



Canine and Feline Geriatric Oncology

Maximizing the Human-Animal Bond



Alice Villalobos, DVM
with Louise Kaplan



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Canine and Feline Geriatric Oncology: Honoring the Human-Animal Bond

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with Laurie Kaplan, MSC**

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To Dr. Gordon H. Theilen, mentor, teacher, researcher, colleague, and inspiration to many creative leaders who helped develop the rapidly growing, multidisciplinary field of veterinary oncology. I dedicate this book to Dr. Theilen, my great mentor, who guided me, a student oncophile, through his visionary and first mock residency program in veterinary oncology at UC Davis, School of Veterinary Medicine, from 1969 to 1972. Dr. Theilen continued to advise and inspire me with his courage, character, and generosity over the years. Dr. Theilen is a notable international forefather in veterinary cancer medicine and research. I am thankful that we are fortunate enough to be planning his 80th birthday celebration in May of 2008. We also plan to compile a special commemorative edition of “Oncology Research and Therapy” (working title) as a tribute to Dr. Theilen’s illustrious career.

To Antonio and Alicia Villalobos, my wonderful parents, who held on to each other and their family with amazing love through thick and thin for 65 years. Their strength, encouragement, and example in dealing with the joys and adversities of life and aging will live as long as their family has life.

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Foreword

The amount of information that applies to contemporary veterinary geriatric oncology is mounting at a frenetic pace. It is generated from the hard work of thousands of clinical researchers and authors of scientific publications in oncology, hematology, gerontology, radiation oncology, internal medicine, surgery, immunology, nutrition, sociology, epidemiology, and research in all related fields. This book draws from the texts and the milieu of references available. Instead of reprinting material, the author delivers applied knowledge to individual cases. For more in-depth detail, readers are referred most notably to the following general references used for this book, listed in alphabetical order by title:

BSAVA Manual of Canine and Feline Oncology, 2nd ed., ed. J. Dobson and D. Lascelles. Quedgeley, Gloucestershire, England: British Small Animal Veterinary Association, 2003.

Cancer Control: Journal of the Moffitt Cancer Center. Geriatric Oncology, Guest Ed. L. Balducci. Vol. 1, No. 2, March 1994.

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Comprehensive Geriatric Oncology, 2nd ed., ed. L. Balducci, G.H. Lyman, W.B. Ershler, and M. Extermann. Oxon, UK: Taylor & Francis, 2004.

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Geriatrics and Gerontology of the Dog and Cat, 2nd ed., by J.D. Hoskins. Philadelphia: Saunders, 2004.

Hematology: Basic Principles and Practice, 4th ed., by R. Hoffman, E.J. Benz, S.J. Shattil, B. Furie, H.J. Cohen, L.E. Silberstein, and P. McGlave. Philadelphia: Churchill Livingstone, 2004.

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Personal Communications from contributors to the *Veterinary Cancer Society Newsletter (VCS NL)*.

Small Animal Clinical Oncology, 3rd ed., by S.J. Withrow and E.G. MacEwen. Philadelphia: Saunders, 2001.

Tumors in Domestic Animals, 3rd ed., ed. J. Moulton. Berkeley: University of California Press, 1990.

Tumors in Domestic Animals, 4th ed., ed. D. Meuten. Ames, IA: Blackwell Publishing Professional, 2002.

Veterinary and Comparative Oncology, ed. D. Argyle and B. Madewell.

Veterinary Cancer Medicine, 2nd ed., ed. G. Theilen and B. Madewell. Philadelphia: Lea & Febiger, 1987.

Veterinary Oncology Secrets, by R. Rosenthal. Philadelphia: Hanley & Belfus, 2001.

Geriatric patient care and client communications are ultimately the attending doctor's responsibility. Readers are encouraged to consult with specialists and view the latest information on the Internet. Some excellent resources available online include:

AOL Private Chat Room chronic renal failure is an online chat room for support of cats with chronic renal failure.

clinicaltrials.gov for access to information on five thousand mostly NIH clinical research studies.

<http://forums.delphiforums.com/CancerPetLoss/start> is a support group hosted by Laurie Kaplan, MSC. It is for people who have lost a pet to cancer. It is the only support group dedicated to grief for a pet lost to cancer specifically.

<http://pubmed.gov/> for full text biomedical articles dated back to 1966.

oncology.medscape.com provides current information on human oncology.

Veterinary Information Network (VIN) for interactive exchange of information.

www.veterinarypartner.com for VIN's client information tools.

veterinaryoncologyconsultants.com for clinician consults with Dr. Anthony Moore.

www.argusinstitute.colostate.edu, the Argus Institute for Families and Veterinary Medicine.

www.avma.org, the American Veterinary Medical Association. Look under Care for Pets.

www.consolepetloss.com, Console: Pet Loss Support System.

www.griefhealing.com for help with grief healing.

www.gulfcoastvetspec.com/oncology/y2k/index.htm for text by Dr. Kevin Hahn.

www.oncolink.upenn.edu/specialty/vet_onc for client information tools.

www.petloss.com for pet grief support and a candle ceremony.

www.petloss.org for pet bereavement counseling.

www.superdog.com/Coping-.html for "a reference to references" on pet loss.

www.vet.cornell.edu/public/petloss/, Cornell University Pet Loss Support Line.

www.vetmed.auburn.edu/distance/clinpath for diagnostic cytology information.

www.vetmed.lsu.edu/oncology for class notes provided by Dr. Neal Mauldin.

Preface

This text is an attempt to distill out the most important useful information for dealing with geriatric cancer patients and caregivers. It draws from an overwhelming deluge of information that overloads practitioners in the rapidly growing field of oncology. The new methods of proteomics (analysis of proteins), metabonomics, and nutrigenomics provide researchers with the keys to unlock the gates of many cellular pathways to map the molecular biology of cancer. These keys are opening doors to targeted therapy, which will enhance the weapons that veterinarians can use to battle cancer. Hopefully the future will allow us to extend the health and longevity of geriatric oncology patients with newer, less toxic targeted technology such as small molecules and vaccine therapy.

Tumors are organized into five large categories according to tissue of origin: carcinomas, sarcomas, blood cancer, nervous system tumors, and miscellaneous/unknown. Tumors are also organized by location: skin, head and neck, chest, abdomen, and bone and blood (lymphoid). Sorting tumors with this perspective may assist practitioners with initial decision making to improve the diagnostic approach and expedite treatment plans, especially with lymphoma patients.

This text is a unique reference for veterinary students, attending doctors, and personnel challenged with the rigors of decision making and caring for geriatric oncology patients. Its greatest contribution may be in the fields of communication, ethics, and philosophy. For instance, a quality of life scale helps the veterinary team negotiate clients through the maze of decision making for older pets in Pawspice care. Certain cases highlight issues in geriatric oncology and management of complex grief and interpersonal relationships with various types of clients. This multidimensional approach offers readers scientific subject matter mixed with cases overlaid with situated knowledge harvested over many years of experience. Victory and frustration are inherent in the management of elderly oncology patients and the reader is cautioned to recognize and avert compassion fatigue.

This tour through geriatric oncology blends elements of attachment, the human-animal bond, and empathy, weaved into the reality of applying cancer therapy tempered by variable client preferences and economics. Of course this is what the veterinary teams does every day in practice, but there are few written guides on how to do this. May this book help you negotiate the ebb and flow of emotions as senescent cancer patients and their deeply bonded families challenge and enrich your career.

Acknowledgements

This book would not exist if it were not for the talented and persistent mind of publisher-editor and book mentor Mr. Dave Rosenbaum. When Dave was with Iowa State Press, he and Bernie Rollin, PhD, coaxed me to step out of the “trenches” and take the time to write a much needed, different type of textbook. David insisted that the book be written in my own personal style. He awakened a sense of duty to give back to my profession. He asked me to share the wisdom and humility that 35 years in the trenches with tumors conferred upon me.

Thinking back to my origins, I thank the good sisters of St. Joseph for their teaching skills at St. John’s Hyde Park and St. Mary’s Academy in Los Angeles. I thank my El Camino Junior College botany teacher, Mr. Charles Luger, who replaced a stolen textbook and encouraged me to pursue my goals. I thank the late professor Julius Sumner Miller for his Einstein-like expertise in teaching college physics on a theoretically practical level.

I thank the amazing faculty at UC Davis Veterinary School in the late ’60s and ’70s. I am thankful for the direction and training provided by my oncology mentor, Dr. Gordon Theilen, to whom this book is dedicated.

I sincerely thank Dr. Frank Lux, who encouraged me to partner with him and open Coast Pet Clinic/Animal Cancer Center in 1974–1982. Coast expanded rapidly into a 24-hour, 12 doctor, 70 staff member clinic with four satellite cancer consultation clinics. I thank Dr. Bill Zontine, who mentored me to look at veterinary medicine more globally. I am grateful for the friendship and encouragement of the late Drs. Greg MacEwen and Art Hurvitz, who inspired me with their brilliance and work at the Animal Medical Center in New York. I thank my founding colleagues, officers, and members of the Veterinary Cancer Society, who forged the specialty of oncology with unwavering dedication. I genuinely thank Dr. Sue Cotter of Tufts University and Angel Memorial for 35 years of friendship, guidance, and faith in me. I warmly thank Ira Lifland, my best friend and husband of 24 years. Ira fills my life with his love and intense multilevel support. I thank Drs. Jane Turrell and Alain Theon for their encouragement in radiation oncology. In 1983, Ira, Jane, and friends helped me build the first dedicated radiation therapy facility in private practice after the banks declined to give us a loan.

These friends, my associates, interns, and the referring doctors of southern California helped me pioneer and develop one of the first comprehensive oncology services in private practice. I also thank organized veterinary medicine for the respect and supportive care given to its members. I thank the American Association of Human-Animal Bond Veterinarians, AAHA, ACVIM, AVMA, Western Veterinary Conference, Wild West, Midwest, NAVC, CVMA, SCVMA, Dr. Bob Pensinger’s Veterinary Post Graduate Institute, Sierra Veterinary Medical Association, and the National Academy of Practice for the energizing effect of learning and networking at meetings. I deeply thank my client

Laurel Hunt for nominating me for the 1999 Bustad Award. It celebrated my natural focus on the human-animal bond and sparked a new career track into the science of the human-animal bond and my new column, "The Bond and Beyond." I thank Brian Hutchins, the editorial staff at *Veterinary Practice News*, and Kristen Kolb. They helped develop the writer in me during five years writing "Oncology Outlook." I thank colleagues Drs. Robert Miller (RMM), Jack Stephens, Robin Downing, Elizabeth Hodgkins, Frank McMillan, Curt Willauer, Chris Hutson, and Kathleen Carson for their moral support, example, and inspiration. I thank all associates, interns, nurses, and staff who worked with me at Coast Pet Clinic/Animal Cancer Center. I will not forget Peter Zippi, Brandi Romain, and Tammy Wood, RVT, who are no longer with us. I heartily thank my oncology nurses Carreen Schuller, RVT, Gary Yumaico, RVT, Travis Bradley, RVT, Carol Merrigan, RVT, and Lisa Teague, RVT, and oncology assistants Bonnie McKinley and Jennifer Dressler. I also thank Mao Mao, Gus Nunez, Jose Alfaro, Lu Storer, and Wendy Triggs for their love, loyalty, and valuable long service to the people and pets of Coast. I joyously thank Leslie Neff, Larry Hoskinson, Linda Washburn, Margaret Norton, Maria and Wolfgang Petersen, Elisabeth Stone, and the Coasters Volunteer Club who are the backbone of the successful placement of over eleven thousand pets through the Peter Zippi Memorial Fund, a big part of my heart. I also thank Chandi Duke Hefner and philanthropists worldwide who help improve the lot of sick, homeless, and mistreated humans and animals.

My deepest appreciation for the creation of this work goes to the amazing organizing and editing skills of Laurie Kaplan, MSC. Laurie contributed enormously by reorganizing my first manuscript. She reconstituted my concepts, articles, lecture notes, and case studies into a big outline and table of contents that evolved into this book. I am grateful for the illustrations provided by Andy Hoffman, Stephen Lewis, and David Perrot and the technical assistance provided by Tamara Coimbra, Keith Fraser, Roberta Karsch, Julie Jennings, Marilyn Wayne, Cyntia Osuna, and my longtime personal secretary, Roni Miyashiro. I am grateful for the editorial and technical support of Sarah Brown, Dede Pedersen, Jamie Johnson, Carrie Sutton, and the entire Blackwell Publishing staff who participated in bringing this work to fruition. I thank Dr. Carl Osborne and the late Dr. Leo Bustad for prioritizing the philosophy of compassion in practice. I thank Drs. John Wright and members of the AAH-ABV for honoring "The Bond" that holds us together. I thank all pet caregivers who ask our profession to help their aging pets when threatened by cancer's intention to deliver its mortal blow.

Introduction

My people are destroyed from lack of knowledge.

Hosea 4:6

This book attempts to bring didactic oncology into a practical format that completely demystifies this specialty for the generalist facing cancer in a geriatric dog or cat. The main purpose and the reason that I accepted the provocative invitation to write this book as a single author is to light a high-touch fuse. This book may serve as a torch or guiding beacon for veterinarians and staff to engage aging pets as highly valued sentient beings. It may help prioritize honoring the humanity of the human-animal bond as we deliver our modern medicine. My career as a “trench oncologist” began in 1972 in battles and skirmishes against cancer at the forefront of the rapidly growing field of veterinary oncology. This work is not intended to be scholastic but rather a force for change to fuse the art of our high-tech medicine with high-touch empathy.

Since cancer kills half of our aging patients, it is truly the single biggest disease responsible for ending the life of millions of highly valued personal pets. Cancer breaks hearts in the companion animal community on a routine basis. The human-animal bond has emerged into a respected life-enriching relationship in our contemporary society. “The Bond” is validated and celebrated as a viable, healthy relationship, one that often takes a priority position in millions of people’s daily routines, their lifestyles, and their economic choices. People purchase pet-friendly vehicles, motor homes, and homes so they can really have their companion animals share their lives and be with them as much as possible. Pet caregivers have created the demand for dog parks, dog beaches, dog hiking paths, and pet-friendly hotels and businesses. While pet owners are at work or on vacation, they hire pet sitters to care for and entertain their animals. Doggie day care and high-end boarding facilities are geared toward quality care and pampering pets. Today’s enlightened pet owners willingly feel that they are their pet’s caretakers or caregivers and, figuratively (not legally) speaking, their guardians. Pet caregivers actively try to learn more about the emotions, thoughts, consciousness, and behavior of their pets. They are convinced that their pets think, have emotions, and can feel happy, sad, lonely, upset, and painful when injured or sick. Pet caregivers want and need relief for their pet’s ailments and discomfort because their own quality of life is impacted negatively when a beloved pet is suffering. Pet caregivers need and demand compassion and understanding from their healers, along with modern medicine and surgery.

When pet caregivers feel the need, they seek the services of veterinarians and a wider growing attaché of pet care services and alternative treatments to find comfort, help, and relief for their pets. Veterinarians contribute not only to the well-being and health of their patients; they have an equally

large responsibility for contributing to the quality of life of the humans with whom those animals live and share all aspects of their lives. Until veterinarians fully appreciate this part of their role in society, they will continue to fall short of their obvious and central role in promoting the health and happiness of people through their pets. One of this book's two key themes is that veterinarians must reach out as much to the pet owner as to the pet, for it is through the owner that the best care of the pet and greatest understanding of the pet's needs are achieved.

Pets age within a mere 10 years. Pet aging happens so quickly that most people are unaware that the routine activities of daily living may place too much demand on an older pet. Clients will often present their senior pets for examination when the pet is exhibiting only mild symptoms or non-specific preliminary signs of illness or cancer. Some caregivers want a thorough examination and screening tests for their aging pet due to the increased risk for cancer. Pet caregivers often request further tests to diagnose a perceived problem or rule out cancer.

More often than not, cancer invades a pet's body insidiously with only few, if any, premonitions or warning signs. When cancer strikes a beloved pet, fear and anxiety fill the exam room. Unfortunately, these gripping emotions often fall on unwilling, deaf ears or are dismissed impatiently by the doctor who is rushing from one exam room to the next in a busy practice. This book serves to reconstruct the initial steps when the veterinarian is working up or presenting the diagnosis of cancer. It can help that first oncology consultation be a life-supporting and client-saving opportunity. This work can also help you understand how to keep your clients affectionately bonded to your practice despite the pet's passing at your facility. Clients will know that you care about them and you care about what happens to their pets.

The typical scenario in the exam room was like the old Norman Rockwell paintings or those beloved scenarios from the James Herriot books. Picture the wise Dr. Smith discussing Fido's cancer problem with Jane (the stay-at-home wife, one child in a stroller and another concerned child in hand). Jane explains Fido's problem to husband, Joe, at dinnertime. Joe calls Dr. Smith to verify the gravity of the situation and the two men make the decision to put old Fido down.

Nowadays, the situation in the exam room is often a single adult (often a man and his cat) consulting with a woman veterinarian who is explaining a disease process and offering multiple tests and high-tech diagnostic and therapeutic procedures and options. The client searches the Internet to educate him- or herself about the disease. This generates the need for further consultation to answer a list of questions. Many caregivers will not be able to afford costly diagnostics and treatment. Others feel philosophically against cancer therapy for an aging pet. However, an increasingly higher percentage of today's pet caregivers are likely to have the willingness and ability to pursue the diagnosis and staging for a cancer pet. They willingly elect special imaging and biopsy procedures and feel compelled to elect definitive treatment, even for their aging pets.

Pet caregivers often want to take the high road and often ask for the best treatment up front or directions for referral and specialty treatment. They openly and proudly regard their older pet as one who has loved them unconditionally for a long time. Older pets are often regarded as "partners" or "best friends" who helped the caregiver during difficult times. The Bond is especially strong if the animal is a guide dog or involved in pet-assisted therapy, service work, agility, or show work. Sometimes the relationship with a pet has outlived friendships, marriages, or loss of family members. It is up to the veterinarian and his or her staff to find out how unique each patient's bond is with the pet's family.

With knowledge from the Internet and other sources, pet caregivers develop the confidence to assert themselves with their doctors because they want to prolong their older pet's life. They are willing to satisfy a sick pet's needs, desires, and quality of life. They want to preserve the lasting relationship with their companion animals at home.

“Family” is used as a very broad term in this text to describe any situation that now includes a pet. “Family” can include singles, partners, and people with or without children. There is no doubt that every generalist would be appreciated more by his or her clients if cancer were recognized earlier and treated with more forethought, expertise, and kindness.

The goal of this book is to provide our readership with a useful decision-making tool rather than a “how to” textbook. That has been done very well. This book arms readers with how to think through the variables and complexity of geriatric oncology while negotiating with the family’s concerns and budget restrictions. The book tells what is unsaid about treating geriatric oncology patients. It unlocks the mystique about cancer so that one may deal with it. The book explains the pitfalls that can be avoided in treating cancer. It spotlights the most common forms of cancer in geriatric pets in a professional, contemporary manner and encourages clinicians to “do it right the first time” for the client and patient.

Part One

Chapter 1

Molecular Biology of Cancer and Aging

The roots of the problems of cancer and aging involve the molecular changes of aging priming aging (cellular senescence). These changes prime aging cells to be more susceptible to the effects of environmental carcinogens. These changes are only partly understood and may or may not be reversible.

Lodovico Balducci, MD

What Is Cancer? How Does It Start?

Cancer is an insidious, nefarious, and obstinate disease. Cancer is an intricate set of biological aberrations that originate in the nucleus of cells and are not completely understood. Cancer results in the uncontrolled and reckless growth of destructive cells that overwhelm the body as they accumulate. Cancer's immortal cells replicate relentlessly via angiogenesis and invasion of vital structures to ultimately kill its host.

Normal cellular division creates a constant flow of injured genes. These defective genes are regularly corrected by innate repair mechanisms present in normal cellular function. Certain genetic point mutations become multifarious if they are not repaired. Genetic damage occurs in cells that lack coordinating signals necessary for self-repair. If those cells are allowed to live and replicate, cancer gets a foothold and proceeds with its fatal agenda.

Each of the trillions of cells that compose a body contains over one hundred thousand genes, arranged in chromosomes. The DNA that composes normal genes is called a "proto-oncogene." A proto-oncogene encodes all genetic information and regulates cell replication so that cells can replenish themselves normally in the bone marrow, intestine, and skin when needed. Genes also regulate normal healing, hair growth, puberty, and gestation (Abeloff et al. 2004).

About one in every million cell divisions undergoes a point mutation resulting in defective, aberrant, or altered genes that clone and initiate tumorigenesis. These genetic mutations can be seen as copy errors and they are normally corrected. If the mutations are involved in the mechanism that controls repair, replication, proliferation, tumor suppression, or telomere (nucleic acid base sequences at the terminal portion of genes, encoding programmed cell death) control, the defective genes are converted into oncogenes and their descendant cells take on renegade behavior.

Cancer evolves on a cellular and sub-cellular level through three basic stages: initiation, promotion, and progression. *Initiation* involves exposure to carcinogens such as sun, tobacco smoke, herbicides (2,4-D weed killer), insecticides, asbestos, free radicals, viruses, and so forth. This initial exposure may result in permanent damage to DNA. Initially this may not be a direct cause of cancer; however, continued exposure increases the risk. Tumor promotion is also seen in chemically induced tumors in experimental animals.

Promotion events are poorly understood. The *promoter* (an abnormal DNA base sequence in genes) stimulates cell division and results in the accumulation of cells that cause the formation of tumors. Aging, poor diet, obesity, toxins, and chemicals injure the stability of genes and are also considered potential promoters.

Progression to malignancy occurs when the tight controls that normally govern cell cycle progression are suppressed or break down. This results in the uncontrolled growth of abnormal immortal cells (cells that do not respond to normal cell death signals). Progression also involves the ability of cancer cells to invade surrounding tissue and metastasize.

These events involve proteins that function by giving and receiving signals on the surface of the cell and along complex and intricate intracellular pathways in the process of cell-to-cell communication. Understanding the specifics of cell signaling can be overwhelming to the busy practitioner. There are basic families and systems of signaling that share certain pathways that aid and abet neoplastic changes. These basic mechanisms are fascinating and do have clinical relevance. Targeting aspects of these basic signaling mechanisms holds the key to promising therapeutics. Scientists attempt to manipulate the proteins that govern the intricate cell signals in ways to prevent, protect, and reverse cancer, especially in the senescent (Ihle 2004).

Tumor Suppressor Genes and Apoptosis

Tumor suppressor genes are responsible for repair of the hordes of copy errors and genetic damage that occurs during normal cell replication. When tumor suppressor genes malfunction, the risk of cancer rises. Tumorigenesis may also arise due to the loss of programmed cell death (apoptosis). All normal cells have a certain life span dictated by telomere shortening after every division and suicide signaling. Suicide mechanisms to self-terminate can malfunction due to mutations of the signaling systems for apoptosis, causing cells to persist and become immortal.

Cell immortality is dangerous to the host. Armed with immortality and lack of suppression by tumor suppressor (p53) genes, these aberrant cells become malignant. They replicate and accumulate into clones of neoplastic cells. The clones undergo successive genetic changes that select for growth factors. Malignant clones acquire the ability to create their own capillary blood supply (angiogenesis). These new capillaries provide nourishment and oxygen for new cell growth, thus allowing more abnormal cells to accumulate and create larger tumors. Tumors send their most vigorous, athletic scout cells into lymphatics and capillaries. These resilient scout cells are able to slip under the radar of the immune system. They travel and metastasize into immortal tumor clonogens (cell clones that are more resistant to treatment). Clonogens may appear anywhere in the body (Khanna 2004; Morrison 2002).

Because renegade cancer cells have minimal cell death, do not curb their telomeres, and bypass senescence, they continue to divide and replicate without repairing. They grow wildly since they lack the ability to terminate themselves through apoptosis. In frenzy, they push, crowd, and dissolve their way into the society of normal tissue cells. *The battle against cancer is often won or lost at this microscopic preclinical stage.*

Most scientists realize that the real and decisive battle against cancer is truly fought at this molecular and immune system level, long before the tumor has expanded and accumulated enough cells to be detected. At this early, preclinical stage, a healthy, militant immune surveillance system could identify and eliminate every renegade cancer cell. Unfortunately, aging is associated with a weakened immunosurveillance system, leaving our geriatric patients at greater risk for cancer.

Cancer and Aging

Cancer is a disease, but aging is not. Aging is the phenotype of the normal phenomenon of cellular senescence. Carcinogenesis is a nefarious multistep process that takes time. Aging animals provide that time as their life span increases. Cancer's multistep process, enhanced by a longer exposure to carcinogens, emerges as a major syndrome associated with aging. Basic research proposes a number of reasons for the increased incidence of cancer in older animals. Aging is associated with a decline in antitumor defenses. Older animals have less resistance, less immune competence, less DNA repair, damaged tumor suppressor genes, and defects in biological responses. Aging is associated with diminished functional reserve of multiple organ systems and an increase prevalence of chronic diseases, which may mask cancer.

Certain proteins or cytokines such as interleukin-6 (IL-6), D-dimer, and C-reactive protein (CRP) are found to be elevated in the aging process. D-dimer is a product of fibrin lysis and CRP is an acute phase protein produced in the liver. These cytokines increase with inflammation and age-related conditions such as osteoarthritis. Cancer creates an immune challenge, which drives the activation and release of a cascade of cytokines including tumor necrosis factor (TNF- α , cachexin), which is responsible for creating the hypermetabolic state of cachexia. TNF- α , IL-6, D-dimer, and CRP also increase with cytokine signaling induced by inflammation, infection, cancer, thromboembolism, and acute illness. Cancer instigates cytokine dysregulation and a domino effect as it disrupts the aging body.

These factors are likely to be responsible for the higher mortality rate from cancer in older animals. Research hopes to provide new prevention methods to deal with the intricate cytokines and signaling steps of cancer as it evolves. The goal would be to "target" cancer out of existence at the pre-cancerous stage, before it embarks on its fatal course.

Cancer Awareness

Client education regarding prevention and awareness of risk factors can help geriatric pets live longer and be cancer free. Educating caregivers about the preliminary stages and early warning signs of cancer may help save a pet. *A well-informed clinician, using improved diagnostics in a timely fashion, can help clients with geriatric pets identify and treat cancer in its earliest stages, which may offset its devastation.*

The most obvious tumors in elderly dogs and cats appear on the body surface, in the skin, subcutis, or fixed to the body wall. Cutaneous cancers may appear as tumors, ulcers, non-healing sores, petechiae, or blood blisters. They may appear as plaques or crusts on the ears, eyelids, and nose and in the non-pigmented skin of sun-exposed senior cats and dogs. The contemporary veterinarian will not suggest, "Let's wait and see if it grows." It is justifiable to examine every mass on a geriatric pet (other than warts) with fine needle aspiration (FNA) cytology to determine whether the mass is truly a lipoma or a malignant tumor.

Environmental Influences, Toxins, and Risk Factors

The multistep process of cancer development over time explains why we see more cancer in aging animals. Some researchers view animals as sentinels that parallel human diseases, including cancers that result from environmental exposure. Certain environmental factors have been found to initiate

and promote cancer. It may take years for environmentally induced cancer to develop in people and in companion animals, but the risk increases with age. The most well-known environmental risk factors for cancer in people are smoking, snuff and betel nut chewing, alcohol, lack of exercise, unhealthy eating habits, obesity, toxins, asbestos, and ultraviolet sun and radiation exposure. Certain food additives such as preservatives, nitrates, chemicals, and aflatoxins are known to be carcinogenic. These carcinogens are associated with gastrointestinal (GI), hepatic, and bladder cancer in humans and presumed to create similar risk for exposed companion animals.

Certain dogs and cats also have additional breed predispositions to environmental toxins. For instance, Scottish Terriers are 20 times more susceptible to bladder cancer than other breeds of dogs and are at greatest risk if exposed to lawn herbicides (Raghavan et al. 2004). Cats ingesting particulate residue from cigarette smoke contaminating their fur are at greater risk for developing oral and GI cancer (Snyder, Bertone, and Moore 2001). Cancer is promoted in the skin by solar radiation, in the lymph nodes by toxins and retroviruses, and iatrogenically by inflammation resulting from adjuvanted feline leukemia virus (FeLV) and rabies vaccines (Ford 2004; Macy 2004). Obviously, there are many more environmental factors in modern living that may initiate the multistep genetic mutations that cause cancer to develop and threaten pets as they age.

Non-pigmented skin in cats and dogs is highly susceptible to mutations from solar exposure. Cats exposed to smokers lick carcinogens deposited on their coats and thus are at increased risk for oral squamous cell carcinoma. Cats exposed to smokers are also at greater risk for lymphoma of the GI tract. Lymphoid tissue, reproductive organ tissue, and growth plates may be more susceptible to mutagenesis by their inherent nature. Lymphoid cells may undergo genetic damage through mechanisms triggered by environmental radiation and toxins. Exposure to 2,4-D weed killer causes lymphoma in dogs. Reproductive tissue is especially sensitive to hormonal influence. Bone cancer most frequently appears in the growth plates of the long bones of large and giant breed dogs.

Retroviral and Infectious Disease in Cancer

Retrovirus infections, such as FeLV and feline immunodeficiency virus (FIV), cause disease related to immune suppression and lymphoma in cats and rank as the main cause of infectious morbidity in cats. Papilloma virus causes self-limiting transmissible oral papillomas in young dogs. As yet, no virus has been found to cause other cancers in dogs.

Cancer is augmented by retroviruses that are found in many animal species from mice to birds to cats to cattle to primates to humans. Retroviruses enter the body and cause mutations in susceptible cells. FeLV and FIV both cause mutations in lymphocytes, immunosuppression, anemia, pancytopenia, leukemias, and lymphoid tumors. FeLV also causes chronic wasting, abortions, and fading kitten syndrome (Theilen, Madewell, and Gardner 1987; Pedersen et al. 1987).

A recent large survey found the prevalence of each retrovirus at 3% in the cat population (Little 2005). Some cats survive into their geriatric years while remaining retrovirus infected. Both FeLV and FIV attack the immune system, causing a drop in the number and activity of T-cells. This results in opportunistic infections, anemia, and weight loss similar to acquired immune deficiency syndrome (AIDS) in humans. Testing and vaccines are available for cats at risk. The FIV vaccine currently available obfuscates detection of truly infected cats due to false positive results following vaccination. Kittens of vaccinated queens test positive up to 3 months of age due to passive transfer of antibodies (MacDonald et al. 2005).

Fortunately, dogs do not exhibit an acquired immune deficiency syndrome. Boxers are more likely to have T-cell lymphoma, whereas Rottweilers are more prone to B-cell lymphoma than other breeds, but no virus has been isolated from dogs with lymphoma as of this writing (Lurie, Lucroy, and Griffey et al. 2004). Infection with *Helicobacter* may stimulate immune responses that may promote GI lymphoma in humans. The increased incidence of lymphoma found in Golden Retrievers may hypothetically be related to infection with *Bartonella* and stimulation of specific immune responses. This arena of tumor immunology and infectious disease research requires epidemiologic studies and sophisticated testing. Polymerase chain reaction (PCR) gene amplification may verify the hypothesis that certain infectious diseases may contribute to tumorigenesis.

Endocrine Influences in Tumorigenesis

Endocrine, autocrine, and sex hormones also play a role in tumorigenesis when the normal cell membrane receptors of target tissues are occupied by stimulatory signals. Altered tissue growth factor genes can also promote cells toward transformation. Dysregulation of normal growth regulatory pathways, ligand binding, and constitutive activation of transmembrane tyrosine kinase receptor activity all promote carcinogenesis. A practical example of this altered microenvironment is the carcinogenic effect of progesterone on the mammary tissue of intact female dogs and cats. They are at risk for developing mammary tumors as they age. The risk is minimal with early ovariohysterectomy and increases with delay past 2½ years in dogs. Carcinomas can be iatrogenically initiated in mammary tissue with progesterone therapy in cats. Testosterone plays a similar causative role for perianal tumors in intact male dogs.

Adjuvant-Induced Neoplasia

Vaccines containing aluminum hydroxide adjuvant may act as carcinogenic promoters of normal inflammatory oncogenes in some cats. Localized inflammatory reactions cause injury at vaccine sites, initiating promitogenic (pro cell division) signaling and genetic mutations and translocations. This genetic damage occurs in the C-myc oncogenes and C-kit oncogenes. They become activated and replace normal oncogenes, resulting in the unregulated stimulation of fibroblasts. If tumor suppressor genes (anti-oncogenes, antisense) such as the ubiquitous p53 genes are damaged, there is too little self-inhibition and autonomous cell death. Consequently, in a variable time period, vaccine-associated inflammation may ultimately direct mutation and mutagenesis and the intricate phenomenon of transition into malignant fibrosarcoma, including other types of sarcoma, in 1/1,000 to 1/10,000 of vaccinated pet cats (Ford 2004; Macy 2004).

How Cancer Kills

Cancer kills because of its freedom from regulatory constraints, which allows for its persistent unrestrained growth and its resistance to treatment. Cancer overtakes its victims with its exponential cell kinetics. After only seven to eight doublings, the cells of a tumor will reach a critical volume that becomes incompatible with host survival. Cancer patients die due to the rapid exponential growth of their tumors.

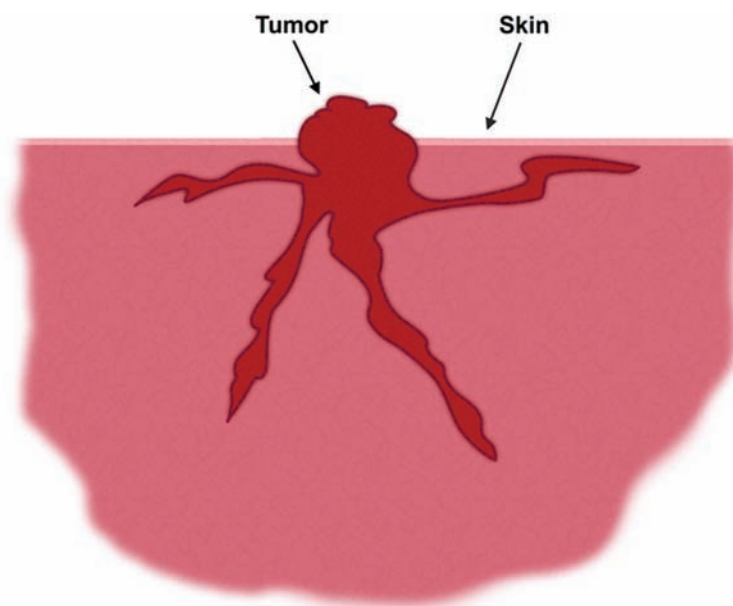


Figure 1.1. The octopus-like shape of a cancerous mass with its head and streaming tentacles that extend into the normal tissues.

A tumor one cubic centimeter in diameter (about the size of a grape) contains one billion cells. Ten percent of these cells are blood vessel cells undergoing angiogenesis to feed and oxygenate the tumor cells and enable them to metastasize. Many tumors, especially soft tissue sarcomas, develop tentacles that use enzymes such as metalloproteinase to dissolve cell walls and invade adjacent normal tissues. They invade tissue along the fascial planes or by direct extension applying pressure to surrounding structures such as nerves, vessels, and organs. It is easy to visualize a cancerous mass as an octopus, with its palpable head and its streaming cells acting as the tentacles that insidiously reach into normal tissues (Figure 1.1).

Cancer also kills by altering and stealing sugar and carbohydrate nutrition from its victims to feed its own troops of invading renegade cells. Cancer-induced weight loss is an involuntary cancer-host interaction resulting in cancer cachexia. Pets with thick fur coats or older pets with mild to moderate geriatric cachexia may camouflage this debilitating condition in its early stages.

Mechanisms of Metastasis

Metastases arise either by direct spread and invasion into areas immediate to the primary tumor and/or by cellular travel to distant locations, especially the lungs, liver, spleen, and bones in humans. Metastatic cells can be thought of as the most outgoing and vigorously athletic cells in the tumor. Metastatic cells creep into the lymphatic and vascular systems. This process is called diapedesis. These resilient cells defy host immunosurveillance and travel to distant locations in the body. Microscopically, scientists can see small clumps of cancer cells sending out “scout” cells that undergo diapedesis as they creep out of the primary tumor. These cancer cells can destroy their surrounding stroma by dissolving the walls of their neighbor cells with a signaling system that regulates lysis by metalloproteinase enzymes. The cells squeeze through or between endothelial cells and pass

into and creep along the walls of capillaries or vessels of the lymphatic system. These scout cells are the immortal “marathon runners” of the clone and are the most resistant to destruction. These circulating malignant cells defy death by anoikis, apoptosis due to loss of cellular contact. They slip under the radar of the immune system and go on to create micrometastases in a new site with tougher, more resistant progeny. These cells divide and survive. They accumulate to become a detectable mass (Khanna 2004).

In part, the ability of neoplasm to grow exponentially is due to the fact that metastases can further metastasize. This biological phenomenon can be used to explain to pet owners why metastatic lesions found in the lungs, liver, bone marrow, or brain are more resistant to the previously used first line chemotherapy and radiation therapy treatments.

Angiogenesis

Cancer cells must create new blood vessels and capillaries to feed and bring oxygen to their progeny of growing renegade cells. The microenvironment allows malignant cells to signal for pathological neoangiogenesis. One mechanism may involve recruiting angioblasts and circulating endothelial precursor cells (EPCs) as with hemangiosarcoma and other solid tumors (Lamerato-Koziki et al. 2005). Cancer cells may also use or co-opt existing capillaries to feed themselves as they grow into clumps of cells. Without angiogenesis, tumors cannot enlarge beyond a few millimeters or become large enough to be detected on radiographs and imaging scans.

Why Are There So Many Kinds of Cancer?

Cancer terminology is generally based on the cell of origin. Although cancer is one disease, there are over one hundred different types of cells in the body, and each one gives rise to cancer. Each type of cancer has its own name with specific unique variations, characterizations, and behavior. This information forms the premise for most practicing oncologists in that if we can name a cancer, we can diagnose it and understand its biologic behavior. Cancer can be classified into five basic groups: carcinomas, sarcomas, blood cancer, central nervous system (CNS) cancer, and cancers of miscellaneous or unknown origin (Table 1.1).

Tissue biopsy and/or FNA cytology provide the cell morphology or structural characteristics that enable us to determine the cell type of a specific tumor for diagnosis. Intricate tests that stain cells for certain protein markers are needed to identify the genetic phenotype of cells that are microscopically and morphologically indistinguishable from one another, such as T-cell and B-cell lymphoma.

The nomenclature that is used in oncology and pathology has its origins in Latin and Greek. Pathologists will change terminology and classifications from time to time. The words describing the molecular biology of tumors and the mechanisms of targeted drug action used in the field of oncology represent by far the largest alphabet soup and the most confusing terminology in medicine.

An understanding of oncology requires familiarity with tumor tissue origins and with the names and various biological behaviors of each cancer, based on its general tissue type. The biopsy report specifies the type of cancer and this is synonymous with its diagnosis. Staging the cancer tells us something about the size of the primary tumor, whether it is localized or has infiltrated local lymph nodes or regional nodes, and if it is metastatic to distant locations in the body.

Imaging helps us to acquire more diagnostic details for staging purposes. The biopsy report also allows the grading of tumors (I, II, III, and well to moderate to poorly differentiated) in the hope that

Table 1.1. Common Terminologies and Abbreviations for Basic Types of Cancer Based on Tissue of Origin

General Tissue of Origin	Specific Tissue of Origin	Basic Cancer Type (Terminology/Abbreviations)
CARCINOMA (CA)		
Skin/epidermis (ectoderm)	Squamous cell: skin, tonsil, respiratory	Squamous cell carcinoma (SCC)
	Basal cell	Basal cell carcinoma (BCC)
Glandular tissue with ducts or tubes (endoderm)	Wax glands	Adenocarcinoma (AC)
	Sweat glands	Sebaceous gland AC; ceruminous gland AC
	Anal sac	Apocrine gland AC
	Reproductive tissue	Anal sac AC
	Breast	Breast cancer (MGAC)
	Prostate	Prostatic AC
	Uterus	Uterine AC
	Testes (may produce sex hormones)	Sertoli or interstitial (Leydig) cell carcinoma
	Ovaries (may produce sex hormones)	Ovarian granulosa cell tumor
	Respiratory tract	Respiratory AC
Hormone-producing ductless glands (may produce paraneoplastic syndromes)	Gastrointestinal tract	Intestinal AC
	Hepatobiliary: liver, bile duct	Hepatocellular (HC), cholangiocellular carcinoma (CC)
	Kidney	Renal cell AC (RCC)
	Bladder	Transitional cell carcinoma (TCC)
		Endocrine tumors
	Thyroid gland	Thyroid AC
	Adrenal gland	Pheochromocytoma, adrenal AC
	Pituitary gland	Pituitary AC
	Pancreas	Pancreatic AC
	Heart	Heart base tumor (HBT)
SARCOMA (SA)		
Connective tissue (mesenchymal)	Fibrous connective tissue	Fibrosarcoma (FSA)
	Vascular: endothelial cells, angioblasts	Hemangiosarcoma (HSA)
	Vascular: pericytes	Hemangiopericytoma (HPCT)
	Skeletal muscle	Rhabdomyosarcoma (RMS)
	Smooth muscle	Leiomyosarcoma (LMS)
	Peripheral nerve	Schwannoma (neurofibrosarcoma) (nerve sheath tumor) (NTS)
	Bone and joint	Osteosarcoma (OSA); synovial cell sarcoma
Combination of epidermal and neuroendocrine tissue	Plasma cells	Multiple myeloma; IgM macroglobulinemia
	Melanocytes containing melanin granules	Malignant melanoma, melanosarcoma (MM)
Allergy cells in skin; gut	Mast cells containing vasoactive chemicals	Mast cell tumor (MCT) Mastocytoma, mastosarcoma

(continued)

Table 1.1. *Continued*

General Tissue of Origin	Specific Tissue of Origin	Basic Cancer Type (Terminology/Abbreviations)
BLOOD CANCERS		
Blood-forming cells	Hematopoietic cells	Leukemias
	Lymphoid cells (in cats +/- retrovirus)	Lymphomas (T-cell, B-cell) (lymphosarcoma) (LSA)
	Lymphoid cells	Cutaneous lymphoma (T-cell, B-cell) (epi- or non-epitheliotrophic) (CL)
	Hemangioblasts/angioblasts (Pluripotent stem cells of bone marrow)	Hemangiosarcoma
CENTRAL NERVOUS SYSTEM (CNS)		
Central nervous system (Neuroendoderm)	Brain	Brain tumors Meningioma Glial, ependymal, neuronal, and embryonal tumors
	Pineal gland	Pituitary tumor
	Choroid plexus	Choroid plexus carcinoma
	Spinal cord	Spinal tumors
MISC. OR UNKNOWN CELL OF ORIGIN		
Unknown cell types of the immune system	Dendritic cells (Histiocytes)	Histiocytosis
	Macrophages	Malignant (MH); systemic (SH); cutaneous (CH)
	Pleomorphic, bizarre fibroblast-like and/or histiocyte-like cells with spindle and round cell characteristics	Malignant fibrous histiosarcoma (MFH) (solitary or multicentric)
	Histiocytic round cells	Transmissible venereal tumor (TVT)
	Pleomorphic atypical lymphoid cells	Pulmonary lymphomatoid granulomatosis (PLG)
	Monocytes	Unknown
	Langerhans cells	Unknown
	Plasma cells that produce IgG or lambda light chains in the cytoplasm	Plasmocytoma, reticulum cell sarcoma, Merkel cell tumor of neuroendocrine origin, atypical histiocytoma, cutaneous plasma cell tumor
Mesoderm (mixed epithelial/mesenchymal) Thymic epithelium	Epithelial lining cells of coelomic cavities	Mesothelioma
	Thymus	Thymoma (infiltrated with mature lymphocytes)

this will help foretell their biological behavior. Naming, staging, and grading are considered essential in order to make decisions and plan cancer treatment.

Some malignancies grow so rapidly that they are difficult to classify by cell type. They are called “un” or “de” differentiated. In such cases, immunohistochemical stains can help to classify cells for diagnostic and subsequent therapeutic purposes. The pathologist will offer these stains when necessary. It is a good idea to pursue such sophisticated diagnostic measures when it will help determine if a tumor has a high or low metastatic potential. This information improves treatment planning and prognosis.

When applicable, tumor markers can be used to identify certain types of neoplastic cells. Tumor markers, which are generally specific antigens, may be found in tissue samples and in serology samples from the patient. Pathologists can now identify certain growth factors and receptors in tumor tissue that can be used for the development of therapeutic strategy as well as to determine disease prognosis. Markers found in blood are commonly used in human cancer patients following treatment to monitor for recurrence. Markers may be positive when a tumor is clinically undetectable but they may also rise due to other factors. This situation places clinicians in a quandary. If the clinician can’t locate the tumor, should he or she interpret rising positive markers as recurrence or as background cross reactivity? This conundrum frustrates decision making for attending doctors and all concerned. Ruling out other causes and good clinical judgment should prevail.

Our profession can look forward to the availability of exciting new tests such as the mast cell tumor (MCT) panel. This panel runs all the special stains for MCT markers. Early indications suggest that a panel of markers like the MCT panel may be helpful in predicting the biological behavior of a patient’s initial tumor. Following tumor markers sequentially may enable early detection of microscopic recurrence. With this information, however, comes the responsibility of ethical and practical decision making. The clinician must deal with the inherent lack of specificity of tumor markers and still make the call to treat or not to treat the patient for suspected recurrence (see chapter 8). This quandary places a huge responsibility on clinicians. Should we treat to be safe or sorry? Should the considerations be modified for aging pets?

New technology using gene arrays (maps) will enhance our ability to know the molecular details of specific tumors. Soon, oncologists will be able to characterize cancers further by genetic markers and mechanisms that may express one growth factor over another or a certain enzyme or cytokine. This information will benefit cancer patients with improved modes for targeted therapy. Although detailed testing with gene arrays is not yet affordable and routinely available for veterinary patients, practitioners still need to comprehend the gross terminology in the field of oncology and stay abreast of the ever-increasing ability and advantages of delving into the molecular structures and functions involved in neoplasia with emerging technology and therapy.

We may change our approach to cancer and treatment philosophy in the future. With new treatment options such as anti-angiogenesis agents, gene therapy, targeted therapy, and stealth antibody therapy, we may soon be able to address cancer on general terms and ambush its basic molecular mechanisms. We may one day abandon the old approach to crisis oncology that dictates us to ask, “What is it? Where is it? Now let’s cut it, irradiate it, or poison it.”

What Are Sarcomas, Carcinomas, and Adenocarcinomas?

Sarcomas are malignancies that originate in connective tissue. Soft tissue sarcomas (STSs) arise from connective tissue other than bone. STSs are tumors that originate in the connective tissue found in skin, muscle, vasculature, and fibrous tissue. These tumors belong to a large group of tumors and

Table 1.2. Soft Tissue Sarcomas of Clinical Significance in Dogs

Mast cell tumor	Malignant melanoma
Nerve sheath tumor (Schwannoma)	Hemangiopericytoma
Fibrosarcoma	Hemangiosarcoma
Neurofibrosarcoma	Plasmacytoma
Myxofibrosarcoma	Rhabdo(myo)sarcoma
Myxosarcoma	Malignant fibrous histiocytoma
Fibroma (invasive)	Liposarcoma
Synovial cell sarcoma	Reticulum cell sarcoma

are often treated similarly (Table 1.2). Because people can see and feel the entire body surface of their pet animals, family members or the groomer initially discovers many STSs.

Sarcomas of bone are osteosarcoma, chondrosarcoma, synovial cell sarcoma, and tumors arising from any other bone constituent. In addition, any other tumor type including metastatic adenocarcinomas may infiltrate bone. Pet owners often misunderstand the basic concept of metastasis to the bone. They may say, “My father died of bone cancer, now my dog has it,” when in fact, the father had metastatic prostate cancer that invaded the pelvic bone. The same is true for metastatic breast cancer in women. Clients tell us that their mother or sister died of lung or bone cancer, but it was actually metastatic breast cancer. Animals don’t have as high an incidence of bone invasion from metastatic cancer as humans do. Most likely, either animal cancer patients do not survive long enough for the metastasis to occur, or their bones are endowed with some unknown sanctuary mechanism.

Blood Cancer

Blood is a connective tissue and sarcomas of hematopoietic cells are commonly referred to as blood cancer or leukemias and lymphomas. They are further classified as to the type of leukemia by the cell of origin: lymphoblastic, chronic lymphocytic, myelogenous, acute myelogenous, granulocytic, multiple myeloma, plasma cell, erythrocytic, and so forth. There are numerous types of lymphomas: large cell, blastic, cleaved cell, small cell, T-cell, B-cell, and so on. It is helpful to differentiate lymphomas by immunophenotyping during the workup phase. This would provide a more accurate expectation of response and overall prognosis, since T-cell lymphomas are more resistant to treatment.

Carcinomas and Adenocarcinomas in Dogs and Cats

The terms “carcinoma” and “adenocarcinoma” (AC) generally apply to cancer that arises in the epithelial tissues of skin and body organs. People often use “carcinoma” synonymously with “cancer” because 80–90% of human cancer cases are carcinomas. ACs originate in abnormal gland cells that are in the lining or inner surface of a cavity or organ. Adenomas are benign tumors of gland cells that, over time, may transition into malignant tumors. ACs and adenomas may originate in any part of the body. The skin and delicate mucous membranes are commonly affected in senior pets. Dogs are prone to develop sebaceous, apocrine (anal sac), perianal, ceruminous, salivary, and sweat gland tumors, while cats are prone to basal cell tumors.

Breast cancer, which is sex hormone related, is commonly encountered in intact female dogs or in dogs spayed after 2½ years of age. It is less common in cats. Squamous cell carcinoma (SCC) that appears in lightly pigmented facial skin of cats and in the glabrous skin of lightly pigmented dogs is solar induced. However, SCC also appears in the oral cavity, tongue, tonsils, esophagus, nasal and paranasal sinuses, respiratory tract, and nail beds. Some reports have associated tonsillar SCC in dogs with environmental pollution and oral SCC and GI lymphoma in cats with exposure to coat-associated carcinogens from cigarette smoke.

ACs in the abdomen may originate from glands such as the liver, colon, intestine, stomach (gastrinoma), kidney, bladder, pancreas, prostate, and adrenal. Widespread dissemination of cancer in the abdomen and throughout the rest of the body is often termed as “carcinomatosis.” The term may also include other tissue types. AC may also originate from any gland in the neuroendocrine or reproductive system such as the thyroid glands, pancreas, adrenal glands, pituitary gland, ovaries, uterus, testicles, and prostate. These tumors often cause paraneoplastic syndromes related to their cell products. Anal sac AC is well known for causing malignant hypercalcemia. However, other malignancies, especially lymphoma, may also cause this potentially life-threatening paraneoplastic syndrome.

Nasal AC in pets may extend past the ethmoid plate into the brain. Primary CNS brain tumors are very pleomorphic. Only choroid plexus tumors of the brainstem, which are poorly responsive to treatment, are classified as carcinomas. AC may appear in the ciliary body in the eye and occasionally in the glands of the eyelids.

Aortic body (heart base tumors, chemodectoma) and bronchogenic AC originate in the chest cavity. Bronchogenic AC is often found as a round solitary mass in the caudal chest. If it is located in the distal lung lobe without nodal metastases, affected dogs may have good survival times following lobectomy. Cats rarely have primary lung cancer, but when they do, it is generally found to be SCC, which may metastasize to the digits and resist treatment.

Mesotheliomas originate from the epithelial lining of the pleura, pericardium, and peritoneum. They originate in the chest and abdominal cavity, causing malignant effusions. In humans, mesotheliomas are associated with asbestos inhalation. They are rare in dogs and cats—most mesotheliomas diagnosed in pets are actually ACs.

Pulmonary lymphomatoid granuloma (PLG) is a rare condition categorized as a precancer that may confuse the clinician. It occurs in middle-aged dogs, appears as massive pulmonary involvement with very large nodules, and infiltrates similarly to an end stage AC or sarcoma. It is important to distinguish this disease from AC as most cases of PLG respond nicely to treatment and have a favorable prognosis despite the enormity of the lesions.

Some malignant tumors have cells that are so undifferentiated or “dedifferentiated” that the pathologist can only report them as anaplastic carcinomas with no indication of the cell type of origin. This was the case with Alfie, the author’s 11½-year-old Australian Shepherd. Ultrasound-guided FNA cytology of Alfie’s mass revealed two populations of bizarre cells appearing to be both carcinoma and sarcoma. The histopathologic diagnosis was undifferentiated carcinoma with no definite gland of origin. Direct visualization at exploratory laparotomy disclosed that Alfie’s carcinoma was hepatic in origin.

The biological behavior of most ACs is aggressive with a persistent tendency for metastasis. Most ACs expand to a detectable size by outward growth (like an onion) and by direct extension into local tissue. The cells use matrix metalloproteinase enzymes to dissolve neighboring cell walls for local invasion. Through diapedesis, AC cells gain entry into lymphatic and capillary vessels and then disseminate throughout the body.

Locoregional recurrence and lymph node invasion is common, followed by widespread metastasis (Figure 1.2). Metastatic AC generally appears as nodular cell clones in the lungs, liver and other



Figure 1.2. The primary mammary gland adenocarcinoma caused edema and swelling of Bear Brown's perineum and legs.

abdominal structures, brain, and eyes. AC may further metastasize to bone and dermis (Figure 1.3). On rare occasions, AC may metastasize to the digits in cats. German Shepherd Dogs may develop a rare form of renal AC, classified as cystadenocarcinoma, that causes the bizarre formation of multiple benign fibrous nodules in the skin.

ACs are commonly visualized as fluffy, or military, infiltrates or nodules in chest x-rays of pets in advanced stage disease. Some pets develop pulmonary effusion and hemoptysis (coughing up blood). Nasal cancer patients exhibit chronic unilateral nasal discharge and/or frank hemorrhage (epistaxis). Some dogs and cats develop occult disease with warning signs of coughing, gagging, exercise intolerance, or dyspnea due to pulmonary compromise from the metastatic disease process.

What Can Be Done to Halt Cancer in Pets?

The overall goals of research and therapy in veterinary cancer medicine are twofold: to cure the cancer while leaving the patient with a good quality of life and, ultimately, to actually and completely prevent cancer cells from colonizing in the body.

Proposed ways to win the battle against cancer also include nutritional concepts such as “starving the cancer cells while feeding the patient” or providing supplements that support the immune system. Some supplements may have anti-neoplastic or protective effects in helping the liver to function and detoxify. Some act as antioxidants that scavenge free radicals.

Future therapies for cancer may control it through medications that will cripple its aberrant angiogenesis capabilities or cripple its ability to create lytic enzymes and cytokines. For example, “targeted” gene therapy, such as the small molecule protein kinase inhibitors, may become the norm. New classes of drugs, including inhibitors of angiogenesis such as Avastin[®], will be incorporated



Figure 1.3. 12-year-old Akita, Bear Brown, with a metastatic mammary gland adenocarcinoma lesion in the skin of her dorsal neck.

into existing protocols. Drugs that inhibit metalloproteinase enzymes will stop cancer cells from dissolving neighbor cell walls. Some of these agents may be recommended for permanent maintenance therapy or used in chemoprevention protocols.

Innovative treatments such as specific gene therapy may control cancer by correcting replication defects. In gene therapy, special genes are transfected into bacterial or cellular vectors and injected into the patient. These therapeutic genes then signal the cells of cancer patients to produce specific proteins that will, it is hoped, suppress or destroy the tumor. In anti-angiogenesis gene therapy, proteins such as endostatin and angiostatin may be used to arrest the angiogenesis process. Gene therapy may offer several ways to fight back at the microscopic level where cell-to-cell signaling in the neoplastic battlefield is most crucial. Researchers are also studying the use of stem cells in cancer therapy to help replace bone marrow and organs that may have been destroyed by treatment or by the neoplastic invasion.

It is quite possible that in the near future, the use of surgery to “cut and slash” at tumors, chemotherapy to “poison” cancer cells (along with trillions of healthy cells innocently undergoing cell division), or radiation therapy to “burn” cancer cells (along with millions of innocent normal bystander cells) will all become methods of the past.

One approach that uses natural or synthetic substances to prevent cancer by interrupting mutation, oncogenesis, angiogenesis, and metastasis is called “chemoprevention” by mainstream conventional medicine (Bergman 1999). An example of chemoprevention for women at high risk for recurrent breast cancer would be the use of anti-estrogen medications such as tamoxifen and raloxifene (Love 2000). Another example of chemoprevention is the use of calcium supplements to decrease the risk of colorectal cancer in humans (Popchain 2004). Research will identify more helpful compounds that may protect or offer support for geriatric pets against cancer.

There are millions of microscopic skirmishes between immune cells and cancer cells in a body on a daily basis. Macrophages, NK (Natural Killer) cells, and cytotoxic T-cells operate by signal cell transduction. Much of this action takes place on cell membranes while the intracellular signaling systems are affected. The body's surveillance cells and tumor suppressor genes (especially p53) work for the immune system and can eliminate renegade cancer cells if they are activated, trained, or empowered. It is at this cellular level, the microscopic field, where the true battle against cancer is won or lost. It is here that the battle should be fought, not when a tumor is already established.

Nutritional and holistic treatment promotes prevention and balance with the use of a healthy diet and supplementation with natural substances such as fatty acids, antioxidants, supplements, and nutraceuticals. The agents used are known or believed to operate at the cell surface signaling level to work on the immune system and/or to protect or detoxify various organs and systems to prevent or lower the risk of cancer. Data regarding the efficacy of large-scale trials is available online from ClinicalTrials.com.

A significant segment of the pet-owning community is drawn toward nutrition and holistic medicine for the prevention and/or ancillary treatment of cancer in aging pets. These methods are popular with the people who believe in them; however, western medicine remains skeptical as few controlled clinical studies can verify claims. Holistic, alternative, and complementary medicine and its many branches of nurturing therapies may have a positive contribution to make in the overall care and well-being of the cancer patient. The holistic approach attempts to care for the entire patient and enhance the quality of life by decreasing uncomfortable symptoms and feelings, seeking to balance the body's systems including emotions, and supporting the immune system. Holistic medicine also actively addresses the nutrition of patients on a preventative and therapeutic basis. There are various types of alternative and holistic medicine including acupuncture, chiropractic, massage therapy, homeopathy, and herbal medicine. Some approaches are under justifiable scrutiny by the watchful and the skeptical, but clinicians should be aware that when faced with advanced and aggressive cancer, the pet caregiver is often compelled to seek information beyond his or her local veterinarian's scope or comfort zone. It is estimated that 8–10% of human cancer patients whose diagnosis has been confirmed by tissue biopsy decline mainstream therapy (Love 2000). This may be true for pet owners as well. This is viewed as potentially harmful to the patient if the pet owner foregoes the opportunity for curative conventional therapy.

Pet caregivers' quests to self-educate may confuse them initially, but eventually these quests empower caregivers with the information needed for comprehensive, personal decision making for their pets. Ultimately, practitioners may use the best from both worlds by combining or interdigitating the most successful conventional treatments with the most supportive complementary treatments to palliatively extend a dear pet's life. This blending and delivery of many different types of medical knowledge is called "integrative medicine."

Much Is Left Unsaid and Unaddressed

Cancer is the grim reaper of geriatric pets. Cancer colonizes from genetic error and environmental insult through the steps of initiation, promotion, and progression. When cancer becomes clinically obvious in a geriatric oncology pet, the battle to save that pet's life will require skill (both interpersonal and medical) and luck. The decisions made at the onset of clinical detection often dictate the ultimate fate of that pet. Those decisions include not only clinicopathological considerations of the patient but also considerations of emotional and psychosocial sensitivities of the family. These issues

may exist with any geriatric oncology case presenting at early, middle, and advanced stage of disease.

This book illuminates emotional and decision-making issues in geriatric oncology that are often left unaddressed in textbooks. It will also clearly outline the information that each pet owner should acquire from a consultation with the primary veterinarian and then, on a more specialized level, from their referral veterinarian. There is a cry for help to the veterinary profession from deeply bonded pet owners because many of their needs, including clear clinician-to-client communication, emotional support, pet pain control, and end of life care issues, are not handled properly.

Too often, volumes of vital interactive information is lost or forgotten in the hurry through exam rooms. Attending doctors and staff leave unsaid much that needs to be said. Veterinarians who learn to understand attachment and how the human-animal bond factors into the geriatric pet–cancer equation will gain a tremendous potential for enriching their practice. Veterinarians who devote time and compassion to the transfer of vital “soft” information to their cancer patients’ caregivers truly serve the contemporary needs and expectations of the companion animal community.

Physiologic and Chronologic Aging Variability

There is no straightforward method for defining the age at which dogs and cats become “senior” or “geriatric.” Of the two species, dog aging is more difficult to pin down due to genetic variability, breed longevity, environmental influences, body weight, and whether or not the dog is obese. Overfeeding and obesity have been shown to reduce the longevity of dogs by 2 years. This may be true for obese cats as well. One study found that almost 30% of our nation’s senior dogs were overweight. By 12 years of age, only 5% of dogs were overweight, and 16% were underweight (Donoghue 1991). The ravages of age interacting with the molecular events and genetic mutations that generate cancer may be potentially reversible with treatment.

Clients often ask, “How can I estimate my pet’s age in comparison with human aging?” A 1-year-old medium-sized dog has accelerated maturation and is comparable to a 15-year-old teenager. During the middle years, the aging process slows down, adding only 4 years per 1 human year. During the last 25% of a pet’s life, aging accelerates.

“Senior” is a term that softens the concept of aging and flows well into “geriatric.” “Senior” prepares pet owners to witness the comparatively accelerated aging of their beloved companion animals. The term “senior” is commonly used to describe dogs over the age of 7 years and cats over the age of 9 years.

I propose that large dogs be considered senior after 5 years of age and giant breed dogs be considered senior after 4½ years of age. Using the term “senior” to describe dogs and cats that have reached 60% of their life expectancy seems reasonable.

“Geriatric” is defined as the state of being in the last 25% of one’s life expectancy (Abeloff et al. 2004). The term “geriatric” is commonly and arbitrarily used to describe dogs and cats over 8 years of age, even though cats and small breed dogs live longer than large and giant breed dogs. The life expectancy for cats and small dogs (less than 20 pounds) is 9 to 13 years. The life expectancy for medium-sized dogs weighing 21–50 pounds is 9–11½ years. Large dogs weighing 51–90 pounds have a life expectancy of 7½–10½ years. Giant breed dogs weighing over 90 pounds have the shortest life expectancy, only 6–9 years.

For this text, all cats and dogs weighing under 90 pounds and over 8 years of age, and all giant breed dogs over 5 years of age, are considered geriatric. Clients are enlightened when they see comparable aging tables showing the variations between animals and humans by species and weight. A

combination of several comparable aging charts for pet cats and dogs stratified by weight was prepared for this text to illustrate the ranges of opinion (Table 1.3).

We often encounter exceptions to the rule when we see chronologically old pets that are physiologically youthful. Some geriatric animals are not afflicted with the usual arthritis, spondylosis, nuclear sclerosis, visual and hearing deficits, muscle loss, and cognitive dysfunction of their counterparts. This

Table 1.3. Comparative Aging Chart for Cats and Dogs

Chronologic Age	Human Age Equivalent Feline	Canine by Weight				
		0–20#	21–50#	51–90#	91–120#	>120#
		0–9kg	10–23kg	24–41kg	42–54kg	>54kg
Human Age Equivalent For Canine In Years						
3 months	5	5	5	5	5	>5
6 months	8–10	10	10	10	10	10
9 months	12	11	11	13	15	>15
1 YEAR	15–24	12–15	12	16	20	>20
2	21–24	19	21–24	23	26	>26
3	25–42	25–28	25–29	29–34	28–39	>39*–40
4	29–32	32	32–34	38–42	43–49	>49*
5	33–48	32–36	36–39	39–49	40–58	>59*
6	37–40	40	40–44	44–49	49–69	>69*
7	41–44	44	47–49	50–61	62–79	>79*
8	45–57	48	50–54	55–63	64–89	>89*
9	49–52	52–53	56–59	61–68	71–99	>99*
10	52–63	56–57	60–64	66–73	78–80	
11	56–60	60–63	65–69	72–76	77–80	
12	61–69	64–67	69–74	77–83	84–94	
13	66–68	68–70	74–79	82	101	
14	71–72	72–73	78–84	88	108	
15	75–80	76	83–89	93	115	
16	80–81	80	87–94	99	123	
17	83–86	84	92	104		
18	88–91	88	96	109		
19	91–96	92	101	115		
20	90–101	96	105	120–123		
21	100	99	109			
22	103	102	113			
23	?	104	117		GERIATRIC	
24	?	107				
25	?	109				
26	?	112				
27	–					

Source: This table is a compilation of several comparative aging charts by William Fortney, DVM, Director of Community Care at Kansas State University School of Medicine; Ron Kurtus, School for Champions, 2005; Fred Metzger, DVM, ABVP, State College, PA, for Senior Care Vet. Ec. Supplement, 1998; Alice Mills, DVM; and Feline Medicine, DVM, Best Practices 2002.

Note: Physiological differences exist between cats and dogs when using their chronologic age. In dogs, the breed, size, and weight create further differences between chronologic and physiologic aging. This table is a compilation of aging tables showing comparable aging for cats as well as for small, medium, large, and giant dogs according to standard weight. Overweight and obese dogs have a greater comparable age and shorter life span than normal-weight dogs.

*Information from William Fortney.

vitality may be the best reason, next to financial limitations, that explains why geriatric medicine is applied on a somewhat arbitrary basis from one clinician to the next.

The clinician who fails to recommend health screening for a senior or geriatric pet because the pet is physiologically youthful deprives that patient of the benefits of an early diagnosis of cancer. The synergism of cancer with aging involves the molecular changes of aging that prime senescent cells to the effects of environmental carcinogens (Balducci 1994). We must individualize our approach to suggest preventative and therapeutic ways to control cancer for each geriatric patient.

A 1998 Gallup Poll found that 39% of the 58 million dogs in the general population were “senior” and that 47% of the senior group was considered “geriatric.” If we use these percentages on the current U.S. dog population of 65 million, we can estimate that there are at least 25.35 million senior dogs and that 12 million are geriatric. Since half of dogs over the age of 10 develop cancer, this translates into 12.675 million canine cancer patients that our relatively small profession will encounter. Over eight thousand dogs are affected by osteosarcoma each year (Eldredge and Bonham 2005), and it can be estimated that as many as 2.5 million dogs may die from hemangiosarcoma overall (Lamerato-Koziki et al. 2005). There are approximately 77.6 million pet cats in the United States. The estimated prevalence of cancer-related death in the geriatric cat population is approximately 32%. It is plain to see that an increasing demand for expertise in geriatric oncology is upon our profession.

Preventable Tumors in Geriatric Pets

As companion animals age, they develop many of the same types of tumors that are found in humans. Since pets don’t smoke cigarettes, they don’t often get lung cancer. There is epidemiologic research from Tufts University and Amherst College, however, showing that cats exposed to carcinogenic cigarette smoke are at greater risk of developing certain cancers. Their surveys found that smoking for 3–5 years in the presence of cats increases their risk for oral and lingual SCC and for GI lymphoma by three to five times. Cats consume coat-associated carcinogens in the form of smoke particles that settle on their fur. It has been shown that smoking stimulates COX-2 in mucus membranes as a mechanism of carcinogenesis. A few reports claim that dogs living in cities where air pollution is heavy may be at a higher risk for tonsillar SCC.

The most preventable cancers in dogs are mammary, ovarian and uterine, testicular, and perianal. Female dogs spayed before the first heat period are protected from reproductive organ cancer for life. Male dogs neutered under 4 years of age are spared testicular and perianal tumors (some of which are malignant).

Another preventable cancer that afflicts the skin of dogs and cats is solar-induced skin cancer. Any unpigmented skin that is exposed to an excess of sun undergoes “field cancerization.” The entire field of exposed skin is more prone to develop actinic SCC or cutaneous hemangiosarcoma. Application of daily sunscreen, keeping pets in the shade, or keeping them indoors during the heat of the day will deter skin cancer. Lesions appear as pets age due to the cumulative genetic damage from solar exposure and field cancerization.

Summary

Understanding theoretical cancer biology is essential for the contemporary veterinarian. The increasing association of cancer and senescence places our aging pet population at greater risk for the many manifestations of neoplasia. How cancer, and its treatment, impacts and affects the geriatric oncology patient is paramount when offering options. Managing cancer in the oldest portion of our diverse

pet population is only anecdotal at this time. Because pets are living longer and the human-animal bond, as a celebrated relationship, has created extremely devoted pet caregivers, there is an increasing demand and need for more information and expertise in veterinary geriatric oncology. Caring for geriatric oncology patients is an arena where academic know-how must be blended with good clinical judgment and honor for the human-animal bond.

Soon, new applications against cancer will involve the routine use of gene therapy. The genetic codes for dogs and cats are available for imaginative and hypothetical research. Soon, it may be possible to correct breed-related predispositions to certain cancers. Perhaps someday we will be able to perform genetic adjustments for pets at risk for cancer. Perhaps, through gene therapy, we will be able to prevent mast cell cancer for Boxers, Bulldogs, and related breeds and reduce the cancer risk for lymphoma and sarcomas in cats and Golden Retrievers. Perhaps we can reprogram large and giant dog breeds to sidestep osteosarcoma and hemangiosarcoma. Frankly, I look forward to the day when the eradication of animal cancer puts my oncology practice out of business!

Medical genetics is rapidly developing. I suspect someone looking at the new edition of Ettinger and Feldman a hundred years from now will laugh at what we all had to say. We must remain alert to growth and changing paradigms in medicine.

Stephen Ettinger, DVM, ACVIM

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Suggested Reading

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- VetMedCenter.com. www.vetmedcenter.com. Consulting editor, Dr. W.B. Morrison.

Chapter 2

Caring for Geriatric Cancer Patients: What Is Needed Aside from Medical Care

More and more, the older cancer patient has become the majority of cancer patients.

Lodovico Balducci, MD

Age Brings More Complexity and Susceptibility

Treating cancer in geriatric pets is more complex than any other discipline in veterinary medicine. Geriatric pets come to us with a smorgasbord of diagnostic dilemmas that may need a wide range of specialty care. The aging pet's skeletal system and organ systems undergo compromise with arthritis and exposure to general toxins, age, obesity, and the impact of other organ failures. For example, heart disease has a negative impact on renal vascular flow and function and may add risk during sedation for diagnostic procedures and anesthesia for surgical tumor removal. Heart disease would exclude the use of Adriamycin due to its cardiotoxic effects. Renal disease would exclude the use of nephrotoxic chemotherapy. Various modalities of therapy including surgery, chemotherapy, and radiation therapy are often used in combination and/or in sequence to deal with specific types of cancer in dogs and cats (Table 2.1).

Age is a condition, not a disease. Many veterinarians are complacent after diagnosing cancer in an old dog or cat past a certain chronological age. Instead of working with the pet caregiver and offering multiple options, some veterinarians are thinking about their euthanasia speech. This cold shoulder attitude is unfair to clients and their geriatric pets. Veterinarians and their professional staff must overcome the doldrums and get rid of the defeatist attitude and not abdicate medical care and individualized oncology management for geriatric cancer patients.

People have preconceived notions about cancer. Aside from those clients who come in self-educated by searching the Internet, many caregivers have little to no knowledge about cancer. Many people hold myths and misunderstandings about cancer and the wide range of available treatments options. Personal biases and ingrained feelings regarding cancer may cause procrastination toward diagnosis and treatment, especially in geriatric pets. One client declined to treat her dog for early stage cutaneous multifocal mast cell tumors with oral prednisone and chlorambucil because her grandfather, a retired veterinarian, was against it.

Each member of the veterinary staff needs to dispel his or her negative notions about cancer. The entire profession must prepare to meet the medical and surgical challenges ahead to help care for the growing number of geriatric cancer patients. By adopting a more contemporary and integrative outlook regarding cancer care, veterinarians and their nursing staff can be successful in meeting the demands for improved geriatric oncology case management.

Table 2.1. Frequently Recommended Treatment Modalities

Type of Cancer	Surgery (Sx)	Chemotherapy (CTx)	Radiation Therapy (RTx)	Adjuvant or Specialized Therapy
Mast cell	*	*	*	H-2 blockers
Skin cancer, SCC	*	+/-	*	Cryotherapy
				Laser therapy
Lymphoma/leukemia	-/+	*	-/+	MoAb, vaccine
Breast cancer	*	*	-/+	Vaccine
Anal, sweat AC	*	*	*	Ck calcium
STS	*	*	*	Targeted therapy
FVAS	*	*	*	Gene therapy
OSA	*	*	samarium *	Limb-sparing, vaccine
Head/neck	*	*	*	Brachytherapy
M. melanoma	*	*	*	Vaccines
Oral cancer	*	*	*	Brachytherapy
Nasal cancer	-/+	+/-	*	Post RTx Sx
Brain tumors	+/-	*	*	Steroids
Endocrine tumors	*	*	+/-	Iodine 131 for thyroid cancer
Abdominal tumors	*	*	-/+	Second-look Sx
Bladder/prostate	-/+	*	-/+	Piroxicam
Hemangiosarcoma (HSAs)	*	*	-	Antiangiogenic therapy
Liver cancer	*	*	-	Percutaneous ethanol injection (PEI). Requires experience with technique
Thyroid tumors	+/-	*	Iodine 131 +/-	
Intestinal AC	*	+/-	-	Downstage with Ctx/RTx before surgery
Colorectal AC				
Lung cancer or metastatic disease	*	*	-/+	Targeted therapy, Nebulized Liposomes
	-/+	*	-	

Note: The most frequently recommended treatment modalities used in combination and/or in sequence for the most common types of cancer in dogs and cats.

Key:

- * Yes
- No
- +/- Often
- /+ Seldom

Aging and senescence are associated with immune system compromise, accumulation of free radicals, and deposition of immunoglobulin in tissues that injure the functional integrity of various organs. This is most evident in old, older, and aged pets as they develop degenerative, hepatic, and renal disease. A list of changes in body systems associated with senescence has been adapted with permission from Dr. Robert Hamlin (Table 2.2.).

Many geriatric pets have pre-existing endocrine disease such as hypothyroidism, Cushing's disease, or diabetes. Many geriatric animals, especially overweight cats on dry food diets, have been fed a less-than-ideal diet their entire lifetime. The multifaceted geriatric companion dog or cat with

all its comorbidities becomes our most complex and medically demanding patient when cancer strikes. The attending doctor and family must set realistic goals depending on the geriatric oncology patient's physiologic age as well as chronologic age. In many cases, quality of life, comfort, and palliation may take precedence over radical curative intent (Kitchell 1988).

Geriatric cancer patients, burdened with comorbidities, often need interventional help. Diagnostics and treatment may require pain control, sedation, anesthesia, surgery, chemotherapy, radiation therapy, immunotherapy, or rehabilitation therapy. Treating the geriatric cancer patient with the philosophy of "do no harm" is a weighty medical and surgical challenge. Unfortunately, this therapeutic goal is lofty and cannot always be achieved, even with the best doctors, specialists, and medical equipment and the know-how. We are unable to make promises that our efforts to help a geriatric oncology patient will not backfire with an adverse reaction.

The human-animal bond is intensified during the special period that the family spends caring for their geriatric cancer pet. Witnessing the debilitating changes of aging and cancer marks an understanding and acceptance of one's own mortality. Seeing an old friend become feeble or experience a bad reaction hurts the inner spirit. Tears and memories come to the surface during medication, feeding, and cleaning times. Goodbyes are said every day with glances toward the resting pet, during walks, and when the pet is being tucked in at night. It is a sad time for the caregiver who is pondering whether he or she is doing the right thing by tending to the geriatric cancer pet even though the cancer is expected to ultimately win.

Surgery, radiation therapy, and chemotherapy are modalities for cancer care that have the potential to do harm or cause adverse side effects before the geriatric cancer patient may realize a benefit. Geriatric patients are not predictable in their responses and reactions to procedures such as dietary changes, anesthesia, surgery, drugs, pain medication, chemotherapy, radiation therapy, or alternative therapy.

Clients need to be made aware of these potential dangers before they agree to a treatment plan. Clear communication is essential. You might tell clients, "We are not treating a machine that needs replacement parts. Our geriatric oncology patient is an aging body with variable organ and tissue responses and sensitivities. If the geriatric oncology patient has a reaction to a drug or a slow recovery from surgery, we feel badly about it. Do not blame yourself or us. We need to stay on the same side, holding hands together as a strong, supportive team to help your old pal live longer with a good quality of life. So let's talk about the options for treatment or palliation and the potential risks and benefits. After that, we can decide together whether or not you are willing to take the risks needed to reap the benefits that we might be able to win."

The Bond Grows Stronger with Age

Living with and caring for a geriatric pet creates a human-animal bond that is often intensified when cancer strikes. Because of the long duration of the relationship, a dog or cat may have a particular meaning to the owner or one of the family members because of an extenuating circumstance. If the pet provided devotion, comfort, and companionship through an illness, divorce, or the loss of a loved one, The Bond is stronger. Some feel that their pet is their last link to a deceased parent or loved one, and so they hold on dearly to that pet's life. Some have a spiritual attachment with a particular pet.

When a pet provides a sense of security, stability, or support, the human-animal bond may be a paramount consideration for the family. A pet may serve as a surrogate, in the role of child, partner,

Table 2.2. Changes in Body Systems with Aging/Senescence

Musculoskeletal	Loss of flexibility
	Loss of muscle mass
	Decreased response to stress
	Loss, graying, and dullness of hair
	Hyperkeratinization of pads
	Brittle claws
	Thick, non-compliant dehydrated skin
	Granulation and fragmentation of collagen
	Hyperplasia of sebaceous and apocrine glands
	Sebum becomes waxier and rancid
	Splitting and fragmentation of cartilage
	Arthritis, painful joints
	Dental calculus and periodontal disease
Gastrointestinal	Decreased salivary secretions
	Esophageal muscular tone decreases
	Constriction of lower esophageal sphincter
	Decreased HCI results in emesis, flatulence, diarrhea
	Fatty liver, nodular hyperplasia, cirrhosis
	Diminished output of pancreatic enzymes
	Decreased absorption of lipids and fats from GI tract due to villous atrophy
Respiratory	Chronic bronchitis
	Decreased volume and increased viscosity of mucous
	Ciliary paralysis and above leads to retention of materials
	Increased histamine release and reduction in cyclic AMP leads to bronchoconstriction, decreased protective airway reflexes
	Weakening of respiratory muscles
Cardiovascular	Fibrosis
	Tracheal collapse
	Decreased oxygen diffusion

(continued)

best friend, confidant, or other family member. Some pet loss heartbreaks will be harder than others. For many, the first loss is the hardest.

The long duration of the relationship is not the only criterion for a strong bond between a person and his or her geriatric pet. In the last decade, we have provided an greater number of oncology consultations for pets that were adopted or rescued as seniors than ever before.

The Bond that pet owners share with a new but aging arrival in their lives is often filled with compassion for the pet’s endurance of an abusive or neglectful past. They feel a strong commitment to nurture the older pet. They want to provide good health care and make the remainder of the pet’s life the best it can be. For all of these reasons and more, many pet caregivers are willing to engage in the battle against cancer for their geriatric pets.

Noodles’s Case (She Needed to Outlive Mom)

Noodles, a 16-year-old F/S Pug, was adopted at age 10 by Robin Birnbaum. Noodles was diagnosed with metastatic mast cell cancer, which extended along the skin of her mammary glands and involved her axillary and inguinal lymph nodes. Robin’s 80-year-old mom routinely called her after every appointment to ask how things went with Noodles. Robin’s mom had been

Table 2.2. *Continued*

Renal Changes	Decreased glomerular filtration rate and renal perfusion, decreased tubular mass Thickened capillary walls of glomerular tufts Ischemic atrophy and fibrosis of peritubular tissue Hypertension, increased vascular resistance Diminished response to ADH Decreased output of erythropoietin Accelerated death of RBCs due to uremia
Urogenital	Loss of sphincteric tone Chronic cystitis, increased frequency of urinary tract infections Pendulous prepuce due to Sertoli cell secretion of estrogen
Endocrine	Relative androgen deficiency, ovarian involution Decrease in hormonal secretion from most glands
Central Nervous System	Decreased neurotransmitters Deafness, blindness, loss of tactile sense Cognitive dysfunction syndrome Behavioral changes Behavioral changes with cognitive dysfunction syndrome Disorientation Reduced social interaction Forgetfulness with house training Sleep disturbances
Molecular, Immune System	Altered and variable levels of activity Decreased T-cell population Decreased tumor suppressor and repair gene activity Increased rate of neoplasia Thymic involution

Source: Adapted from Geriatric Medicine I, 1988, Veterinary Post Graduate Institute, Santa Cruz, CA, with permission from Drs. Robert L. Hamlin and Robert R. Pensinger, 2005.

battling lymphoma for 11 years and she had recently been told that she only had 2 or 3 weeks to live. Robin said that she thought her mom felt a deep kinship with Noodles (“They were both old ladies with terminal cancer”), linking her own survival to Noodles’s. During her chemotherapy treatments, Noodles became the poster dog and mascot for the local wellness community dog walk in Redondo Beach, CA. Robin carried Noodles for most of the walk due to Noodles’s declining health (Figure 2.1). The mast cell tumors that were once in remission had returned and developed along her mammary lymphatic vessels.

We added lomustine to her chemotherapy protocol. This helped Noodles achieve a partial stable remission. When Noodles’s platelet count dropped below 40,000, Robin’s mom was especially concerned. Eight months went by. After Robin’s mom passed away, Robin told me that she worried that Noodles would die before her mother. If Noodles had died, she said, it would have dashed her mother’s will to live. Instead, Noodles went into a complete remission and delighted everyone with her longevity and vitality.

Geriatric oncology requires us to do much more for our clients than to merely understand treatment and provide good medical care. We must also be resourceful and compassionate to assist caregivers in decision making and comprehensive caretaking for the benefit of their pet and other family members.



Figure 2.1. 16 year-old F/S Pug, Noodles Birnbaum, during difficult days with metastatic mast cell cancer. The cancer was resistant to initial treatment but responded to a change in protocol that incorporated lomustine. Noodles achieved a durable complete remission, which lasted 10 months.

Individualize Client Character

At each appointment, the veterinarian should take note of the love bond that exists between a particular client and his or her pet, not to judge but to appreciate and respect its power. Taking note of this relationship with a comprehensive focus gives each office visit intensity and purpose. This is no less important than the physical examination or the analysis of scientific data. This client interview will also help determine the best way to communicate with that client.

Some clients have strong personalities. They may be impatient if they have to wait to see you. Some may not want a detailed medical explanation. Most clients are used to having control of most aspects of their lives until cancer strikes their pet. They feel awful because they have no control over their pet's aging process or the cancer. A good approach to these issues would be to acknowledge them. Explain that we have no control over aging and may be able to offer some help with the cancer. Point out the areas where they still have control, such as pain control, quality of life, and how and when their pet will pass.

Other clients with more subdued, dependent personalities may slump into a depression and go blank. They may not be able to comprehend the necessary information for decision making.

In addition, the diagnosis of cancer may be critical if the geriatric oncology patient has another worrisome concurrent morbidity such as incontinence or chronic renal failure (CRF). The client may already be stressed with the rigors of long-term care for the geriatric pet (Schoen 1991). The diagnosis of cancer on top of an age-related disability may be too stressful for the caregiver to deal with at the moment.

Both personality types need information handouts to read in privacy at home. Give them a few days to absorb the information and suggest Internet information sources and consultation with an

oncologist. Let clients know that you will partner with them to help them make the best decisions regarding options to pursue for their geriatric cancer pet.

Sensitivity Self-Assessment

After every appointment, assess your own performance as a veterinarian by asking yourself three simple questions: Did I serve the client? Did I serve the pet? Did I serve The Bond? The human-animal bond is an entity unto itself, bigger than the pet alone or the client alone. A veterinarian may perform superbly as a medical practitioner to the pet and communicate accurately and clearly to the client, but without an understanding of The Bond, we are no more than mechanical engineers trying to fix a broken pet, or liaisons explaining to a client what's wrong with his or her pet. Our understanding of The Bond is the aesthetic that elevates our work into one of the most meaningful, passionate, and compassionate arenas of health care.

Defining the Human-Animal Bond (The Bond)

A working definition of The Bond was proposed in a 1998 statement from the AVMA Committee on the Human-Animal Bond: "The human-animal bond is a mutually beneficial and dynamic relationship between people and other animals that is influenced by behaviors that are essential to the health and well-being of both. This includes, but is not limited to, emotional, psychological, and physical interactions of people, other animals, and the environment. The veterinarian's role in the human-animal bond is to maximize the potentials of this relationship between people and other animals." Dr. John S. Wright, past president of the American Association of Human-Animal Bond Veterinarians (AAH-ABV), proposes a simpler, more expansive definition: "The relationship between people, animals, and their environment. The AAH-ABV mission is to provide education, resources, and support that enhance the ability of veterinarians to create a positive and ethical relationship between people, animals, and their environment" (Wright 2005).

Because of The Bond, pet owners in the early 2000s began spending more money than ever before on their pets. They also spent more time to become educated about their pets' medical conditions. This is good news for our profession because of its potential income. The bad news for those who entered veterinary medicine for monetary reasons is that this increase in pet owner spending is accompanied by more stringent standards in choosing medical caregivers. Clients no longer simply use the veterinary office nearest their home. They choose veterinarians and a veterinary staff based, in part, on their sensitivity and compassion. They rely on their chosen pet(s) for spontaneous moments of playfulness, joy, and physical contact. Pets give people opportunities to give care and that enriches their lives with meaning, identity, and a closer connection with nature. Pet caregivers want their veterinarians to be cognizant and respectful of their special relationship. They want more than scholars; they want healers with intellectual charity who are not judgmental (Bustad 1996).

Keno's Case (If You Don't Communicate Well, Clients Will Go Elsewhere)

The Mannings were given a poor prognosis for Keno, an old M/N Beagle. He had epistaxis 1 week after his adoption. The initial computed tomography (CT) scan, rhinoscopy, and biopsy

were negative for cancer. Two months later, Keno had a second episode of epistaxis. The new CT scan and biopsy confirmed nasal chondrosarcoma. The attending doctor immediately referred the Mannings to a radiation oncologist. During our phone consultation, they told me that they felt that the specialist was abrupt and looked bored and aloof during their consultation time. They said the doctor would not speak frankly with them or answer their questions to address their concerns. Mrs. Manning said, “We felt that we were talking to an attorney and not our veterinarian.” When they asked if there were any more specific survival data that might favor Keno, they said that the doctor started doing math to show them what a median survival meant. Mrs. Manning said to me, “I’m an architect and my husband is an engineer. We both have MBA degrees. We did not need a math lesson!”

The radiation oncologist told the Mannings that Keno needed a third CT scan. Apparently, the second CT scan “was not good enough to determine if the cancer was in one side or in both sides of Keno’s nasal cavity.” She estimated the cost of treatment at \$6,500.00. The Mannings asked what side effects Keno might have and the doctor told them she couldn’t say because “it depends on the dog.” She said that some get a bit of a burn and some develop blindness. Then the doctor gave some statistics and started to explain the averages in yet another math lesson. The Mannings asked the doctor, “If Keno were your dog, would you do it?” The doctor said, “That is a terribly unfair question—I get a discount. It was inappropriate of you to ask. How can you ask me that?”

Needless to say, the Mannings had a confidence crisis with this consult. When they asked for a record transfer, the office manager apologized. She said that the doctor may not have the best bedside manner but the techs and the treatment provided are excellent.

The Mannings told me that they were also looking for a Chinese medicine doctor to help Keno. They ultimately decided to drive 2½ hours in the opposite direction of the facility that provided the disappointing consult so Keno could have his radiation therapy elsewhere. Mrs. Manning said, “If the doctor treated us with boredom and indifference, we are afraid she would be like that with our dog too.”

Ideally, the contemporary veterinarian looks at each person-pet relationship freshly and applies a caring focus on client concerns and the geriatric pet’s well-being in the face of cancer. Celebrating the meaningfulness of The Bond between your clients and their geriatric pet(s) will be a constant and powerful practice refresher. The uniqueness of each client-pet relationship is inspiring and gives meaning to work for the veterinarian. Take an interest! Enjoy the various facets in the relationships that create your practice. Treasuring The Bond will keep you afloat and help you avoid feelings of drowning, burnout, and compassion fatigue (see section on compassion fatigue in chapter 11).

Providing medical care for geriatric dogs and cats with cancer can be depressing. It is especially disheartening if the pet was presented in an advanced stage of disease or if the client has money constraints that prohibit treatment. Often, the client can sense that the attending doctor has already written the pet off. The client sees through the doctor’s professional veneer and finds a lack of sympathy.

A client can sense when his or her veterinarian doesn’t have a clue about The Bond or is withholding compassionate care. The client may feel underappreciated by a veterinarian who doesn’t seem to value the client or the pet enough to offer supportive suggestions and medical care to help manage the geriatric pet’s cancer. Pet owners can tell when their veterinarian prefers to euthanize their geriatric cancer pet rather than be bothered with the complexity of treating that pet’s multiple problems. If the veterinarian steers the client toward euthanasia and the client doesn’t want this, he or she will either find compassionate care for the pet elsewhere or will comply—only to endure intense guilt and regret for years to come.

The textbook case is the exception. Textbooks are great. Where would we be without them? Oncology topics are covered with great detail in reference textbooks and in the veterinary literature. Each geriatric oncology case has a unique element if one looks for it. Many cases are atypical. With the volume of material that a contemporary veterinarian has to have in his or her head, it is a lifelong challenge just to keep all of the facts in place and up to date. But this isn't enough. Aside from having medical knowledge, veterinarians must also be able to think outside of the box. It is easy to fall into the trap of quoting textbook material, statistics, and so forth and be completely unable to provide individualized consultations or think outside of the box.

This may result in missed diagnoses and treatment delays and limit the quality and type of care that can be offered. Many patients have symptoms that would indicate a diagnosis that is true in 90% of cases. However, for the other 10%, don't automatically rule out the possibility of a diagnosis that is less common. Approximately 12% of the cases that look and feel like cancer are not cancer. Lead the client to as much information as he or she can handle. Let clients know what you are thinking and where you ideally would like to go with the workup of their pet's case.

Rodney's Case (One Enlarged Kidney May Lead to Another)

Rodney, a 14-year-old DSH M/N cat, developed an enlarged kidney. Fine needle aspiration (FNA) cytology was non-specific. The attending doctor recommended nephrectomy. The biopsy report diagnosed renal lymphoma. Rodney was given time to recover from surgery and then he was referred for an oncology consultation. Unfortunately, Rodney's remaining kidney enlarged during his 2-week recovery.

In situations like Rodney's, a geriatric oncologist would think differently, especially about masses in the abdominal cavity of old cats. Oncologists would strongly suspect lymphoma while ruling out differentials such as hydronephrosis, polycystic kidney disease, perirenal pseudocyst, or renal carcinoma. An oncologist would work hard to establish the diagnosis of renal lymphoma without the surgical intervention of nephrectomy in a geriatric feline oncology patient.

FNAs for large abdominal masses are often inconclusive due to cellular necrosis, cellular fragility, and heterogeneity within the mass. It is not unusual for me to examine up to 20 FNA slides from various sites of an abdominal mass. It takes patience to locate and identify the neoplastic cells that you are looking for. The extra effort is well worth it because it spares the geriatric patient the morbidity of surgery.

Before recommending nephrectomy for a patient like Rodney, it would be best to collect more FNA cells using a 22-gauge needle with a non-aspiration technique or a 1½-inch 27-gauge needle with gentle aspiration from multiple sites of the kidney. The next best step would be to get several percutaneous Tru-cut needle core biopsy samples using ultrasonography. This would be less invasive and a better next step considering Rodney's age and the prevalence for lymphoma (Caruso 2005). Rodney received unhelpful surgery that delayed his diagnosis and definitive treatment. Rodney was in poor condition at our first consultation and his family was so alarmed that they declined chemotherapy.

Conversing with Clients

Conversation skills are a top priority for successful communication. How you say it is often more important than what you say. Clear explanations and written information will help you acquire your client's confidence and compliance for the complex care often required in geriatric oncology.

Maintain an Unconditionally Positive Attitude

The contemporary veterinarian must strive to show each client an unconditionally positive attitude. This is essential when addressing a geriatric cancer patient's specific issues and when answering questions about a disfiguring procedure such as amputation, mandibulectomy, or enucleation, or an upsetting condition (Small 1991). We must also strive to keep the client's "reality buttons" in focus. In addition to all of the other roles you will play as a veterinarian, you are also your client's barometer. What you say and how you say it can either help or hurt your client and your patient as well. Be aware of and sensitive to your client's state of mind and always seek balance in your communications.

Balance: Helping the Client's State of Mind

People get emotional when their geriatric pets are seriously ill. Cancer evokes fear, dread, and irrational behavior. Client education helps people understand which cancers are treatable. The family needs to be assured that many geriatric patients diagnosed with cancer can be cured, placed in remission, palliated, or maintained with an acceptable quality of life in Pawspice care. It is important to help clients stay rational and involved in the decision-making process.

Help Your Clients Keep Their Balance by Addressing Them on Their Level

People with all types of personalities own pets. Clients want and need your full attention. You need to keep a healthy two-way balance with the client. Make sure that you have your clients' full attention when you are speaking to them. Make sure you are concentrating on them while they are talking to you. Focus on them while you are listening to the pet's history, description, and duration of clinical signs. Some clients have the need to provide some personal information that impacts how they relate to their pet. Remember that because they live closely with their geriatric pet, they possess vital information that you, with all your education and experience, cannot possibly know. Be respectful of their intimate knowledge of their pet and be careful not to give your clients the impression that their intuitive feelings and knowledge are of no value to you.

If you find that your mind was not focused for charting information and you did not hear what the client said, simply ask the person to repeat it. The client knows that there is a lot on your mind. Asking a client to repeat the history or the duration of illness and the exact symptoms is a way of saying that you don't want to miss anything and that you want to chart it properly.

You may have to repeat your questions if the person seems evasive. For instance, it may take several questions to establish the rate of growth of a mass. When did you first notice it? What size was it at that time? When was it half the size that it is now? All of these questions need to be asked and answered to ascertain the history properly. Sometimes it's hard to get the client to commit to an answer, yet with patience and positive persistence, the information can be documented for the record.

Use good communication gestures such as looking directly at the client, sitting at his or her level, patting the patient, avoiding barriers such as the exam table. Use plain non-medical words to help your client understand the diagnosis and extent of cancer for the geriatric pet. If you need to use medical jargon, you should clearly define each term. Medical jargon is a sure way to lose a client's attention. The contemporary veterinarian counsels caregivers with appropriate hope balanced with realism, instead of the old "test and slaughter" philosophy (Butler et al. 1991). That old philosophy was prevalent 20–30 years ago, yet this bias still lingers with some clinicians. You understand many aspects of the medical situation regarding the pet better than the client. It is your obligation to share this information with the client any way you can; use handouts and web sites.

The first question you can ask a pet owner is, “What do you know so far about your pet’s cancer?” It is surprising to find that many pet owners are inadequately and hastily informed about their pet’s cancer problem.

There is a certain personality type who will chatter at you non-stop. Knowing when and how to politely excuse yourself from the rambling is essential. Look for a break in the chatter and let the person know that you would like to talk with him or her more but that your main focus must remain with the patients. Tell the client that you have another patient waiting to be seen or a procedure that needs to be performed. Just excuse yourself politely when you can.

Another personality type with high needs asks the same questions repeatedly in different ways. These clients are hoping you will tell them what they want to hear (Butler et al. 1991). They need to hear both the upside and the downside of what the cancer and its treatment options would entail.

There is a certain personality type who will NOT be interested in understanding the technical details of the geriatric cancer pet’s medical situation. We should not force these clients off their balance with information overload. They don’t want to listen to medical explanations. They only want to know how to care for the pet’s medical condition properly. This type of client needs user-friendly information handouts the most, but will probably not read them.

Mimzi’s Case (Keep Clients Well Informed)

Mimzi, a 12-year-old F/S Pug, was due for a routine dental check-up. She had a few warts and some small bumps in her skin. A mass on her right shoulder bled after a visit to the groomer, and it seemed to bother her. The warts and bumps were removed at the time of her dental check-up. Biopsy samples were not submitted. A few weeks later, Mimzi’s right prescapular lymph node was enlarged. Antibiotics were given to fight the suspected infection. When the node did not reduce in size, FNA cytology slides were sent to the lab. The attending doctor telephoned the family and told them that Mimzi had a mast cell tumor.

Our consultation found that the family was poorly informed about mast cell cancer and the gravity of Mimzi’s situation. It may have been a case of owner denial. However, the attending doctor’s responsibility in geriatric oncology is to ensure that clients have a basic understanding of the extent of their pet’s cancer and a general idea of the prognosis.

Dealing with Inappropriate Depression and Grief

When clients learn that their elder pet has cancer, they are understandably depressed and frightened about what will happen. When delivering the diagnosis of cancer, be aware that the client may become very depressed. Check to be sure that the client is hearing and understanding what you are saying. When delivering the prognosis, always explain that the survival data is generally derived from reference statistics about other animals with the same type of cancer.

Illustrate a bell curve and show the family that the majority of patients are in the middle part of the bell curve for survival time. Show them that there are always a small percentage of animals that have shorter and longer survivals at each end of the curve. Assure the clients that your oncology team will do everything possible to position their geriatric cancer patient in the longer survival group. If

there is hope, an encouraging statement would be, “We can’t change the given prognosis, but we can try to outlive it.” Clients need to understand that your treatment at the clinic and their caregiving at home might help position their pet within the longer survival group of the bell curve.

Dealing with Anticipatory Grief

Pet loss is a special kind of grief. Much of it is anticipatory grief. It robs caregivers of energy and the ability to treasure and enjoy the precious time that they have left with their pet (Meyers 2000). It is important for veterinarians to identify this profound sorrow. It often pops up at the time one receives the diagnosis of cancer and again with any bad news. Anticipatory grief is often not recognized by the veterinarian, even though most highly bonded pet owners will verbalize or act out their grief. Veterinarians and their staff members need to validate the caretaker’s attachment for the pet and feelings of pending loss (Voith 1985). Sometimes the right words from the veterinarian can make the difference. It is also important to recommend pet-loss counseling. Group therapy sessions may be available through individual therapists who are qualified and interested in pet-loss counseling.

At times like this, I might say, “You are experiencing life’s richest emotions of love and loss. You will live through this and you will be okay. Your pet won’t leave you until his job is done and you will know when his mission is completed. Do you feel the passion that Buddy gives you right now? Some people will never know the depth of your grief for Buddy. Their lives were not enriched in the way you have been enriched with Buddy.”

Pet owners often tell me that they became more insightful and compassionate through pet loss. For Judy (see Buddy’s case later in this chapter), I said, “You will be a much wiser person for the experience that Buddy gives you so that you will be prepared when a family member or close friend passes on. You can learn how to use these tools of insight to help others who feel that they are in the same hopeless situation that you learned about so well with Buddy.” Judy responded, “Buddy is my best friend. I wouldn’t leave his side until it is over. Thank you for helping me. After Buddy is gone, I would like to help other people who are having trouble and feeling hopeless about losing a pet, like me.” This statement was a good indicator that Judy was beginning to progress through the stages of grief. She was accepting that Buddy would go and she was thinking about helping others and creating new attachments.

To ensure further support for the client, we also inform the referring veterinarian of the situation. We ask the attending doctor to call the client and to alert his or her staff to provide as much comfort and support to the pet owner as possible during the pet’s end of life care or “Pawspice” program. We also directly encourage the doctor to instruct the pet owner to seek counseling.

Disenfranchised Grief

A client’s grief and sadness may be heightened by feelings of being disenfranchised. Few people truly understand the enormous emotional burden that pet illness and loss places on a person’s morale. Many pet owners suffer from the insensitivity that others show in regard to how they feel about their beloved pet’s medical condition or impending death. This makes them feel disenfranchised because they can’t share their caregiving burden and their grief (Corbin 2004). Certainly you and your staff members should not be among the people who do not understand how they feel.

Ask your clients if there is anyone they can count on for moral support. Let clients know that you and your staff understand what they are going through. Assure them that you are aware of their needs and that you and your team will help them to help their pet. Use creative optimism and present a positive, action-oriented attitude about solving each one of the geriatric pet's concurrent issues and medical problems. This gives clients more confidence that their geriatric cancer patient will be given every chance to survive as long as possible with a good quality of life.

Inappropriate Optimism: Keep Reality Buttons in Place

If, after a diagnosis of pet cancer, your client seems inappropriately optimistic, not understanding the seriousness of the pet's illness, communicate realism. You might say something like this: "You are paying me for my opinion and I want to make sure that you understand the gravity of Bullet's condition and prognosis. We need to make sure that you keep your reality buttons in place. We can't change the poor prognosis that is dictated by the pathologist or the advanced stage of illness, but if you want us to treat him, there is a chance that we may be able to help Bullet outlive his prognosis."

Expect Shock and Dread

Many clinicians have told me that they are uncomfortable and don't know how to respond to clients who exhibit fear and grief. Some deal with this discomfort by just going on with the consult and ignoring the client's emotional display. They might point to the box of tissues, or offer a tissue, but they don't address or validate the client's sadness in a helpful way. This omission of counsel, this lack of verbal acknowledgement, further disenfranchises that client's grief experience. It also alienates the client from your practice. Hire a grief counselor to come to a couple of staff meetings to provide skills and drills to provide emotional comfort to those who need it. Once you and your staff have the tools, the discomfort turns into the a positive feeling of knowing you can acknowledge and offer empathy and help the client through the issues of pet illness, palliative therapy, and loss. Following are two true case scenarios with some verbal suggestions on how to address fear and grief on the phone or in the exam room.

Dori's Case (Wear Both Hats When Needed)

Maxine had a tissue in her trembling hand and was on the verge of tears when I entered the exam room. We discussed Dori's biopsy report, which diagnosed lingual squamous cell carcinoma (SCC). Oral examination was difficult, but the SCC invaded the entire base of Dori's tongue, making it stiff, ulcerated, and painful. I verified the poor prognosis that accompanies this type of cancer. Maxine looked at her 12-year-old F/S German Shepherd Dog-mix and burst into tears. She could not suppress her intense feelings of loss, injustice and regret. She said, "I love Dori. And I don't want her to suffer." Maxine had previously declined surgery and radiation therapy for Dori after learning that chemotherapy would have been only palliative.

Maxine reported, "Even though Dori lost 17 pounds and had trouble eating, she was still behaving close to normal and was cheerful in every other way." She asked me to do whatever I could for Dori to help her live a quality life until the end. When I introduced the concept of

Pawspice and how to recognize and alleviate pain for Dori, Maxine burst into tears again. My other two exam rooms were full and there were people in the waiting room. But it was more important to focus on Maxine's distress for a few precious moments. I told Maxine that I was going to put on the pet loss counselor's hat for a few minutes. I knew that my other clients would understand completely.

I began by letting Maxine know that we would be there to help both her and Dori get through the next several months and that she was not alone in her grief. I said that pet loss often has the power to bring all of our personal losses to the surface and that grief makes one feel raw all over. I suggested that her tears were shed not only for Dori but also for other past losses—that these tears that come so freely may be called “tears of the ages.”

Maxine then confided that she rescued Dori from the pound just after her brother had committed suicide. She said that her father had recently died, and that she was holding his hand when he died. She said, “I just can't take another loss.” Now we both recognized that Maxine's deep grief was truly for all of her losses. I suggested to Maxine that Dori might be helping her to deal with her repressed grief in a very special way. I told Maxine that Dori's cancer would give her time for reconciliation and that her passing may be a liberating gift to her. Maxine remained in distress.

When a client remains in distress, reach out and try to bring them to accept the situation. Even though I was behind schedule, it was important to help Maxine. It was time to share my personal beliefs with her by saying, “Each pet that shares our life comes to us with a special mission. Dori has a mission in your life and she won't leave you until it is accomplished.”

This message is a very powerful tool that can bring deep meaning to the feelings that the caregiver is experiencing. It can also help to bring the grieving client to focus onto his or her personal life and the role that the old pal has played in the caregiver's life. Maxine told me that she was a smoker since childhood and that Dori would be her teacher to help her quit smoking.

When it seemed appropriate, I told Maxine that I needed to put my other hat back on, as Dori's doctor, and help to provide care and medical treatment to the best of my ability. We continued the office visit and made a treatment protocol for Dori that consisted of pain control, hand feeding, and immunonutrition. The daily protocol included monitoring Dori's weight, hydration, food intake, and scheduled rechecks in order to monitor the well-being of both pet and pet owner. Two days later, a follow-up phone call found Maxine feeling much better, as was as Dori, who lived well for another 4 months.

Over the years, this message has helped uplift many of my upset clients: “The energy that you use to be anxious, depressed, and upset about Max's cancer is very powerful and it has a negative impact on both you and Max. Instead, harness that energy and use it in a positive way. Then, you will be able to do more to help Max. Use your powerful energy to keep your appointments and learn more about the cancer and how to best care for Max. Your positive energy will help Max have a better chance and improve his quality of life.”

Buddy's Case (Address Suicidal Tendencies)

Judy shared her life with Buddy, an 11-year-old M/N Golden Retriever who achieved a prolonged, stable remission with cutaneous lymphoma. When Buddy came out of remission and became resistant to treatment, Judy told me that she wanted to die if her sweet Buddy died.

Ignoring such a statement from a client would be very dangerous. When clients express this degree of depression, they are asking for your help. Never leave such an expression unanswered. If you are unable to help clients with their emotional responses to bad news, be sure to have a staff worker ready to step in. This is one of the other hats that we must wear as veterinarians. We are not therapists and should not delve too deeply into the client's emotions or thoughts, but we can be a friend.

An appropriate, helpful response will validate the importance of the pet in the person's life, and express that you understand their feelings. For example: "I know how important Buddy is to you. Pets like Buddy come to us with a special mission on earth. Only you know what that mission is, because it is very personal. Your love and the joy that he gives you are the reasons for your deep sadness. Your sadness is a rich emotion, just as beautiful and rich as the love bond that you share with him."

It is helpful to ask distraught clients to tell you something special about The Bond that they share with their old pal. You can comfort clients with words like, "Buddy will always be with you, but in a different way. He will be in your sweet memories. Buddy will be like a jewel that you place in a special box and store safely away in your memory shelf. You can always open the memory box to see and hold the jewel whenever you want to. Our pets were not designed to live as long as we do. They come to us with an internal time clock, like an hourglass, that runs out long before ours. In fact, if you have one to three pets at a time, you will have up to 27 heartbreaks in your lifetime. Some of these heartbreaks, like how you're feeling about Buddy right now, will be harder on you than others." Many people remain stuck in their grief but are unable to express it. You might be able to help such a client by saying, "If you keep the grief inside, it will make a hard knot in your throat. If you release it and let it out, you will then be free to just be sad and go on with the business of living your life."

Consider Extenuating Circumstances

Veterinarians are constantly adjusting the puzzle of patient care based on time and money constraints of the client. Every person-pet combination has extenuating circumstances. Take these given factors, add into the equation the health issues and habits that are intrinsic to the geriatric cancer patient, and the result is the challenge of geriatric oncology. We need to know about all of these factors and their summation, in order to determine if there can be complete or partial compliance to a particular chemotherapy, radiation therapy, or maintenance protocol.

Ask the client, "What is going on in your lives that may interfere or compete with the time commitment you need for your pet's treatment?" Some families have overwhelming interpersonal issues, or a concurrent crisis, or health issues that impact how they are able to care for their pet's cancer. Travel time and transportation issues for repetitive treatments may be difficult for people without cars or for those who are in and out of town due to work, parent care, or second homes. Money issues may exclude the preferred treatments and force the oncology team to treat the patient with a compromise protocol that has been adjusted to be more affordable. The pet's caretakers should not be judged or made to feel guilty. They should participate in the choices that are being made for the adjusted protocol. The oncology team must also inform these clients that the results may not be as successful when using the compromised protocol.

Pawspice Care Philosophy

Pawspice is about veterinarians and their nursing staff helping clients to provide end of life care at home for their ill pet. Family members need to fully understand that the word “palliation” actually means treatment for comfort, not cure. Often palliation is clearly the preferred mode of care for a geriatric oncology patient instead of curative treatment or euthanasia.

As pets glide into their geriatric years, the bond they share with their caregivers gets stronger. The American Pet Association estimates that 16 million pets die each year in the United States. Cancer claims at least half of dogs and cats over the age of 10. Organ failure erodes health in geriatric pets and ranks as the second most common cause of death. Most geriatric cancer patients are in physiologic decline with the aging process along with organ compromise and/or failure concurrently with their malignancies.

We must face the fact that many geriatric cancer patients will not be treated due to owner reluctance, financial constraints, concurrent illness, or a logistical problem. We can and should still offer reluctant clients an up-to-date consultation or a referral so they can be fully informed of their options. Concern for the well-being of the patient is first and foremost. It is time to wholeheartedly admit to ourselves that despite our great medical advances, compassionate supportive care for the patient and emotional support for the family is often the best medicine that we can provide at the end of the road for the human-animal bond.

If a geriatric pet is in the advanced or terminal stages of cancer at the time of diagnosis, various levels of palliative care and or Pawspice (pet hospice) care should be recommended as highly effective priority options. The contemporary veterinarian offers palliation and Pawspice over the insensitive suggestion of euthanasia as per the old “test and slaughter” philosophy. The Pawspice option keeps pet and caregiver comfortably close to their familiar places and satisfies the need to nest for a private farewell. This is often *THE* very best care that veterinary medicine can offer honoring the human-animal bond.

The most important ingredient to look for in yourself, your staff, and your clients is the willingness to provide comfort care for the geriatric cancer patient to assure peacefulness and quality of life. The purpose of Pawspice is to allow more time for the client to let go of his or her old pal with a longer, kinder, and intimate farewell. As long as the pet is peaceful and pain-free, many tender private moments of quiet emotion and sweet conversation can be gratefully shared between the caregiver and the dying pet (see chapter 10 on Pawspice).

Summary

No matter how the case turns out in the end, be assured that many caregivers with geriatric pets want and need you to help them fight for their geriatric pet’s life. The intensity of this cry for help places all veterinarians and their hospital staff on the emotional front line to help pet caregivers in the battle against cancer. It is always appropriate to acknowledge the reality of the geriatric oncology patient’s prognosis and say, “We are working against the odds.” If you accept this challenge with compassion for your clients’ feelings, your efforts will be appreciated and your practice will earn a positive reputation (Bustad 1996). Assure clients that you will partner with them and offer the best guidance for them for decision making. Then deliver the best care that you and your consultants can provide for the geriatric oncology patient while honoring the human-animal bond.

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Part Two

Chapter 3

The Warning Signs of Cancer in Geriatric Pets

The analysis of many a success or failure (in cancer management) often reveals the important role played by the physician or physicians who dealt with the case in its inception and their decisive influence on the eventual result. Where temporizing guesswork, amateurish approaches and defeatist attitudes may fail, intelligent understanding, prompt skillful treatment and a hopeful, compassionate attitude may succeed.

L. V. Ackerman, MD, and J. A. del Regato, MD

Principles and Practice in Geriatric Oncology

The warning signs of cancer in geriatric dogs and cats may be subtle and masked by obesity, pre-existing arthritis, and dental disease. Cancer is underestimated in geriatric pets because it is camouflaged by general signs of aging, such as “slowing down,” lethargy, reduced appetite, and weight gain or loss of muscle mass causing a distended abdomen. It is important to practice anticipatory medicine with geriatric dogs and cats. Be vigilant and look for cancer behind every warning sign no matter how subtle the sign may seem to be.

In order to provide geriatric patients the best chance of survival from cancer, we need to detect the cancer in the earliest possible stages. The veterinarian’s most important clinically relevant task is to recognize the premonitory warning signs of cancer. Most types of cancer exhibit specific early (prodromal) warning signs. Following this, the geriatric patient begins to exhibit more location-specific or function-specific signs. As tumor size progresses further, the geriatric patient exhibits more obvious warning signs, such as evidence of a mass or the interruption of a routine function.

It is generally the owner, the groomer, or the attending veterinarian who first detects a warning sign of cancer in an older pet. In my experience, there seems to be more owner reluctance, overprotection, and detection delay in geriatric pets. In many case histories, the pet caregiver and/or the attending veterinarian elected inaction. They took a conservative stance despite the presence of prodromal warning sign(s) because of the pet’s advanced age.

Cancer in geriatric pets is often allowed to progress due to ignorance, owner denial, overprotection, and various other circumstances and reasons resulting in detection delay. Clients are often unaware of the early signs of cancer in pets—client education is the best solution to this problem. The veterinarian can play an important role by educating clients one-to-one during office visits, with slide shows, videos, handouts, newsletters, web sites and downloads, and so forth. Incorporate client education during the waiting room time.

Some caregivers suspect that their geriatric pet may have cancer, but subconsciously or intentionally they delay taking the pet to their veterinarian. They may dread spending money (lack of health insurance in humans delays visits for over 6 weeks); they may be in denial. Some are afraid of finding

a terminal problem. Others simply do not want to put their old pal through the inconvenience and stress that they fear cancer treatment will entail.

Detection delays are not all caused by uneducated or reluctant clients. In some cases, the client reported a problem based on existing warning signs, and the veterinarian failed to diagnose or delayed tests that would have revealed the diagnosis of cancer at an earlier stage.

Such detection delays can seal the fate of an animal that might have been treated successfully. For example, some owners report that they suspected that their old cat had cancer because of a chronic bleeding facial ulcer. The attending doctor did not diagnose the lesion(s) as facial squamous cell carcinoma (SCC), but instead prescribed an ineffective topical ointment. Many cats with solar-induced SCC can be saved or spared nosectomy and pinnectomy if treated properly at the earliest stages using cryotherapy, imiquimod cream (Aldara[®]), or laser therapy.

Warning Signs of Cancer in Dogs and Cats

It might be easier to think of the warning signs of cancer if we group them into three tangible symptom groups: palpable, physiologic, and behavioral. Please refer to the following list of clinical warning signs of cancer and illness in pets.

Palpable Warning Signs

1. Lymphadenopathy, abnormal swellings, or plaques that continue to grow in the skin.
2. Abnormal masses in the oral cavity, mammary glands, testicles, vaccine sites, organomegaly.
3. Sores or ulcers that do not heal in 2 weeks, on the nose, ear tips, and face of white cats and ventrum of non-pigmented breeds.

Physiologic Warning Signs

4. Weight loss, cachexia.
5. Pale mucous membranes, icterus, jaundice, or hyperemic areas on membranes.
6. Halitosis, more than one loose tooth at the same location.
7. Abdominal distention, organomegaly, ascites, hemoabdomen.
8. Petechia, ecchymosis, hemorrhage at any location, especially orifices.

Behavioral Warning Signs

9. Anorexia.
10. Reduced energy or exercise intolerance, dyspnea, coughing, gagging.
11. Dysphagia, salivation, regurgitation, voice change, emesis.
12. Chronic sneezing, unresponsive ocular discharge, unilateral nasal discharge.
13. Dysuria, stranguria, hematuria that persists after initial therapy.
14. Diarrhea, tenesmus, constipation, hematochezia, change in shape of stools.
15. Lameness, painful movement, painful joints, hesitation to exercise.
16. Polyuria and polydipsia (PUPD): rule out CRF, endocrinopathy, hypercalcemia, and hepatic disease.
17. Syncope, muffled heart beat, pericardial effusion, pleural effusion, tachypnea.
18. Weakness, ataxia, paresis, behavior changes, pain, pleuralgia.

A revised list has been prepared in lay terminology for the general public of warning signs of cancer and illness in pets. This list, along with an illustration for locating lymph nodes (Figure 3.19), is at the end of this chapter (see Table 3.2). Clinicians are invited to copy and distribute this list and illustration to clients and the companion animal community as educational material. An excellent form to assess pain and illness in pets from NAVC *Clinician's Brief* can be downloaded for use at www.cliniciansbrief.com (Giving Seniority to Senior Pets 2005).

Cancer mimics many other diseases, and unless a mass is diagnosed, it is free to behave insidiously. Certain tumor types are well known for aggressiveness and ruthless behavior. However, almost every type of neoplasia has a premonitory sign that can be identified in its preclinical stages. If definitive action is taken at the advent of the premonitory/prodromal signs, a resolution of disease, or at least a better outcome, is possible.

The “let’s wait and see” attitude of the veterinarian of the past must give way to a more contemporary “let’s get a diagnosis” attitude. A veterinarian advising a client to “watch” a mass lesion is practicing illogical medicine. Most pet caregivers do not have the skills to know if a mass is behaving in a malignant manner. Secondly, because any time that a mass is not clearly benign to the clinician, it is always best to remove the mass and submit it for definitive diagnosis immediately. If the tumor is benign, that is good news. If the tissue is neoplastic, early detection will be invaluable in the ongoing management of that pet (Moore 2004).

Commonly Overlooked Prodromal Warning Signs of Cancer

Sadly, too many companion pets that experienced prodromal signs, which their caregivers were concerned about, progress into advanced stages of neoplasia before a diagnosis is made. Listen carefully to your clients. A red flag should go up when you hear a client casually or assertively report a specific or vague problem or a changed behavior in an older pet. It may be a sign that you discovered in this text or one you intuitively feel or scientifically know may indicate cancer.

Oral Cancers are Discovered Late

Geriatric pets (especially cats) with oral tumors are often diagnosed late in the course of their malignancy, despite the presence of early warning signs. Many caregivers don’t pay attention to their pet’s oral health. Signs that forewarn oral cancer are often noticed with mild curiosity and procrastination. Cats with bad breath or awkward chewing may be suspected as only having a minor dental issue. The family is not alarmed particularly when the pet remains alert and joyful and continues to eat. Think of an old cat with hyperthyroidism and an oral tumor driven by an increased appetite despite oral cancer pain. People detect oral tumors in dogs more readily because they pant and display an open mouth.

Prodromal Signs for Oral Cancer

Some of the early prodromal signs of oral cancer that pet owners often neglect to act upon are:

1. Pawing at the mouth, salivating, or leaving drops of blood in the water dish.
2. Holding or chewing food on one side of the mouth, dropping food, trouble picking it up.
3. Dysphagia or an awkward motion of the tongue while trying to chew.

4. A cat attempting to grasp food but dropping it.
5. A cat ignoring or walking away from food a moment after being very interested in eating it.
6. Halitosis: one person told me that her 15-year-old Beagle was frisky but had developed the worst halitosis. She told me that the dog was no longer allowed in the house.

Oral cancer can be difficult to diagnose in geriatric pets because some neoplastic lesions have no mass. This is especially true in senior cats with oral SCC. Lesions may appear only as lytic sites in the mandible or maxilla with loose infected teeth. Secondary infection automatically accompanies loose teeth. A typical scenario is the old cat with an infected oral SCC lesion. SCC clandestinely mimics dental disease and halitosis. The cat is taken to the veterinary hospital for a dental. The loose teeth are extracted, antibiotics are prescribed and the patient goes home. The cat returns in 30–90 days with obvious neoplasia at the old extraction site. The diagnosis could have been made at the time of the previous dental extraction had the attending clinician's index of suspicion been on high alert to rule out neoplasia. Dental radiographs might have identified abnormal lysis of bone at the lesion. At the previous dentistry, a deep socket tissue biopsy containing bone from the infected site could have been diagnostic.

Early detection of oral cancer and quick, aggressive action can save a pet's life. If the veterinary profession methodically educates the pet-owning public to link the subtle warning signs of oral cancer with a visit to a well-trained, suspicious veterinary clinician, more pets will be saved.

The Veterinary Team Can Educate Clients to Detect Oral Cancer

The veterinary team can be invaluable in teaching clients about oral cancer by doing the following:

1. Explain to clients that their pets will instinctively try to maintain a normal routine despite the pain and discomfort that oral cancer inflicts.
2. Show clients how to teach new pets to allow routine grooming and inspection of the entire mouth including visualizing the tonsils and under the tongue.
3. Demonstrate how to perform a mock oral inspection while pets are young (< 13 weeks). It is never too late to ask clients to acclimate their geriatric pet to oral inspections so the pet is easier to examine on rechecks.
4. Instruct pet owners to brush their pet's teeth frequently and to schedule routine dental exams. If gingivitis, tartar, and halitosis are present, dental prophylaxis is essential.

Pet owners educated in this way will be more likely to detect oral neoplasia in its earliest stages.

Patches's Case (Blood in the Mouth 4 Months Before Diagnosis of Malignant Melanoma)

Janice Wilkinson allowed her dog, Patches, a F/S 8-year-old Springer-Retriever-mix, to run back and forth along the fence, teasing and playing with the dog next door. Janice saw streaks of blood coming from Patches's mouth periodically. She thought that Patches cut herself chewing on the fence while taunting her canine neighbor. Janice did not see anything unusual when she inspected. Four months later, Janice noticed a fleshy red mass medial to Patches's upper left third premolar (LmaxP3). She took Patches to her local veterinarian immediately. A biopsy of the mass diagnosed spindle cell sarcoma but it could not rule out amelanotic melanoma. Our first consultation was at this point. Since the biological behavior of these two tumors is so different, a specific diagnosis was necessary. Janice authorized an immunohistochemical stain for differentiation. The tissue tested positive for the special tissue markers, MITF and S100. The presence of these protein markers on the spindle cells confirmed the diagnosis of oral malignant melanoma.

Knowing the aggressive nature of malignant melanoma helps us plan our treatment strategy to deal with metastatic disease as well as local control. Patches had a CT scan to determine bone involvement and define the borders of her lesion. She then had a caudal maxillectomy with 1 cm clean margins around the mass. This was followed by three sessions of chemotherapy with carboplatin and then she was entered into the Canine Melanoma Vaccine Study with the University of Wisconsin. This experimental vaccine is comprised of irradiated canine melanoma cells that have been genetically engineered to produce human GM-CSF (an immune stimulant). Data obtained from this study is pending from the Animal Cancer Treatment Program at the University of Wisconsin. Another more promising xenogeneic vaccine for canine melanoma that targets the enzyme tyrosinase has gone through clinical trials and United States Department of Agriculture (USDA) approval under the direction of Dr. Phil Bergman at the Animal Medical Center in New York.

Jake's Case (Ocular Discharge Was Jake's Early Warning Sign for SCC)

Jake Neff, a 12-year-old M/N DSH, had a “runny” right eye for months. There was no response with ophthalmic medications. Lisa, his caretaker, occasionally saw Jake pawing at the left side of his mouth. Her attending veterinarian could not find any abnormalities on physical examination. A few weeks later, Lisa noticed that Jake was chewing food in the left side of his mouth. It took several months and a third trip to the veterinary hospital for Jake's problem to be recognized and diagnosed as oral cancer. Jake's attending doctor detected a softening of the hard palate on the right side due to an infiltrative lesion involving Jake's right maxilla. The biopsy diagnosed oral SCC.

Max's Case (Arthritis Treatment Masks Osteosarcoma)

Max Boman, a 10-year-old M/N Doberman Pinscher, exhibited periodic lameness due to osteoarthritis of his elbows and hips beginning when he was 7 years old. His attending doctor dispensed Rimadyl® to ease the painful symptoms. At each episode of lameness, Max seemed to do well for about 6 weeks, as long as he had his medication, but one such episode with left foreleg lameness did not respond. The Bomans noticed a firm swelling in the mid-caudal aspect of his left foreleg. Radiographs disclosed a lytic, demineralized lesion at the distal left ulna characteristic of osteosarcoma.

The opportunity for early diagnosis was missed because Max's symptoms were masked by concurrent arthritis and the usual treatment. Symptomatic treatment for arthritis provided enough palliation against cancer-induced bone pain. This scenario is more common today since dogs are receiving powerful non-steroidal anti-inflammatory drugs (NSAIDs) for arthritis pain. The prudent veterinarian must periodically recommend radiographs for lame senior and geriatric dogs—especially for large and giant breeds with a high prevalence for osteosarcoma (Figure 3.1). If the client declines radiography, it is best to note his or her refusal in the medical chart before prescribing a course of symptomatic relief for the patient.

Warning Signs of Skin Cancer in Cats

With the exception of feline vaccine-associated sarcomas (FVAs), elderly cats are six times less likely to develop skin tumors than dogs. Benign tumors in cats may appear at any age and in any breed but are most likely to appear in geriatric Persian and Siamese cats. The median age for occurrence is 12 years. The most common benign tumors in geriatric cats may be present for many years



Figure 3.1. Lameness and swelling of the distal radius in a senior dog (a) is a common warning sign of bone cancer. This radiograph shows a lytic bone lesion, (b) typical of osteosarcoma.

without causing clinical concern. Benign skin tumors often appear as small, raised solitary masses covered with haired skin located on the head, back, trunk, or legs. They are superficial and generally do not cause alopecia, ulceration, pain, or invasion of surrounding tissue. These tumors may be solid, cystic, or pigmented and are generally cured with surgical excision. Basal cell tumors are the most common benign skin tumors of older cats.

Most malignant skin tumors in cats appear on the head, back, dorsum, legs, and mammary glands. They may be multiple, invasive, inflamed, ulcerated, coalescing, large, and erosive. They are locally invasive. Regional lymph node invasion and metastasis is uncommon except for mammary carcinoma, malignant melanoma, and at least 22.5% of long-term FVAS cases (Hershey et al. 2000). FVASs initially appear in the dermis and subcutis at typical vaccine or injection sites.

Initially, a small inflammatory reaction nodule arises following vaccine. If the nodule fails to regress within 1–3 months or if it enlarges to 3 cm in size, it should be biopsied (Figure 3.2).

Malignant SCC, fibrosarcoma (FSA), mast cell tumor (MCT), and mammary carcinoma (MGAC) are the most common types of cancer afflicting geriatric cats. The feline sarcoma virus (FSV) causes multiple dermal masses in young cats infected with FeLV. It is rare and non-responsive to conventional treatment (Theilen, Madewell, and Gardner 1987).

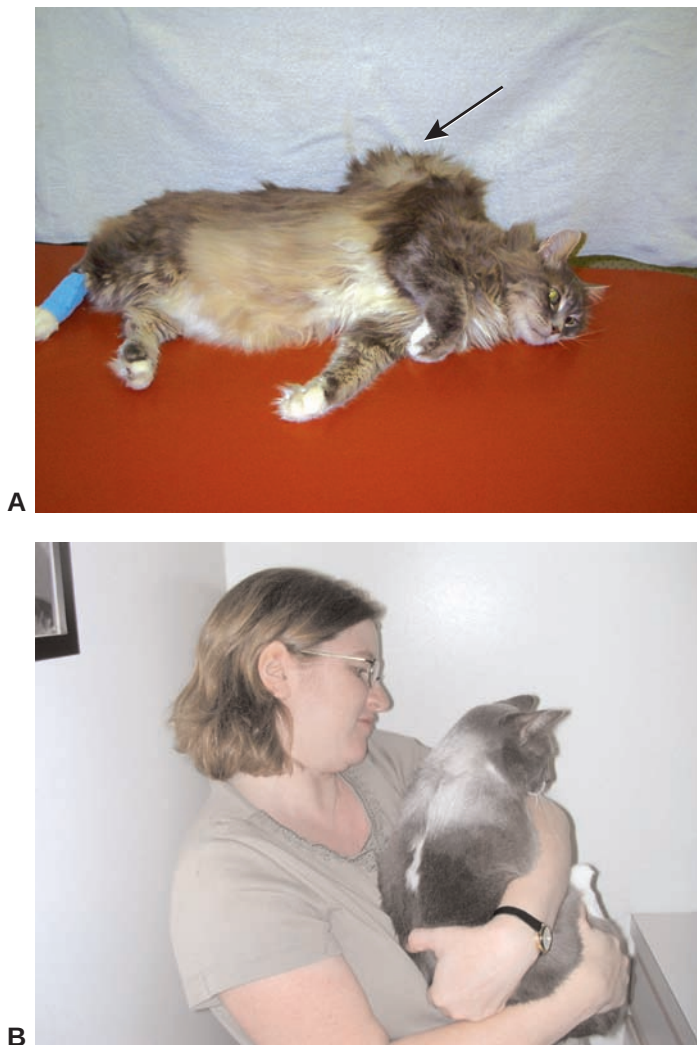


Figure 3.2. FVAS arises as a small nodule, which enlarges at vaccine sites. Tumors can become very large (a). Abby shows her radiation therapy site where the hair grew in white. She is celebrating her fifth anniversary of survival from FVAS, with her caregiver (b).

Solar-Induced Skin Cancer in Cats: Non-Healing Lesions

SCC appears as chronic superficial crusting ulcers in the non-pigmented facial area of cats. Lesions most commonly appear on the ear tips, nose, lips and temporal skin. Here are some typical quotes from cat owners: “I didn’t know that it would be cancer”; “I thought he had dirt on his nose”; “I thought he scratched his nose”; “He always rubs his nose on the screen door”; “I thought he got his ear scratched in a fight”; “I thought it was a sty in her eyelid” (Figure 3.3).

Initial lesions appear as inflamed sunburned skin with crusting sores. If the sores persist for over 2 weeks, carcinoma in situ is the most likely rule out. A presumptive working diagnosis for actinic lesions or SCC would be warranted whether or not the owner permits a biopsy for verification. The superficial ulcerative lesions of carcinoma in situ are easily treated with cryotherapy or laser therapy and may respond to topical use of imiquimod (aldara) cream. Instruct pet owners to keep white cats inside between 10:00 a.m. and 4:00 p.m. to avoid sun exposure.



Figure 3.3. Solar-induced nasal planum SCC in a cat (a). Solar-induced SCC on the pinnae and the temporal areas of a 20-year-old white cat (b). SCC lesions appearing on upper (c) and lower (d) eyelids of white cats exposed to the sun.

Warning Signs of Solar-Induced SCC

Dogs with non-pigmented ventrum skin are at risk for SCC and from solar exposure. Breeds most commonly affected with solar-induced SCC in my practice are Pit Bulls, White Boxers, Dalmatians (Figure 3.4a), and Harlequin Great Danes. Typical warning signs of SCC on sun-exposed skin include prodromal lesions that first appear as inflamed patchy sunburn (Figure 3.4b). Early SCC lesions appear as patchy red blemishes, which may ulcerate. Advanced lesions become proliferative fleshy masses, which may hemorrhage. American Pit Bull siblings Bella and Stella developed a full array of SCC lesions (Figure 3.5). They are shown before and after therapy.

Warning Signs of Cutaneous Hemangiosarcoma

Actinic cutaneous hemangiosarcoma is a solar-induced vascular skin cancer that occurs in the non-pigmented ventral skin of dogs that like to sunbathe. Greyhounds, Italian Greyhounds, Whippets, American Pit Bulls, American Staffordshire Terriers, Basset Hounds, Beagles, Dalmatians, White Boxers, English Springer Spaniels, and Salukis are among the breeds more commonly affected. Early lesions appear as flat red spots, red blisters, or bluish blood-filled dermal cysts. Some tumors may appear as raised cystic lesions that easily hemorrhage.

Non-actinic cutaneous hemangiosarcoma is rare. It is a cutaneous manifestation from multicentric hemangiosarcoma (Figure 3.6b). Breeds reported with greater prevalence are Bernese Mountain Dogs, Boxers, German Shepherd Dogs, and Golden Retrievers (Goldschmidt and Hendrick 2002).

Penny's Case (She Had a Rash That Would Not Go Away)

Penny Burchfield, an 8-year-old F/S Pit Bull–mix, was plagued with skin allergies. She developed little red spots on the skin of her underside. Her family thought the red spots were “just another rash,” but the spots did not go away with topical or systemic treatment for allergies. Penny was referred to a dermatologist, who diagnosed cutaneous hemangiosarcoma by punch biopsy. It is a cancer of the superficial capillaries in delicate skin and generally does not exhibit the aggressive biological behavior of visceral hemangiosarcoma. Penny was given Accutane[®], an expensive retinoid, for a year and a half. The lesions did not regress. She developed a small, fleshy mass on



Figure 3.4. SCC in a Dalmatian's unpigmented ventrum skin due to solar exposure. The lesions metastasized to the inguinal lymph nodes (a). Patient with chronic sunburn: a prodromal sign (b).



Figure 3.5. Both Pit Bull siblings, Bella (a) and Stella (b), have solar-induced SCC, which responded to a combination of surgery, cryosurgery (c, d), and oral maintenance with *Agaricus* immunonutrition.

her right flank that was removed during a routine dental examination. Her attending veterinarian submitted the mass for histopathology and found that the mass was an incompletely removed grade II MCT.

We met Penny for consultation regarding the MCT. She had over 50 cutaneous hemangiosarcoma lesions (Figure 3.6a). Since acutane was not helpful, we recommended cryotherapy for the numerous cutaneous hemangiosarcoma lesions. It has been over 3 years since that first consultation. Penny develops new cutaneous hemangiosarcoma lesions every few months and comes in for periodic cryotherapy as needed. New MCTs appear yearly and are widely excised.

Cutaneous Lymphoma: Often Misdiagnosed as Dermatitis

Cutaneous lymphoma (CL) has many manifestations that may run over a variable length of time. It may first appear as flaky and/or inflamed, hyperemic skin with or without pruritis. One client commented that his pet's skin looked as if it was producing ashes. In many cases of CL, the owner and the attending doctor notice flaky skin, dandruff, dermatitis, folliculitis, macules, plaques, and pododermatitis for several months, or longer, before skin biopsies are taken. Lesions may be crusted, ulcerated, alopecic, pigmented, and pruritic and may wax and wane. CL is rare in cats.

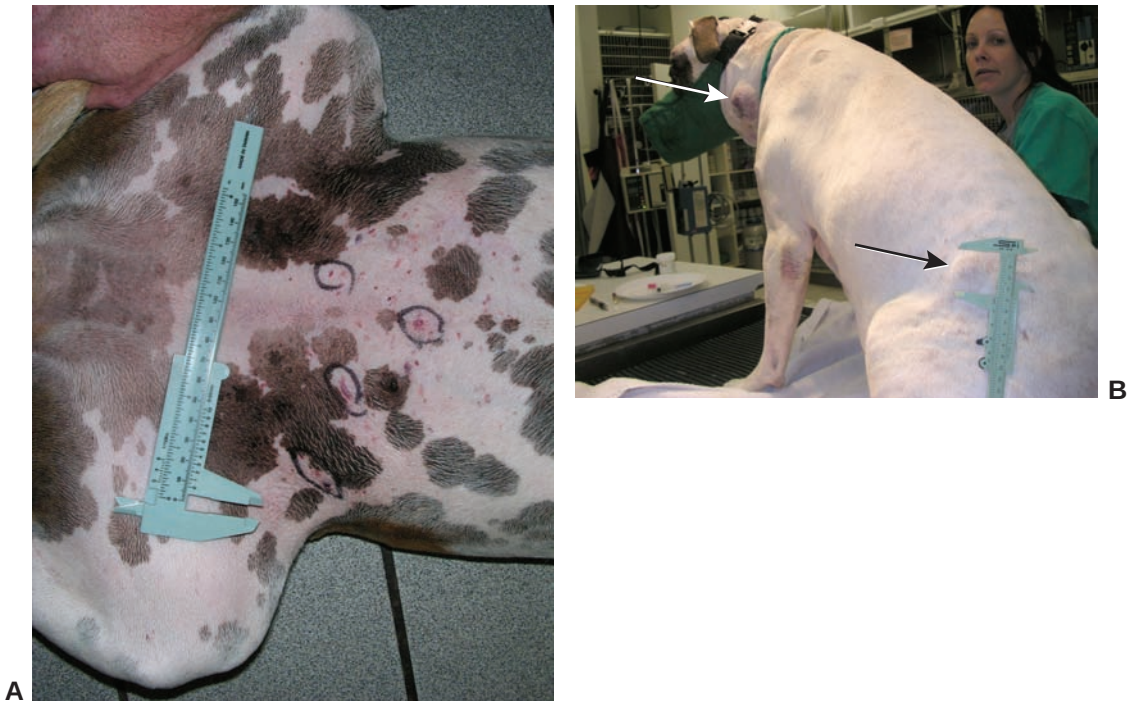


Figure 3.6. Actinic dermal hemangiosarcoma lesions during a cryotherapy session for Penny Burchfield (a), an 11-year-old Pit Bull. Penny needs periodic cryotherapy for new lesions as they emerge over a 3-year period. Cutaneous non-actinic hemangiosarcoma is due to multisystemic hemangiosarcoma in Buddy Lebuarn, a 9-year-old American Pit Bull (b).

Most cases of CL are histologically diagnosed in older dogs as cutaneous T-cell epitheliotrophic lymphoma. It is also known by its old misnomer, mycosis fungoides (MF), because the lesions mimic fungal disease. Non-epitheliotrophic cutaneous lymphoma lesions may be B- or T-cell. Painful, inflamed lesions often appear in the oral cavity, eyelids, and body orifices. CL may respond to initial chemotherapy for short remissions but most patients die within a year of diagnosis (Figures 3.7 and 3.8).

Jack's Case (CL Can Easily Be Misdiagnosed as Dermatitis)

Jack Watson, a 10-year-old M/N Golden Retriever, developed non-pruritic, flaky, scaly skin. His attending doctor treated the differential list that included flea allergy dermatitis, atopic dermatitis, pyoderma, and food allergies. Over a period of 6 months, Jack's skin appeared inflamed and would dry, causing large pieces of dried skin to peel and flake. Later, Jack developed macules and plaques of thickened skin. Several punch biopsy specimens were sent for histopathology. He was diagnosed with cutaneous T-cell lymphoma.

Mast Cell Tumors

One in five skin tumors, which appear as innocent fatty tumors or fleshy wide-based warts, may actually be an MCT. Boxer and Bulldog breeds are at greater risk although any breed may be affected. Mast cells are normally present in all tissues of the body and function in allergic reactions and local



Figure 3.7. Shar-Pei with cutaneous lymphoma. Most cases are diagnosed as T-cell epitheliotrophic lymphoma.



Figure 3.8. Cutaneous lymphoma appeared as inflamed hyperemic dry skin, which mimicked allergic dermatitis, for several months before diagnosis in this 16-year-old Poodle (a). Notice the late stage lesions in her eyelids (b). Mitzie also had painful oral lesions.

control of vascular tone. There are greater numbers of mast cells in airways and around body openings. Some MCTs appear rapidly on the face, feet, or axilla resembling insect bites. Don't cling to this diagnosis if the swelling lasts over 2 days. MCTs may also arise in the feline spleen or along the intestinal tract or in the liver. On occasion, some MCTs acquire the behavior of infiltrating lymphomas. In these cases mast cells are found in the bone marrow and in the peripheral blood as mast cell leukemia.

Lucy's Case (The Family Thought She Had Hairballs)

Lucy, a 12-year-old F/S DSH, started vomiting once or twice daily for several weeks. The family initially felt Lucy's problem was hairballs. The vomiting episodes were unresponsive to initial treatment. When her vomiting episodes became more frequent and more dramatic, she was referred for consultation. Endoscopic exam found a fleshy red lesion involving the pylorus, which was diagnosed as MCT. She responded well to surgical excision and chemotherapy for at least 6 months until lost to follow-up.

Mast cell tumors behave variably depending on their grade and location. Lesions in mucocutaneous junctions, groin, axilla, and mammary chain are more aggressive in my experience, although one report found no difference (Sfiligoi et al. 2005). Rapid growth rate (doubling time), geriatric age greater than 8 years, metastatic disease at the time of diagnosis, and relapse are factors that negatively affect prognosis.

Buddy's Case (An Innocent-Looking Skin Mass Can Kill)

Buddy, a 10-year-old M/N Boston Terrier, had a pedunculated mass on his left caudal thigh for 3 years. At first, the mass looked like an innocent skin tag. It changed suddenly one day, and looked more like a mushroom. The mass was removed during a routine dental procedure without a biopsy. Within a month, Buddy's thigh and his left popliteal lymph node became swollen. FNA cytology revealed malignant mast cells. The lesion was metastatic to Buddy's inguinal node and the mammary lymphatic vessels (Figure 3.9).

All brachycephalic dogs are prone to MCTs. Therefore, it is best to perform an FNA on even the most innocent-looking indolent skin lesions in a brachycephalic dog prior to removal. In this way, a wider surgical excision and biopsy for grading, staging, and treatment can be planned.

Hanny's Case (MCT Present for 3 Years, Then Lymphoma)

Hanny Jackson, a 9-year-old F/S Golden Retriever, had a recent history of hypothyroidism, urinary tract infection (UTI), and a grade I MCT. Thyroid supplementation helped Hanny shed



Figure 3.9. Buddy had a pedunculated mass on his left caudal thigh for 3 years. It was removed without a biopsy. The lesion was metastatic to Buddy's inguinal node and the mammary lymphatic vessels.

16 pounds over 4 months. She developed several new dermal and subcutaneous masses. The attending doctor recommended removal and biopsy. If the biopsy indicated MCT, then a second deeper excision may be needed. He also warned that more lumps might develop.

It was at this point that Mr. Jackson was referred to our service for consultation. Hanny had six skin tumors. A mass in her right axilla was 1.2 x 1.2 x 0.5 cm. It was a pearl-colored, hairless dermal tumor of 3 years duration (Figure 3.10). Mr. Jackson said that he had asked his veterinarian about the mass but was told that it was not a problem.

Three of the six skin tumors revealed sheets of mast cells on FNA cytology, including the right axillary mass. The MCTs were removed widely and diagnosed as grade I-II MCTs on histopathology. Hanny received oral chlorambucil and prednisone and weekly vinblastine IV chemotherapy for 8 weeks followed by a tapering schedule. Six months later, Hanny exhibited generalized lymphadenopathy. FNA cytology was consistent with lymphoma. Immunohistochemical stains were positive for CD79a, which classified it as a B-cell lymphoma.

This scenario illustrates the vulnerability of geriatric cancer patients to second primary cancers, especially for Golden Retrievers and Boxers. It would be expected that Hanny's lymphoma would be more resistant to treatment due to previous use of steroids for her MCT. Fortunately, she achieved remission with induction chemotherapy.

Rapidly Growing Masses in the Skin

Mast cell tumors may appear suddenly. They may appear as angry, fleshy, inflamed masses that epilate. Some MCTs have a glassy appearance on denuded skin. Some have a very rapid growth rate. Some may appear as a bee sting and cause a large swelling.

Max's Case (MCT Misdiagnosed as a Bee Sting, Then a Spider Bite)

Max Anselmo, a 10-year-old M/N Aussie, suddenly developed a swelling on the right side of his nose that was treated as a bee sting. The swelling shrank marginally with antihistamines

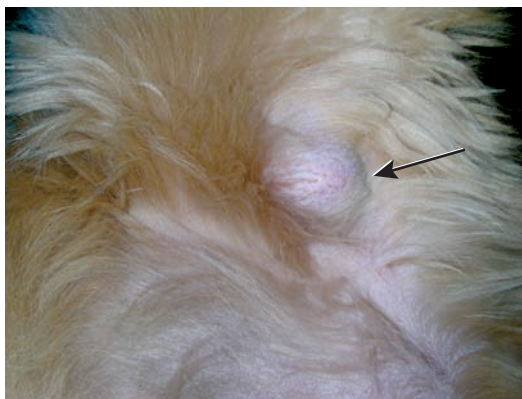


Figure 3.10. This innocent-looking mast cell tumor was present for 3 years in the right axilla of Hanny, an older Golden Retriever.

and steroids but returned. Mike took Max back to the vet, who then suspected a spider bite. Four weeks went by on symptomatic treatment while Max's muzzle remained swollen. Mike noticed that a lymph node in Max's neck was enlarged. The attending veterinarian took FNA samples that diagnosed both the muzzle and node swelling to be mast cell cancer. He responded to radiation and chemotherapy for several months; however, he developed systemic involvement. Diagnosis a month earlier might have changed the outcome for Max.

Some MCTs appear and then disappear and may go undiagnosed because of this transient feature.

Katie's Case (An Educated Owner Was Suspicious of MCT)

John Haddon read one of my local newspaper columns about MCT. It said that some MCTs could appear and then disappear due to histamine release causing a local inflammatory response. John's 3-year-old F/S Rhodesian Ridgeback, Katie, had a marble-sized mass in the skin behind her ear that disappeared. A few days later, John noticed that another mass appeared on the opposite side of Katie's neck. Because of what he read, John brought Katie to our clinic for an examination.

FNA cytology of each site found sheets of mast cells present at both locations. A third MCT was found on her proximal hind thigh. We surgically excised a section of skin that contained both the palpable mass and the regressed mass. We also removed the mass on her thigh with wide margins. The tumors were grade II MCT on histopathology. Katie developed a new crop of MCTs about every 3 years and lived to age 11.

Warning Signs of Mammary Cancer in Dogs

Many people feel guilty that they didn't recognize the early warning signs of mammary cancer in their dog. Here are some typical quotes: "I thought it was a cyst"; "The tumors didn't bother her"; "My vet said to keep an eye on it"; "One thing led to another and we didn't get back to the pet hospital when they grew"; "We wanted her to have a litter first but we never got around to it"; "My husband wants to keep her natural"; "We didn't know that if you spay a female dog or cat before she goes into heat, it protects her from breast cancer" (Figure 3.11).

One out of four intact female dogs over 4 years of age is at risk for developing one or more breast tumors. Malignant carcinomas are diagnosed in 50% and half of these carcinomas metastasize to draining lymph nodes and lungs via a plexus of lymphatic vessels within 1 year. Ovarian hormones, progesterone and estrogen, cause sensitization and promotion in mammary tissues resulting in point mutations in the genes that initiate tumor growth causing field cancerization. Ovariohysterectomy (OVH) surgery prior to 6 months of age is preventative while OVH surgery prior to 2½ years of age has a sparing effect.

Ginger's Case (Biopsy All Mammary Tumors at Initial Surgery)

Ginger Meeks, a female 10-year-old Australian Shepherd, went to work every day at various construction sites and herded sheep on the family's ranch. She had one litter and was never spayed. Ginger developed two mammary tumors that were probably not noticed for some time



Figure 3.11. Breast tumors in an intact female geriatric Poodle.

due to her thick coat. When the family noticed the tumors, the masses felt like walnuts. Ginger's veterinarian performed a lumpectomy but submitted no biopsy at that time.

Shortly after, several tumors recurred at the site. A second surgery was performed; this time, a mastectomy and biopsy verified mammary adenocarcinoma. The biopsy did not detail the margins because only a small sample of tumor tissue was submitted for diagnosis (see chapter 5 section on biopsy techniques and pathology and chapter 6 on surgical margins).

Within a month, Ginger developed angry red, weeping, raised dermal rashes emanating up to 6 cm in all directions from the incision site. At that point Ginger's family came to our service for consultation (Figure 3.12a). She was in severe pain from the lesions to the point where she had trouble walking. Mammary cancer invasive into the cutaneous lymphatics is known as inflammatory mammary adenocarcinoma or inflammatory carcinoma. It has a very aggressive biologic behavior. The family declined chemotherapy due to the poor prognosis. We provided palliative anti-inflammatory therapy and pain medication and entered her into Pawspice care. It may not be fair to speculate, but Ginger may have had a different course if the first surgery had been a mastectomy with a biopsy. However, the mechanisms that cause inflammatory carcinoma are not fully understood (Figure 3.12b).

Cancer of the Nasal Passages

Nasal passage cancer develops insidiously in older pets. It composes up to 2.4% of reported canine tumors and is more common in long-nosed (dolichocephalic) dogs and rare in cats. The most common tissue types found in canine nasal passage cancer are nasal respiratory carcinoma, SCC, fibrosarcoma, chondrosarcoma, and lymphoma. Lymphoma and respiratory adenocarcinoma are the most common tissue types found in feline nasal tumors. Treatment is frustrating because 68% of dogs with nasal cancer do poorly with the best of treatment. There is encouragement from a study that employed follow-up CT scan and surgical exenteration of residual disease following radiation therapy, which more than doubled median survival times (Adams et al. 2005).



Figure 3.12. Breast cancer in the cutaneous lymphatics is known as inflammatory mammary adenocarcinoma or inflammatory carcinoma. It exhibits a very aggressive behavior and is universally fatal. The lesion infiltrated the suture line (a). Notice the swollen right rear leg in this patient (b).

The early warning signs of nasal cancer in dogs or cats are unilateral nasal and or ocular discharge, epistaxis, stridor, loss of smell, facial or palatine deformity, loose teeth, and, sometimes, pawing at the face. Late-stage signs would exhibit a deformity along the dorsal aspect of the maxillary bones or over the paranasal and frontal sinuses. Some pets present a raised or pitting facial deformity. The deformity may involve the maxilla. Some pets exhibit a firm or soft focal, raised mass protruding below, around, or between the eyes. Some cases may have a softening and bowing out of the hard palate due to demineralization of the palatine bone. In every case of facial deformity, there is bone lysis and tumor invasion at that site. There may be a tremendous amount of mucus and phlegm clogged in the passages and sinuses. The stridor, discharge, sneezing, and epistaxis cause great distress for the family.

Most cases of nasal cancer exhibit sporadic signs, which show progression over a period of about 3 months before they are actually diagnosed. Initially the clinical signs fit the assumption that the pet has one of a various number of afflictions of the nasal passages.

Most clinicians would rightly suspect that the geriatric patient has rhinitis or allergies or an inhaled foreign body. Initial rhinoscopy may find no lesions while cultures find the usual pathogens. The diagnosis of rhinitis may suffice for a time. The presence of oral-nasal fistula or pain from infected or extracted teeth may complicate matters and mask the diagnosis.

Rufus's Case (One Episode of Epistaxis Can Forewarn Cancer)

Rufus, a 10-year-old M/N Black Lab belonging to Trudy Gleason, had a single episode of epistaxis. He started snoring over the following 4 months. After a second episode of epistaxis, his attending veterinarian performed rhinoscopy and biopsy, which yielded the diagnosis of nasal passage chondrosarcoma. Rufus was referred for radiation therapy. Trudy was told that nothing else could be done for Rufus and that his chances for survival past another 3–6 months would be all that she should expect. Trudy did not want radiation for Rufus and came in for a second opinion. Treatment with carboplatin and immunonutrition helped Rufus survive another 3 years.

Blue's Case (Episodic Epistaxis Forewarns Nasal Cancer)

Blue Monahan, F/S, an 11-year-old Aussie, had an episode of nasal bleeding. A CT scan and rhinoscopy with biopsy were negative. Three months later, Blue had a second episode of nasal bleeding. This time around, the CT scan and biopsy confirmed nasal chondrosarcoma. Blue was given essentially the same poor prognosis that Rufus (just discussed) had been given. The family asked me for a second opinion, which led me to recommend radiation therapy, carboplatin, and immunonutrition.

Suede's Case (Clients Don't Report Some Warning Signs)

Suede, a 9-year-old male Chocolate Labrador Retriever belonging to Susie Saddle, had a senior wellness “tumor watch” exam including chest and abdominal x-rays. The exam showed no signs of tumor activity. Two months later, Suede sneezed out a chunk of tissue. Susie took the mass to her local pet hospital to submit for pathology. Suede was diagnosed with SCC. It was at this point that Susie admitted that Suede had been sneezing for 5 months. She did not mention the sneezing or occasional epistaxis during Suede's wellness exam because she thought the sneezing was from allergies or inhaled weeds or dust. She admitted to not reading our brochure that describes the warning signs of cancer. Don't assume that your clients will take the time to read handouts or newsletters.

Instruct your room assistants to review the checklist of warning signs for cancer and illness during senior wellness exams and geriatric checkups (Table 3.2).

Warning Signs of Hypercalcemia

Malignant hypercalcemia is a paraneoplastic syndrome that is associated with some cases of lymphoma, anal sac carcinomas, and miscellaneous other tumors. PUPD and lethargy are early warning signs of this potentially fatal paraneoplastic syndrome.

Harley's Case (If a Lymphoma Dog Is Sick, Check the Calcium)

Dr. Harlan called to brief me about the Jones family and Harley, their M/N 8-year-old Boxer, with generalized lymphadenopathy. A fine needle aspirate confirmed the diagnosis as lymphoma. The Jones's were his favorite clients and would be calling to speak to me before making an appointment. When Mr. Jones called, he had the usual questions about prognosis with treatment. I asked him about Harley and sensed that Harley was not feeling well. He had a poor appetite and PUPD. He was not on any steroids.

I instructed the family to go immediately back to Dr. Harlan's office and have a serum calcium level check and chest radiographs. Sure enough, Harley had malignant hypercalcemia causing slight elevations of his renal values. He did not have an anterior mediastinal mass or symptoms of myasthenia gravis. Harley spent a few days in the hospital on fluids, diuretics, and steroids to resolve the hypercalcemia. He was feeling much better by the time we started

definitive chemotherapy. Most Boxers have T-cell lymphomas, which are more resistant to treatment and long-term survival (Lurie et al. 2004; Modiano and Helfand 2005). Harley is 24 months into his first complete remission as I write.

Warning Signs of Abdominal Masses

Geriatric dogs and cats are very deceiving as they develop indolent abdominal tumors. They may appear to be slowing down, or look as if they are gaining weight. Some pets show subtle reluctance or a change in behavior with lethargy. Others develop nausea, vomiting, weakness, straining, obstructions, diarrhea, hematochezia, lethargy, and so forth. Unfortunately, most abdominal masses are detected late in geriatric pets.

Warning Signs of GI Lymphoma in Cats

Although there has been a drop in FeLV-related lymphomas in cats, there is a rise in non-viral intestinal lymphoma with and without pre-existing inflammatory bowel disease (Louwerens, London, and Pederson 2005; Cotter 2005). Soft stools, diarrhea, and chronic weight loss in older cats are important warning signs to rule out GI lymphoma. These skinny old cats often have normal values in their blood work and normal x-rays on their workup. Intestines may feel ropey on palpation. Many of these cats do not have palpable masses in the abdomen. If there is no response to dietary management, further diagnostic tests are indicated.

Endoscopy and biopsy of inflamed and suspicious (cobble stone) looking lesions may establish the diagnosis of intestinal lymphoma. At times, the only way to get a definitive diagnosis is with exploratory surgery and full thickness tissue samples taken from several areas of the intestinal tract. For cats with abdominal masses, FNA cytology or Tru-cut needle core tissue samples may establish the diagnosis without subjecting the geriatric oncology patient to the stress of exploratory surgery (Figure 3.13).

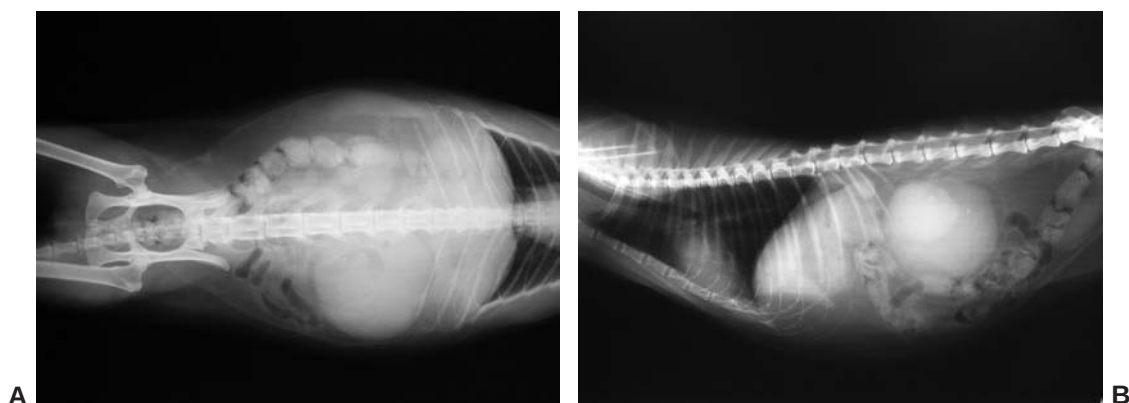


Figure 3.13. Radiographs showing renomegaly.

Warning Signs of Hepatic Tumors

Geriatric pets are more prone to develop hepatic neoplasia as they age. The warning signs are non-specific during the early stages but may include polydipsia, abdominal distension, nausea, anorexia, elevated liver enzymes, icterus, vomiting, pain, and lethargy. Obesity, hypothyroidism, and Cushing's disease are concurrent conditions that may camouflage the warning signs of hepatic tumors in geriatric pets.

Mitzie's Case (Elevated Liver Enzymes Are a Clue)

Mitzie, a 13-year-old F/S Beagle belonging to Roberta Karsch, had a history of colitis with acute episodes three to four times a year. Mitzie gradually developed an enlarged abdomen and drank more water as she aged. Her doctor considered Cushing's disease and ran all the tests. The liver enzymes were up but she was negative for Cushing's. Radiographs indicated a large hepatic mass or hepatomegaly. Abdominal ultrasound detected a 15 cm mass in the central caudal liver displacing her gallbladder caudal and to the left of midline. Roberta elected exploratory laparotomy. The surgeon performed a right liver lobectomy and gallbladder excision. The diagnosis was biliary adenocarcinoma. We treated Mitzie with chemotherapy for 4 months. She developed multifocal recurrence in her liver with elevations of her hepatic enzymes, ascites, and abdominal distension (Figure 3.14).

Alfie's Case (My Own Dog's Liver Cancer Was Insidious)

Alfie, my own 11½-year-old Australian Shepherd, showed some hesitation to go on his morning walk without his rimadyl. In retrospect, it was out of character for Alfie to stay on the floor during a car ride. He usually jumped on the seat to look out the window with Alaska, our



Figure 3.14. Mitzie Karsch, a 13-year-old F/S Beagle, had a right liver lobectomy and gallbladder excision for a 15 cm hepatic mass. The diagnosis was biliary adenocarcinoma. Early warning signs were masked by colitis, an overweight body condition, and Cushing's disease. Mitzie's abdomen distended again. MRI showed a large inoperable mass in parasagittal frontal lobes invading through the ethmoid plate.

Great Pyrenees. Alfie was alert, active, and still interested in food when my associate, Dr. Kathleen Carson, commented on him, saying Alfie looks “a little geriatric.” I examined him carefully and palpated a large, firm mass in his anterior abdomen. I could feel his ribs and realized that Alfie had mild muscle wasting from cancer cachexia.

From that moment forward, Alfie knew that I knew. He acted like the sick dog he truly was, dutifully enduring his workup with radiographs, ultrasound, and FNAs, which indicated a bizarre sarcoma. Exploratory celiotomy found metastatic lesions throughout the entire hepatic parenchyma, mesenteric nodes, gallbladder, and serosa. We had said our goodbyes to Alfie before he went under anesthesia. When the surgeon told us the malignancy was inoperable, we sent him scampering carefree over the rainbow bridge. The histologic diagnosis was a highly malignant undifferentiated carcinoma of unknown origin.

The Warning Signs of Splenic Tumors

German Shepherd Dogs, Golden Retrievers, and other large-breed dogs are prone to develop splenic tumors. Geriatric dogs show very few warning signs during the early indolent stages of splenic hemangiosarcoma. It is a very aggressive vascular cancer, which is thought to arise from CD34-positive stem cells (hemangioblasts) from bone marrow origin (Modiano and Helfand 2005). Pale mucous membranes, slowing down, hesitation to exercise, or distended abdomen may be signs of splenic hemangiosarcoma, but most dogs are diagnosed only after acute abdominal hemorrhage of a splenic mass.

It makes sense to screen all susceptible breeds over the age of 5. Proactive screening would include survey abdominal x-rays and/or ultrasound examinations every 6 months to check for splenic hemangiosarcoma. We may be able to extend the survival times in cases that are detected before splenic rupture. Very few dogs with splenic tumors are lucky enough to be diagnosed early. That situation may change with new tests to detect circulating hemangioblasts by sorting with flow cytometry. Soon you will be able to send 3 ml of anticoagulated blood for detection in dogs at risk and then suggest using a new endothelial vaccine (in clinical trials) that may help dogs survive this dreaded cancer.

Chloe's Case (Screen High-Risk Breeds; Surgery Is Best Before Splenic Rupture)

Chloe Foreman, a 12-year-old German Shepherd Dog, accompanied her pal, Max, for his final farewell after a 1-year battle with nasal chondrosarcoma. Mr. Foreman admits that he focused all his attention on Max's radiation therapy, recurrence, and overdue bills. He did not take Chloe for an exam when her coat turned dull; she lost weight and started itching. Right after Max was euthanized, Mr. Foreman asked the attending doctor to examine Chloe. He said, “The doctor's face turned white when she palpated Chloe's abdomen.” The doctor discovered a large mass in the area of the spleen. That day, Chloe had blood work, radiographs, ultrasound, and exploratory surgery. She was referred to our service for consultation and follow-up care. Mr. Foreman could not afford costly chemotherapy. He settled for vincristine, Cytoxan, piroxicam, doxycycline, and immunonutrition. Chloe gained back 15 pounds and her shiny coat. She is 16 months post-splenectomy as I write.

Marty's Case (Not All Bleeding Spleens Are a Death Sentence)

Marty Lloyd, a 19-year-old, 90-pound M/N Collie belonging to Gary Lloyd, presented with acute onset of weakness and pale mucous membranes. Abdominal radiographs and a four-quadrant abdominal tap indicated that this crisis was due to a bleeding tumor in his spleen. Ultrasound-guided FNA of a 6 × 6 cm cavitated splenic mass failed to confirm hemangiosarcoma on cytology. The mass was confined to Marty's spleen. Radiographs showing three views of the thorax were clear and his organ function panel was within normal limits. He had anemia (PCV 20%). We felt that Marty, despite his advanced age, would survive exploratory laparotomy and splenectomy because his performance assessment and body condition to this episode was excellent for a dog of 19 years. We told Gary that 80% of bleeding splenic tumors are malignant hemangiosarcomas or cancer of some type but that 20% are benign hematomas. If the bleeding was controlled with splenectomy and if Marty survived the post-operative period, there was an 80% chance that Marty would only have another 3–4 months to live.

Gary responded with an amazing look of relief and said, "Why wouldn't I want to do this? You are telling me that if you operate that he has a good chance to live 3–4 months and a 20% chance of living longer than that! Why would I not want to give him a chance?" Gary turned my grim statistics into his golden window of opportunity. Old Marty made it through the surgical procedure. He lived 3 more years, with the help of acupuncture and chiropractic, to the ripe old age of 22.

Chronic Hematuria Heralds Bladder or Prostate Cancer

Transitional cell carcinoma (TCC) of the bladder causes disturbance of urine flow and hematuria and mimics a urinary tract infection. Antibiotics often create an apparent improvement, masking symptoms, which can delay detection and diagnosis of this insidious cancer. Persistent hematuria should urge pursuit of the diagnosis with ultrasound and cystoscopy. A tumor antigen test (V-BTA Test, Bion Diagnostic Sciences, Redmond, WA) may help diagnose TCC in its early stages as a screening test. Unfortunately, hematuria causes false positives. Since hematuria is the chief symptom in TCC, the test is limited. Most labs will run the test but its application in hematuria cases may need to be interpreted alongside ultrasound or double contrast radiography that visualizes lesions.

Sacsha's Case (Persistent Hematuria Signals Bladder Cancer)

Sacsha Podowski, a 17-year-old Samoyed-Shepherd mix, was treated for three episodes of UTI and hematuria over an 18-month period. He was on soloxine for hypothyroidism and carprofen (rimadyl) for chronic arthritis. Abdominal ultrasound revealed a large mass along the left wall of the bladder. A urethral catheter was used to aspirate cells from the wall lesion for cytology. Sacsha was diagnosed with TCC. He responded to chemotherapy with mitoxantrone for a short period.

Winter's Case (Bladder Stones and UTI May Mask Bladder Cancer)

Winter Tobo, a 15-year-old M/N Cocker Spaniel who had been successfully cured of MCT 5 years previously, presented with a history of UTIs and chronic hematuria. The condition was

initially responsive to antibiotics, but recently, the hematuria persisted. Two large bladder stones were identified on plain radiography, which explained the hematuria. At cystotomy, the bladder mucosa appeared fleshy and abnormal. Tissue was submitted for biopsy, which diagnosed TCC. Winter's cystotomy incision dehiscenced and he was taken to an emergency clinic for care. Budget constraints forced the family to opt for euthanasia.

The Warning Signs of Colon Tumors

Colorectal neoplasia is associated with maldigestion, weight loss, hematochezia, tenesmus, diarrhea, abnormally shaped feces, and obstruction. Many geriatric patients are at advanced stages of disease when tumors become large enough to cause symptoms. One of my geriatric oncology patients exhibited sporadic hematochezia over 5 years before the family consented for a workup.

Lucky's Case (Tenesmus and Change in Stool Shape Warned of Cancer)

Joan Scheid noticed that her 14-year-old M/N Scottish Terrier mix, Lucky, was straining and that his stools were flattened or leaf shaped. A rectal exam was normal, but a barium enema found a solitary mass in the colon. Joan opted for exploratory laparotomy. The mass was removed with wide margins followed by anastomosis. The mass was diagnosed on histopathology as a leiomyosarcoma. The mass could have been intestinal adenocarcinoma or MCT but Lucky was indeed a lucky dog because this sarcoma is associated with long survival following excision. Lucky lived to be 17 years of age.

Warning Signs for Anal Sac Carcinoma

Anal sac tumors may become quite large before a dog exhibits symptoms due to the innate elasticity of the anal sphincter. Some tumors protrude and may be noticed at an early stage. Most grow alongside the distal rectum and may expand to 5–8 cm in large dogs before being noticed. Straining to defecate (tenesmus), bleeding, malodorous anal discharge, abnormal bowel movements, or stool drifting off to one side during elimination are all warning signs of anal or perianal tumors. Some dogs are not diagnosed until they have trouble defecating due to metastases and enlargement of the sublumbar/iliac nodes from the primary anal sac mass. These lymph nodes may expand enormously, placing firm pressure on the colon and causing tenesmus, change in the shape of the patient's stool, and ultimately obstruction.

Dealing with Geriatric Caregivers with Geriatric Pets

Veterinarians need to be especially careful when dealing with elderly pet owners and their geriatric oncology pets. They may have trouble remembering instructions and keeping things in order. Elderly people are also burdened with their own doctor visits and concurrent conditions such as arthritis, heart disease, diabetes, and hearing and vision deficits. We can't expect them to wrestle with their pet to give pills or be responsible for difficult home care procedures and wound care.

Lady, Jax, Prince, and Boy's Case (Screen All Geriatric Pets in the Same Household)

The Conners, an elderly couple, shared their lives with three cats and a dog that were all geriatrics. Lady, their beloved 13-year-old F/S DSH, developed a third recurrence of FVAS and was referred to our service. One year into Lady's treatment, Jax, their M/N 12-year-old DLH, started salivating. He was in too much pain to allow an oral exam. Under sedation, we found that a huge fleshy mass had completely obstructed his pharynx, making intubation impossible. We were amazed that Jax's problem had gone unnoticed in the Conner household for so long. Mr. Conner said that Jax had quit eating dry food a couple of months before. Somehow Jax had been able to swallow soft food without dysphagia, gagging, or pawing at his mouth.

A few months later, the Conners noted a large firm mass in the right axilla of their 12-year-old M/N Shepherd-Malamute, Prince. The mass was $8 \times 8 \times 8$ cm and diagnosed as sweat gland adenocarcinoma. Prince was a big, energetic dog and difficult for the elderly couple to manage for brushing, bathing, or walking. Mr. Conner did not see or feel the mass until it was obvious due to Prince's thick undercoat and hefty appearance.

At age 16, Lady (a 3-year FVAS survivor) started losing weight. Her appetite remained excellent. On physical exam, we palpated a small thyroid nodule and small tumors in her caudal left mammary glands measuring $1.5 \times 1 \times 1$ cm. Hyperthyroidism and mammary adenocarcinoma were diagnosed and treated. Six months later, Lady developed diarrhea and weight loss. GI lymphoma was diagnosed and treated. Lady succumbed to renal failure at age 17. A year later, Lady's son, Boy, developed loose stools and weight loss. He was diagnosed with GI lymphoma at age 17 and treated.

This scenario is not uncommon in households where human and pet are aging together. Mr. Conner was burdened with doctor visits and hospitalizations for Mrs. Conner's diabetes and heart condition. Veterinarians need to be proactive with elderly clients who have elderly pets. We can establish routine visits to carefully examine and screen their geriatric pets. Hopefully, we will identify problems, including cancer, at early stages.

Acute Warning Signs

Cancer creates acute symptoms due to its insidious indolent nature. Cancer can bypass prodromal signs and build momentum within the host. Some caregivers reported that the cancer figuratively burst out like the creature in the movie *Alien*. Acute signs are more than warning signs; they are often so obvious that they are direct indicators. Acute signs put attending doctors on high alert to strongly suspect cancer in their geriatric patients. Older patients admitted for acute collapse, seizures, dyspnea, obstruction, pathological fractures, blood dyscrasias, septic fevers, and low blood glucose should be worked up to rule out neoplasia.

Acute Collapse: May Be a Ruptured Abdominal Mass

A dog with a splenic or hepatic mass might be playing, then suddenly lie down and be unable to move. A dog with an insulinoma may have a seizure or collapse. A cat with spinal lymphoma may become paralyzed. A dog with a brain tumor or a cat a meningioma may have seizures. A dog with

a bleeding hemangiosarcoma of the right atrium may collapse due to cardiac tamponade and pericardial effusion. A geriatric oncology patient with coagulopathy may suddenly collapse.

Jinx's Case (It Can Happen at Your Clinic)

Jose, who worked at our clinic for 15 years, lifted Jinx, a 13-year-old M/N Old English Sheepdog, to place him in the bathing tub. Jose called out “code blue” because Jinx collapsed in the tub. Abdominal centesis and ultrasound led to the immediate clinical diagnosis of ruptured splenic hemangiosarcoma with metastatic foci in the liver. The family declined further care due to Jinx’s advanced age and poor prognosis.

Acute Dyspnea: May Indicate Thoracic Masses or Effusions

Anterior mediastinal masses (AMMs), especially in cats, are very insidious because they grow without much attention until they reach a critical mass. They cause pleural effusion and may cause esophageal obstruction. A cat with AMM may exhibit acute respiratory distress, tachypnea, and vomiting. A cat with anterior mediastinal lymphoma may have acute collapse after exercise. Geriatric oncology patients with occult disseminated disease may develop respiratory distress syndrome or acute systemic inflammatory response syndrome (SIRS).

Shelby's Case (She Died Suddenly without Complaint)

Shelby, an intact 8-year-old Rottweiler, had a decreased appetite and mild lethargy. The only abnormality on her database was thrombocytopenia. Abdominal ultrasound found metastatic cancer in her liver. On her first visit, Shelby jumped out of the car, walked into our office, collapsed, and died on the spot, releasing copious amounts of fluid from her lungs. We presume she had SIRS. Shelby’s family was in shock because she did not act like she was dying.

Acute Pathological Fracture: May Be Osteosarcoma

Many working breed dogs with osteosarcoma are able to hide their pain. The first warning sign that a pet caregiver may have to herald osteosarcoma may be an acute pathological fracture.

Ozzy's Case (Greyhounds with Osteosarcoma May Not Know It)

Ozzy Marquod, a 9-year-old M/N Greyhound, had a pathological fracture as the first warning sign of bone cancer for his family. Ozzy was jumping out of the car when he went suddenly lame. Radiographs identified the characteristic lesions for osteosarcoma of the left distal radius. Ozzy had an amputation and is receiving carboplatin chemotherapy and immunonutrition at this writing.

Noodles's Case (Indoor Cats Can Have Pathological Fractures)

Noodles Marcus, a 17½-year-old indoor Siamese cat, was found acutely limping on his left hind leg. Noodles had been diagnosed with advanced stage GI lymphoma 3 years previously. Noodles was considered one of our miracle cats because his cachexia was extreme, yet he regained

his weight on chemotherapy. All the while he had CRF. Mr. Marcus leaves the country often, so Noodles received maintenance chemotherapy sporadically. Radiographs identified a left tibial fracture with displacement and demineralization of the bone. The fracture was repaired with a plate and a biopsy was taken to rule out lymphoma. The histopathology report diagnosed osteosarcoma at the fracture site. Noodles recovered from surgery but his loose stools and cachexia returned due to recurrence of his GI lymphoma, which seemed to be exacerbated from the stress of surgery. We started Noodles back on chemotherapy but he did not do well and was lost to follow-up.

Acute Pain or Paresis: May Be from Spinal Cord Tumors

Acute onset of severe pain or paresis may be the first warning sign of a spinal cord tumor. Vertebral body masses or any primary or metastatic tumor that invades the spinal canal or impinges on the spinal cord may cause acute onset of pain and/or paresis. This type of compressive pain is very difficult to control with analgesics. Imaging is the best way to diagnose these lesions.

Seizures and Behavior Changes: May Be from Brain Tumors

Many brain tumors are not malignant but because they compete for space in the cranial vault, by their very nature, they kill the host. Many geriatric oncology patients with brain tumors are not diagnosed until a precipitating acute warning sign appears.

Amanda's Case (Meningiomas in Cats Grow Slowly to a Point)

Amanda, a F/S 17-year-old DSH, started howling around the house more frequently and during the day over a 6-month period. The symptoms seemed to abate with anti-anxiety medications. She became more aloof, which was attributed to the medication. Then 1 day she started circling to the left. Magnetic resonance imaging (MRI) found a large mass consistent with a meningioma in the left posterior fossa/cerebellopontine angle. The mass explained Amanda's behavior changes.

Misty's Case (Something Was Wrong for 6 Months)

Misty D'Amico, a 13-year-old F/S West Highland White Terrier, was in and out of the hospital for 6 months with general complaints about weak rear legs, chronic UTIs, hypothyroidism, ear infections, chronic gagging, lethargy, occasional loss of balance, and a dwindling appetite. One night Misty had a massive seizure and was rushed to the emergency room. An MRI found a large inoperable mass in her parasagittal frontal lobes that had invaded through the ethmoid plate (Figure 3.15).

Painful Maxillary Swelling: May Indicate Oral Cancer

Cats have variable early warning signs for oral cancer such as ocular discharge, pawing at the mouth, loose teeth, and halitosis. However, they are often not diagnosed until the caregiver notices a swelling either in the mandible or maxilla.



Figure 3.15. Misty, a 13-year-old F/S West Highland White Terrier, had vague prodromal warning signs for 6 months prior to diagnosis.

Shandi's Case (Ocular Discharge and Pawing at Her Mouth Were Her Warning Signs)

Shandi Payner, a 14-year-old DSH calico cat, had early warning signs of a “runny eye” and occasional pawing at her mouth on the right side. She quit eating dry food. When she had overt dysphagia, the family took her to their veterinarian for an exam. A firm swelling of her right maxilla was discovered (Figure 3.16). The family elected to place a feeding tube when Shandi could no longer eat but declined conventional therapy due to the poor prognosis.

Scrappy's Case (Sudden Enlargement of the Mandible Can Signal SCC)

Scrappy Irvine, a 12-year-old M/N DSH, suddenly developed a firm swelling on the rostral mandible. The family was familiar with our warning signs of cancer brochure because their family dog, Ebony, a 10-year-old Blue Heeler cross, was successfully treated for splenic hemangiosarcoma during the previous 18 months. They called immediately requesting tests and treatment for Scrappy. Biopsy of the mass verified SCC. They elected mandibulectomy, feeding tube placement, and follow-up radiation therapy to the surgical site and neck nodes. Scrappy had 3 follow-up chemotherapy treatments with carboplatin. Scrappy had no recurrence of oral SCC during a 5-year follow-up.

Paraneoplastic Syndromes

Paraneoplastic syndromes (PNSs) are plentiful in geriatric cancer patients. Older animals may bypass the prodromal warning signs of cancer and exhibit a PNS, which is secondary cancer, as their first warning sign. A good working definition for PNS is: An aberration of physiology, function, or structure that is mediated by the production or the release of chemicals, hormones, or hormone-like molecules or cytokines that exert an effect that is distant from and unrelated to the size or mass of a primary tumor. Older pets are commonly rushed to emergency rooms due to acute onset of severe

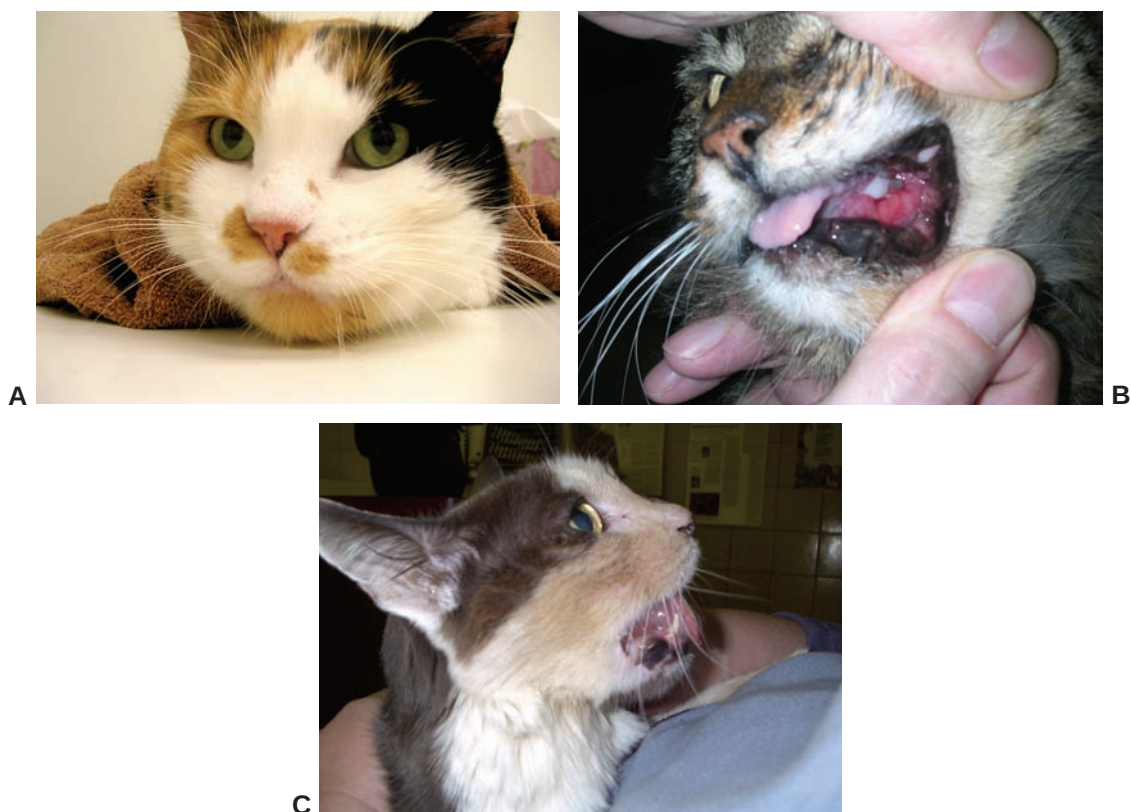


Figure 3.16. Oral tumors are generally discovered late in cats. Shandi Payner had an ocular discharge, increased salivation (a), and dental extractions prior to the diagnosis of SCC of her right maxilla. Oral SCC in the left mandible (b) and sublingual area (c) in an older cat.

PNS symptoms, which evoke the emergency room clinician (criticalist) or attending doctors to pursue the diagnosis of cancer as the primary problem.

PNSs have some of the longest names in medical terminology with prefixes of “hypo” and “hyper” followed by “inemias” (e.g., hyperheparinemia, hyperinsulinemia, hypergammaglobulinemia). The syndromes affect multiple sites and systems and have variable morbidity. These aberrant conditions torment the geriatric cancer patient with adverse metabolic changes and hormonal imbalances. Geriatric patients are often subdued and less active, which can divert the discovery of a metabolic imbalance until the patient is in advanced crisis.

A host of cytokines and endocrine substances have been discovered in the past 4 decades in the study of cellular metabolism (metabolomics). These “new players” are produced or over-expressed by neoplastic cell clones originating from organs and tissues. Many of these cellular products were unheard of when half of our profession attended veterinary school. A cadre of interleukins, interferons, prostaglandins, enzymes, and co-factors regulate intracellular and extracellular functions and cell surface signaling. Any one of these proteins may be overproduced (over-expressed) by neoplastic transformation of their progenitor cells. As researchers gain more understanding of the intricate chemistry of cellular metabolism and cancer, we may be able to exploit their underlying mechanisms as therapeutic targets (Hahn 2005).

Any malignancy that originates in or affects the bone marrow and its hematopoietic stem cells may induce a PNS. The most common hematologic effects from malignancy are anemia of chronic disease followed by blood loss anemia, microangiopathic anemia (common in hemangiosarcoma), and immune-mediated hemolytic anemia. Thrombocytopenia and coagulation disorders are also common. Hyperestrogenism from Sertoli cell tumors, Interstitial (Leydig) cell tumors of the testes of older dogs, and ovarian tumors may induce hypoplastic anemia, leucopenia, and thrombocytopenia. Degranulating mast cell tumors release heparin (hyperheparinemia) and may induce petechiation, ecchymosis, and hemorrhage due to PNS coagulopathies. FeLV and FIV retroviral infection exert effects in the bone marrow tissue of cats resulting in immunosuppression, anemia, leukopenia, pancytopenia, leukemias, and lymphomas that can produce any number of PNSs.

The dramatic effects seen with PNSs often create life-threatening complications for the already compromised geriatric oncology patient. Renal failure and heart failure can be sequelae from severe malignant hypercalcemia. But if the geriatric oncology patient has pre-existing CRF and/or heart disease, the patient is impacted more heavily by the PNS and the window of opportunity to respond is diminished. Insulinomas cause hypoglycemia, inducing seizures, weakness, and coma. PNS-related epistaxis may occur in a geriatric dog due to hyperviscosity syndrome resulting from immunoglobulin production from malignant plasma cells in multiple myeloma. Hemangiosarcoma induces fatigue and acute collapse due to chronic anemia, acute blood loss anemia, immune mediated anemia, and coagulopathies. Gastrointestinal ulceration is commonly found in mast cell cancer patients due to hyperhistaminemia or due to hypergastrinemia in patients with gastrinoma. Any one of these PNSs is an urgent care challenge that requires intense supportive care with 24 hour per day management.

Cancer cachexia, anemia, fever, and hypoproteinemia are commonly encountered in geriatric oncology patients. Hypercalcemia, GI ulceration, protein-losing enteropathy (GI lymphoma in cats), and hypoglycemia are commonly seen syndromes. Glomerulonephritis and neurologic problems, hyperestrogenism, hypertrophic osteopathy, and hypergammaglobulinemia are also frequently encountered. Many problems that parallel the symptoms of PNS are actually iatrogenic, due to perioperative complications or to adverse effects related to chemotherapy or radiation therapy. It is up to the attending clinician to establish the cause of the paraneoplastic condition.

Endocrine PNS

Most endocrinopathies in geriatric pets are oncologic in nature. Feline hyperthyroidism and hyperadrenocorticism or Cushing's disease, by definition, fit the PNS category. Thyroid tumors cause distant effects on the function and condition of the heart and kidneys in feline hyperthyroidism. Either primary cause (pituitary tumor or adrenal tumor) in Cushing's disease is essentially neoplastic in nature. Feline hyperthyroidism and hyperadrenocorticism may be among the most common PNSs seen in geriatric pets.

Endocrine-Like PNS

In addition to hypercalcemia of malignancy (HM), veterinarians may encounter other endocrine-like PNSs. Any malignancy that originates from an endocrine organ or tissue that upregulates the production of a product of an endocrine organ may induce a PNS. Pancreatic tumors produce a variety of biologically active hormones that adversely affect the geriatric oncology patient.

Insulinomas are pancreatic beta-islet cell tumors that secrete insulin, causing elevated levels, which cause hypoglycemia and are manifested by the patient as weakness, ataxia, seizures, and coma. PNS hypoglycemia may also be caused by disturbances of other metabolic pathways by non-islet cell tumor functions or products such as insulin-like growth factors.

Gastrinomas are non-islet cell pancreatic tumors that secrete gastrin, which causes gastroduodenal ulcers, blood loss, vomiting, and pain. This PNS is known as the Zollinger-Ellison syndrome in human medicine. Increased epinephrine and norepinephrine from pheochromocytoma (adrenal gland neoplasia) causes PNS hypertension, restlessness, and related disorders.

It is up to the diagnostic acumen of the clinician and good laboratory support to feather out the various causes of any one of the panoply of PNSs that can potentially affect aging companion animals.

Hematologic PNS

PNSs are commonly manifested as hematologic abnormalities, such as anemia, monoclonal gammopathies, thrombocytopenia, thrombocytosis, platelet dysfunction, hypoproteinemia, coagulopathies, and disseminated intravascular coagulation (DIC). These PNSs are most often associated with hemangiosarcoma in older dogs. Overproduction of red blood cells (erythrocytosis) and neutrophils (leukemoid reaction or neutrophilic leukocytosis) and eosinophils can be due to excess secretion of stimulatory glycoproteins and cytokines from tumor cell clones.

Dermal PNS

The skin is a target organ that may reflect distant effects from primary tumors. Some cutaneous PNSs have been described in animals such as alopecia, cutaneous flushing, necrolytic migratory erythema, nodular dermatofibrosis and ischemic necrosis of the hind digits, pemphigus vulgaris, and pruritis. We should also include calcinosis cutis and feminization and virilization syndrome in this category. There are certainly other cutaneous manifestations of neoplasia that are yet to be reported.

Some PNSs are manifested as abnormalities in the skin, such as nodular dermatofibrosis on the legs of Shepherd breed dogs with renal cystadenocarcinoma, vasodilation, and cutaneous flushing from adrenal tumors or mast cell degranulation and release of vasoactive substances such as histamine and heparin. Pancreatic alpha cell clones can secrete glucagon and cause erosive blisters (necrolytic migratory erythema). Older cats may develop ventral alopecia and painful footpad disease from biliary and metastatic pancreatic carcinomas in the liver.

Simply put, PNSs are disorders that accompany or precede the diagnosis of certain malignancies. Encountering one of these varied disorders may be the pet owner's first warning sign and your initial clue to work up the geriatric patient for cancer. The most dramatic PNS is HM. It is generally associated with T-cell lymphoma and various adenocarcinomas, most notably, anal sac apocrine adenocarcinoma. Older dogs may develop other endocrine-like PNSs such as hyperadrenocorticism from pituitary adenomas, adrenal tumors, or, rarely, primary lung tumors. Older dogs may develop hypoglycemia, which is most commonly caused by insulinoma. Other common PNSs are anorexia, cachexia, protein-losing enteropathy, fever, and pain.

Of the many PNSs, several merit description and more attention to help familiarize you with the most important features of these baffling syndromes.

Anorexia and Hepatic Lipidosis

Cancer-related anorexia and hepatic lipidosis are common problems in feline geriatric oncology patients. The condition may persist on a long-term basis and become the overriding cause of death. When owners encounter a change in eating behavior, we should consider it a red flag for anorexia. Anorectic cats may approach the dish, stare at the food, and then back off, appearing to be nause-

ated. Some gag. Some cats will make a grinding sound with their mouth as if they have temporomandibular joint disease. I associate this grinding sound with a poor long-term prognosis. In my experience, it appears in cats with weight loss, poor hydration, and one of the viral infections, FeLV, feline infectious peritonitis (FIP), or FIV.

Thoughts on Feline Anorexia

Scholars have long wondered about the odd, aloof psyche of the anorectic feline. One viable theory can be found in the April 15, 1999, *JAVMA*, where Dr. Frank McMillan comprehensively reviews the vast data about how stress causes neuropeptides (“negative endorphins”) to form in the body, which negatively affects emotions and health. Cats are very “oral”-based animals. They seem to enjoy using their tongues to clean themselves and they socially enjoy licking others. It is easy to conclude that gingivitis, stomatitis, or any illness (especially oral and GI neoplasia) would cause pain and stress in cats and a “negative neuropeptide” flood resulting in loss of appetite. It is obvious that other factors such as mood, texture, smell, or change of food also alter the mental states that influence a cat’s appetite.

Because cats are independent and do not pant, their oral tumors are usually discovered in advanced stages. Geriatric cats with lingual tumors seem more demoralized than cats with tumors located in the dental arcades and the hard palate. The prognosis for long-term survival in cats with oral tumors is generally poor, especially with lingual SCC.

The first positive article on the subject of mandibulectomy in cats came from our oncology practice (Hutson et al. 1992). It reported on a series of seven cats that had mandibulectomy followed by radiation therapy for SCC of the mandible. This small series of cats had prolonged tumor-free intervals, and this report is referred to as an encouraging reference article. Our cats did well because they all had feeding tubes placed at the time of their mandibulectomy. They did not lose weight because we kept them in a positive nutritional status despite the predictable loss of appetite during the course of therapy. The esophageal feeding tubes remained in place well after completion of radiation therapy.

Treatment for Anorectic Cats: The Feeding Tube

An essential facet of treatment for geriatric cancer cats with hepatic lipidosis and anorexia would be feeding tube placement. Old malnourished cats with CRF need feeding tube placement when they are unable to consume enough calories to maintain a positive energy balance. It is best to recommend placing a feeding tube in any old cat with a history of unresponsive anorexia and cachexia. When planning cancer treatments that would initiate the recurrence of anorexia or stress the already anorectic geriatric cancer cat, a feeding tube should be considered as standard supportive care. At any given time, we have approximately half a dozen cats in Pawspice care that need feeding tubes.

Missy’s Case (Offset Anticipated Anorexia)

Missy, a geriatric feline, refused to eat for 2 weeks following mastectomy for mammary adenocarcinoma. Missy needed a second chain mastectomy for breast cancer management. I recommended that a feeding tube be placed as a prophylactic measure. This precaution was not only important to the success of the surgery but was also a factor in the family’s decision to have the second surgery done.

Oral medications such as Xanax[®] (1.5 mg per day) and ciproheptidine (2 mg twice daily) can stimulate the appetite and are often helpful. An IV injection of diazepam (1.5 mg) may arouse a cat's appetite for 30 minutes, but it is troublesome to repeat frequently. There are ways to coax a cat to eat. Petting the cat, putting food on the paws or on the nose, and warming food to room temperature to release aroma may help. Because cats love the ritual of eating, dramatizing the preparation and sounds (the can opener) of serving the food often spark interest.

Cats don't particularly love the way mice taste, but they do love to chase moving things and play. Maria Peterson of Santa Monica, CA, found that tossing food (chase) or tying it to a string (play) will often prompt an anorectic cat to start eating again. Offering different flavors of food, especially fresh shrimp and salmon, may spark an anorectic geriatric cat's appetite.

Assess hydration in front of the cat's owners and show them how to monitor it by stretching then releasing the skin to see if it springs back. Many anorectic cats go home with bags of fluids and vitamins for subcutaneous injection by their owners.

Before sending the client home with a geriatric cat that needs medicating and home care, always make it a point to clearly demonstrate the proper method of giving pills, liquids, vitamins, capsules, and especially SQ fluids. It is easy for the veterinary staff to administer SQ fluids and force feedings, but often impossible for the caregiver to muster up the courage to use a needle or force-feed their sweet, independent-minded, stubborn feline. With detailed preparative coaching, most clients feel that they have made a real "breakthrough" when they master the technique and gain the skill.

Teach clients several ways to force (hand) feed their geriatric cat. Opening a cat's mouth can be difficult, but with skillful instruction, most pet owners are willing and able to hand feed if necessary. Patrick Strong of Los Angeles used hand feedings for his 16 ½-year-old M/N cat, Montgomery, following splenectomy for mast cell infiltration. Montgomery enjoyed an excellent quality of life until age 21. Gene Behrman of Manhattan Beach, CA, kept Biggs, his 16-year-old M/N cat with CRF, on daily SQ fluids until age 22.

Some caregivers are willing to hand feed their cat but the cat will not accept it. This causes great stress to the family and it obligates the attending doctor to solve the problem. If a cat is losing weight rapidly, we strongly and enthusiastically suggest a feeding tube as the best solution to this problem. The placement of a feeding tube is widely accepted as a necessary step for resolving hepatic lipidosi. Encourage feeding tube placement as routine supportive care for all stubborn cases of feline anorexia. It should not make a difference if the reason a cat won't eat is terminal or temporary. Providing good nutritional support is imperative on a daily basis.

Esophagostomy feeding tubes are the most commonly utilized method for tube feeding anorectic cats. Nasal feeding tubes are utilized on a temporary basis but are too cumbersome and easily removed by the patient. We used to place gastric feeding peg tubes via endoscopy at surgery. Since the more practical technique for placement of an esophageal feeding tube was described, we use it almost exclusively (Ogilvie and Moore 2001).

Once the esophageal feeding tube is in place, the nightmare of force-feeding an unwilling cat is over. Recommend a healthy liquid diet designed to meet the feline patient's specific nutritional needs. It can be fed along with pulverized medications through the tube. Pet owners truly appreciate the opportunity to provide proper nutrition to their geriatric cats without the angst that force-feeding entails. In fact, caregivers may become dependent on the feeding tube. They may feel fearful and frustrated if the feeding tube accidentally comes out. In this case, simply comfort the client and replace the tube if the patient still needs it. Once the feeding tube is removed, the caregivers have to resume the work of directly administering medications over the objections of their cat.

Cancer Cachexia, an Insidious PNS

Prior to the clinical detection of cancer, many geriatric animals lose body condition and drop weight. Companion animals with cancer cachexia are in a hypermetabolic state, which causes involuntary weight loss. This insidious process occurs while the pet may still maintain a good appetite, attitude, and activity level. For a time, the geriatric oncology patient may be able to fool the best and most highly bonded caregivers. Weight loss starts to become obvious when 6–10% of the pet's normal weight has been lost. Some people explain away their elder pet's weight loss with the rationale that this is just part of the aging process. In reality, their pet is wasting away before their eyes (Figure 3.17a).

In some cases, cancer cachexia is the only visible warning sign of illness or neoplasia. The mechanism for this profound involuntary weight loss is still not fully understood. Some scientists feel that the mechanism of cancer cachexia is put into action due to abnormalities in carbohydrate, protein and lipid metabolism, and cytokine dysregulation (Figure 3.17b).



Figure 3.17. Cancer cachexia: Weight loss becomes obvious when 6–10% of the pet's normal weight is lost. Some people feel their elder pet's weight loss is part of the aging process.

Metabolic Abnormalities in Cancer Cachexia

Cancer cells metabolize glucose differently than normal cells. The end product of the abnormal cell's anaerobic glycolysis is lactic acid. It requires energy from the body to convert the lactate back into glucose. In addition to this metabolic disturbance in carbohydrate metabolism, cancer patients have abnormal glucose formation, disposal, oxidation, and turnover. Cancer patients have been shown to have elevated insulin levels and exhibit more insulin resistance than normal. If the geriatric oncology patient is overweight or has diabetes or Cushing's disease, insulin resistance may be compounded.

Cancer patients have lower levels of amino acids and high-density lipoproteins (HDL) and high levels of low-density triglycerides, resulting in disturbances of protein and lipid metabolism. Some cancer cells can't access fat as an energy source. This situation has opened the door to the concept of starving the cancer and feeding the patient as a nutritional approach to managing the cancer patient.

Along with the metabolic abnormalities of cancer cachexia, the cancer patient experiences immune system suppression and extreme physiologic stress. After several months of weight loss, the debilitated pet may start to exhibit signs such as decreased exercise tolerance, GI disturbances, or lethargy. This behavior is what most often prompts a visit to the veterinarian. Decline in the condition of pets with cancer cachexia may leave the animal in such a state of debilitation and dehydration that attempts to help them surgically or medically may be fraught with complications.

The oncologist and the referring doctor must determine if the pet is capable of surviving suggested procedures and protocols that are generally used to diagnose and treat the cancer. Unfortunately, despite the removal of the primary tumor or the achievement of remission in lymphoma via chemotherapy, the metabolic abnormalities of cancer cachexia persist. It is unsafe to deliver cancer therapy to debilitated geriatric oncology patients. We must first restore them to a metabolically balanced state of hydration and nutrition. Encourage the pet owner to rehabilitate his or her pet at home whenever possible with quality nutrition and supplements so the pet will be able to better tolerate the treatment modalities selected to battle the cancer.

When cancer cachexia is identified, many caregivers are shocked that their companion pet has lost so much weight. They feel cheated that the cancer was so insidious. This very situation happened in my own household. My 11½-year-old Australian Shepherd, Alfie, developed cancer cachexia without me noticing it. His case was described earlier.

Weight Loss: An Insidious Warning Sign of Cancer

Soft stools, diarrhea, and chronic weight loss in older cats are important warning signs to rule out GI lymphoma. Cachectic cats often have normal values in their blood work and normal radiographs for their preliminary workup. The intestines may feel ropey on palpation. Many cases do not have masses in the abdomen. If there is no response to dietary management, further diagnostic tests are indicated. Endoscopy with biopsy of inflamed and suspicious (cobble stone) looking gut lesions may establish the diagnosis of intestinal lymphoma. At times, the only way to get a definitive diagnosis is with exploratory surgery with full thickness tissue samples taken from several areas of the intestinal tract. For cats with abdominal masses, FNA cytology or Tru-cut tissue sample may establish the diagnosis without subjecting the patient to the stress of surgery.

How Cancer Causes Anemia

As cancer cells gain momentum in the body they acquire the physical ability and the cellular mechanisms that cause various types of anemias. This makes anemia one of the most common paraneoplastic syndromes encountered in practice. Up to one in four pets with cancer may have an associated

anemia. Since geriatric dogs and cats frequently have concurrent illnesses, such as hypothyroidism, CRF, or chronic active hepatitis (CAH), they may not have the regenerative abilities needed to deal with their anemia. Anemia is more common and may be profound in dogs with hemangiosarcoma and Sertoli cell tumor due to estrogen suppression of the bone marrow. Anemia is found in cats infected with FeLV and FIV. It may accompany the diagnosis of lymphoma especially if they have advanced renal lymphoma. Any animal with myeloproliferative disease will also have anemia due to myelophthetic crowding of the bone marrow. Anemia may appear with any type of cancer. The types of anemia most commonly encountered with oncology patients are described as follows:

1. Anemia of chronic disease (ACD) exhibits normochromic, normocytic red cells.
2. Blood loss anemia (BLA) exhibits hypochromic, microcytic red blood cells.
3. Microangiopathic hemolytic anemia (MAHA) exhibits schistocytosis (shearing of red blood cells [RBCs]) and hemolysis often due to disseminated intravascular coagulation (DIC).
4. Immune mediated hemolytic anemia (IMHA) exhibits spherocytosis, hemolysis, and regeneration of RBCs with elevated reticulocytes. The tumor releases tumor-associated antigens that prompt the immune system to react to and destroy its own RBCs. Consequently, the victimized RBCs are fragile and undergo hemolysis.

The mechanisms that result in anemia may be intertwined with one another to complicate matters for the geriatric oncology patient and the clinician. Dogs with hemangiosarcoma often experience BLA due to acute rupture of a splenic mass and hemoabdomen. Yet the dog may have been “slowing down” for several weeks while the tumor caused MAHA and low-grade DIC. Circulating RBCs and platelets get fragmented as they bump into strands of fibrin that clog the tiny abnormal blood vessels and microvasculature that compose the matrix of the tumor. Fibrin strands also form in small capillary vessels when animals develop DIC, further pushing the intravascular injury and destruction of red cells.

5. Myelophthetic anemia (MA) results when the bone marrow is invaded with cancer cells. The normal precursor cells for erythropoiesis are crowded out with pressure from the neoplastic cells. This type of anemia is often associated with the leukemias and it may be complicated with ACD. Myelophthetic anemia, as a paraneoplastic anemia, may also be caused by other yet-to-be-described cytokines. There may be other functions and other inhibitors of growth factors produced by malignant cells that have the power to dysregulate the function of normal bone marrow cells.
6. Bone marrow hypoplasia (BMH) is found in dogs with Sertoli cell tumor due to the hypersecretion of estrogen, which is suppressive to RBC formation in the bone marrow. This condition is likely to occur in senior cryptorchid dogs (most commonly reported in German Shepherd Dogs) that have not been surgically explored for removal of their retained testicle(s). Prevention for this type of BMH in any case would be early neutering.
7. Hypersplenism causes anemia with an exaggerated hemolytic function that clears RBCs from the circulation.
8. Erythrophagocytosis can also cause anemia. It occurs due to an aberration of phagocytic macrophages found in malignant and systemic histiocytosis of Bernese Mountain Dogs and malignant fibrous histiocytoma of the spleen.
9. Iatrogenic anemia may result from chemotherapeutic suppression of blood precursor cells in the bone marrow. Aging is associated with a reduced stem cell reserve, which makes the geriatric oncology patient more susceptible to chemotherapy-related anemia. The anemia is slowly progressive with long-term chemotherapy and may cause the hematocrit to be as low as 20 as opposed to a normal low of 37. Chemotherapy-induced anemia is an expected side effect in treating people

because higher doses are used. The dose range and frequency of veterinary chemotherapy protocols is generally lower than that used for humans and therefore not injurious to the animal's bone marrow. The anemia caused by veterinary chemotherapy does not become a clinically significant issue. The offending drug should be suspended, reduced, or given less frequently if the anemia becomes a problem. Erythropoietin may help boost the hematocrit in cases where we cannot safely discontinue chemotherapy (such as resistant lymphomas).

Treatment for Paraneoplastic Anemias

Geriatric pets often have chronic borderline anemia due to stem cell depletion, lack of regenerative responses, myelofibrosis, diminished reserve, and physiologic stress.

Treatment of the geriatric oncology patient for the any of the paraneoplastic anemias just described should be aimed at correcting the anemia while targeting the primary tumor with surgical intervention or chemotherapeutic control. Transfusions or the use of Biopure® (an oxygen carrying solution) may be necessary as a rescue measure in cases with life-threatening blood loss and myelophthetic and hypoplastic anemias (Hale 2005).

Erythropoietin (Epogen®) is a glycoprotein growth hormone secreted by the kidney, which acts on stem cells of the bone marrow to stimulate RBC production. Recombinant DNA technology allows erythropoietin to be commercially available for use in the treatment of anemia. It is of great value in cases that are responsive. Antibody formation is a problem in both dogs and cats. New erythropoietin products made specifically for dogs or cats or both may become available. Ideally, it would be great to have a megakaryocyte-stimulating factor but as of this writing, there is no product on the market.

It is wise to advise caregivers to feed small amounts of highly digestible food at 1–2 hour intervals to their severely anemic pets to keep their blood flow from diverting to meet the demands for digestion of a large meal.

Noche's Case (Anemia Reduces Tolerance to Pre-existing Airway Disease)

Noche Holbrach, a 14-year-old F/S Lab mix, was being treated for resistant small cell lymphoma. She developed chronic anemia presumably from chemotherapy. Noche had concurrent chronic obstructive airway disease that caused hypoxic episodes when she was excited. The anemia lowered her threshold of endurance during these respiratory distress episodes. We used epogen to stabilize Noche's hematocrit. The anemia resolved when we increased the interval between treatments during her remissions. It recurred when she needed chemotherapy dose escalation to treat her lymphoma as she developed resistance.

Frisco's Case (Limb Sarcomas Can Induce PNS)

Frisco Antonelli, a 12-year-old male Yellow Lab, was limping for 10 days by the time Ms. Antonelli felt that he was in pain. She suspected a muscle pull. Frisco's doctor found a soft tissue swelling in the left thigh. Radiographs found no bone involvement. Frisco was sent home on etogesic 300 mg as needed with the plan to rule out trauma, lipoma, or neoplasia. Two weeks later, Frisco started whining and limping again. A biopsy of the mass was scheduled for several days later.

On the day of anesthesia, an in-house PCV was 34% and a panel was sent to an outside lab. Chest radiographs showed a possible metastatic lesion in the left caudal lung lobe. Five to six

tissue samples were taken. The tissue appeared to be blood clots but were surgically taken and submitted for histopathology. The following day, the panel reported low hemoglobin of 10.8 g/dl and a low hematocrit of 32% with nucleated RBCs of 9% along with 4 comments: polychromasia +2, macrocytosis +1, hypochromasia +1, and anisocytosis +2. The pathology report was inconclusive.

Ten days after the procedure, Frisco was referred to a surgical specialty clinic for another surgical biopsy. During the pre-anesthetic workup, chest radiographs demonstrated progressive metastatic disease. Frisco was referred to an oncologist who suggested a repeat biopsy procedure, palliative radiation therapy, or euthanasia. He was given a prescription for Tramadol® 50 mg BID for pain and Tussigon® 5 mg 1–2 tablets BID or TID as needed for coughing. The family was referred to our service for emotional support for themselves and Pawspice care for Frisco.

We made the presumptive diagnosis that we were working with an aggressive soft tissue sarcoma such as hemangiosarcoma. This would explain the coagulation disorder, the metastases, and the anemia. We gave the family information on hemangiosarcoma and explained the biological behavior of this relentless cancer and entered Frisco into Pawspice care. A week later, Frisco was doing much better clinically, although he remained anemic. Three weeks later, his hematocrit dropped to 18% and his platelet count was 80,000. We explained that the anemia and thrombocytopenia were from internal blood loss, a myelophthesic effect of the cancer and/or immune mediated pathways. The family declined a blood transfusion or Biopure. We advised strict rest for Frisco. He did very well for 2 more days. He ate a big breakfast on the third day and slowed down during the day and declined his dinner. Late that evening Frisco became dyspneic and weaker. That is when the family called me for advice. We decided to let him pass away in his loving home. Ms. Antonelli brought me yellow roses. They are blooming their hearts out on my deck today, reminding me of Frisco as I write.

Malignant Hypercalcemia

Hypercalcemia of malignancy is a very distinctive and one of the most urgent paraneoplastic syndromes. Unfortunately, geriatric oncology patients with concurrent diseases, such as Cushing's disease, CRF, or hepatic disease may already be polydipsic and have polyuria. Paraneoplastic syndromes are aberrations of function or structure associated with cancer that are not related to the actual mass itself. Dogs and, less often, cats may develop classic malignant hypercalcemia associated with, first and foremost, lymphoma and then a host of other tumors, most notably apocrine gland anal sac adenocarcinoma, multiple myeloma, thymoma, thyroid carcinoma, bone tumors, squamous cell carcinoma, mammary gland carcinoma, and, of course, primary parathyroid tumors.

Certain clones of cancer cells produce a parathormone (PTH) like hormone PTH-rp (related peptide). It parallels PTH secreted by the normal parathyroid gland with related gene sequences identical to real PTH. PTH-rp pulls calcium from the bones and causes electrolyte and metabolic havoc and can precipitate renal failure in the geriatric cancer patient.

The clinical signs are polydipsia and polyuria with an inability to concentrate urine followed by lethargy, vomiting, dehydration, bradycardia, hypertension, weakness, constipation, depression, and, in severe cases, stupor, coma, and seizures. Whenever the calcium level is near or greater than 18 mg/dl,

the case must be considered a medical emergency as the kidneys undergo life-threatening vasoconstriction. With such reduced blood flow through the kidneys, the glomerular filtration rate (GFR) drops and cellular degeneration and calcification set in.

Workup and Treatment of HM

HM patients may be so sick that emergency fluid therapy (0.9% saline diuresis) must first be given for stabilization *before* the cancer can be treated. It is tempting to use steroids immediately because steroids reduce HM by inhibiting prostaglandins, osteoclastic activity, and calcium uptake. In order to establish a diagnosis and determine the underlying cause, it is important to do a rectal exam, harvest samples of enlarged lymph nodes, and take x-rays of chest and abdomen to rule out a thymic or abdominal mass *before* the administration of steroids. If no evidence of cancer is found on this initial assessment, it is wise to do a bone marrow aspiration and FNA of the liver and spleen. Use a 1½-inch 27-gauge needle for FNA. If the cytology is negative, proceed with abdominal ultrasound in pursuit of a definitive diagnosis and then proceed with corticosteroids.

Steroids will obscure the diagnosis of lymphoma. Steroids have a direct cytotoxic effect on lymphoblasts, causing the cell surface membrane to become more fragile. The cells undergo lysis and appear as non-diagnostic cellular debris on the FNA cytology slides. If the lymphoblasts are in cytotoxic lysis, they may not be diagnostic on cytology or on histopathology slides. It is possible to run immunocytochemistry or immunohistochemical stains on the intercellular debris present on FNA cytology samples and non-diagnostic tissue samples. For example, the presence of positive staining for CD79a and negative staining for CD3 protein markers in the cell debris would suggest a B-cell immunophenotype of the lymphoma.

The best plan of action is to gather all FNA slides and Tru-cut biopsy samples during the initial hours that the pet is in the hospital on IV fluid therapy. Use saline diuresis to rehydrate the patient and increase the GFR. Once the patient is rehydrated, it is safe to follow with furosemide at 1–4 mg/kg at 8–24 hour intervals to directly inhibit further calcium absorption. Use prednisone orally at 1 mg/kg once or twice daily. Treat the primary tumor with chemotherapy or surgery as quickly as possible while maintaining diuresis and monitoring renal and cardiac function. Induction chemotherapy protocols for lymphoma and more detailed treatment for refractory HM are covered in many texts.

Generally speaking, hypercalcemic lymphoma patients have more trouble maintaining prolonged remissions and survival, especially if they also exhibited an anterior mediastinal mass. Most of the hypercalcemic lymphomas are of the T-cell phenotype. Unfortunately, T-cell lymphomas are generally more resistant to chemotherapy treatment than the B-cell phenotype lymphomas. This holds true in both dogs and cats.

JR's Case (Perianal Anal Tumors Go Unobserved for a Long Time)

JR Radke, a 13-year-old F/S German Shepherd Dog mix, was referred with a history of bilateral pannus, urinary incontinence, and a large right-sided perianal gland carcinoma. Looking back, her warning signs dealt with the primary tumor with an 8-week history of licking her anal area. The referring hospital treated JR for an impacted anal gland without much improvement. The large mass was discovered on a recheck and considered inoperable. An incisional biopsy was performed for a definitive diagnosis. The pathology report described the mass to be a well-differentiated perianal gland carcinoma. Mr. Radke was referred to our service for definitive treatment.

After a thorough consultation, with full disclosure of the potential side effects including anal sphincter incontinence, Mr. Radke elected to proceed with definitive treatment. JR's presurgical workup radiographs and blood work revealed HM. Her reported calcium level was 14.4 and her corrected calcium was 13.3 mg/dl. JR responded well to preoperative aggressive saline diuresis followed by excisional biopsy with intralesional chemotherapy and intracavitary (intraoperative) radiation therapy (directed into the tumor bed). The margins were clean and the HM resolved.

Five months later, JR presented with a 3×3 cm firm mass at 4 o'clock on the right side of her anal sphincter. Mr. Radke thought that this was a recurrence but she did not have HM with this mass. I felt the mass was a de novo tumor, pointing out the lack of HM and its location on the opposite side of the sphincter. The new mass was excised with the earlier intraoperative protocol. Histopathology revealed a poorly differentiated rhabdomyosarcoma. There was no recurrence of HM during JR's 20-month survival.

Harley Jones's Case (When a Lymphoma Dog Feels Sick, Check the Calcium)

Harley Jones, a 5-year-old male Boxer, was referred for multicentric lymphoma. During our pre-visit conversation, Mr. Jones mentioned that Harley had a poor appetite. I asked about his water intake and discovered that Harley had PUPD. This was an indicator that Harley may have an anterior mediastinal mass with HM or sepsis. Since stage III lymphoma cases should be feeling well, I advised Mr. Jones to take Harley directly to his attending doctor for an exam, chest x-rays, and to check the calcium level. Harley had a serum calcium level of 14.7 and a corrected calcium level of 13.1 mg/dl and slight elevations of his BUN and serum creatinine. The chest x-rays were negative for AMM. Harley was given the appropriate treatment with fluids and diuretics and was able to avoid renal damage.

Harley Stall's Case (HM May Result with Bone Metastases)

Harley Stall, a 9-year-old Yellow Lab, was referred following incomplete removal of a large apocrine gland adenocarcinoma of the anal sac. Harley responded well for 3 months until he developed PUPD. His corrected serum calcium was 14.68 mg/dl. A large firm mass was palpated on rectal exam. Lateral abdominal radiographs demonstrated enlarged sublumbar/iliac nodes. Calcium levels were not taken prior to his first surgery. Harley received intense saline diuresis, steroids, and furosemide to reduce his serum calcium.

At exploratory laparotomy, the mass was declared inoperable by the attending board-certified surgeon performing the surgery, as the mass had the density of bone. Harley recovered and was discharged with instructions for the family to give one liter of saline SQ BID, etidronate, and gastroprotectants. We presumed Harley's hypercalcemia was due to bone metastases releasing osteoclast-activating factor or tumor-associated prostaglandins because his primary tumor did not manifest clinical signs of malignant hypercalcemia.

We entered Harley into Pawspice care and continued medical management of the HM. Our strategic plan was to offer supportive comfort care with SQ fluids, chemotherapy, steroids, and other measures (diet modification with low calcium content). With teamwork and great home care, we were able to keep Harley's calcium level down for 3 months. Without the SQ fluids, his serum calcium level would rise to 14.3 mg/dl. With time, the tenesmus increased and the

family became exhausted with Harley's medical management and the chore of administering the SQ fluids to such a big dog over a prolonged time. The Stalls were pleased that Harley had a good quality of life and that he was able to give them a long farewell.

Pain Is a Warning Sign and a Paraneoplastic Syndrome

As a warning sign, cancer pain is all too often overlooked in the geriatric oncology patient. Pain is considered a paraneoplastic syndrome. It is estimated that up to 20% of the 65 million dogs in the United States may suffer from osteoarthritis pain and less than half receive veterinary care. Pain neglect may become an important welfare and ethical issue (Robertson 2005). Since pre-existing pain is commonly present in older animals with other concurrent geriatric conditions, cancer pain is often accepted as part of the problem and misinterpreted. Chronic pain in sedentary geriatric dogs and cats is generally undertreated when compared to pain in more active younger animals. Geriatric pets may have a lower threshold to pain and many seem to accommodate to their chronic pain. Older animals may be more stoical than younger, more active, excitable animals. Most geriatric dogs and cats have periodontal disease and arthritis. Pet caregivers feel that their old pets have adjusted well to living with chronic low-level pain.

The warning signs of cancer pain in geriatric oncology patients are associated with reduced energy, exercise intolerance, trouble breathing, coughing, gagging, dysphagia, regurgitation, vomiting food or bile, tenesmus, constipation, lameness, stiffness, reluctance to move, hesitation to exercise, painful extremities, breathlessness, increased panting, anxiety, disorientation, dizziness, paralysis, behavior changes, teeth grinding, vocalizations, agitation, crying, and so forth (French et al. 2000).

Chronic pain in the geriatric oncology patient may wax and wane with variations in the weather and activities and concurrent conditions (Figure 3.18). Pet owners interpret this waxing and waning as good days or bad days for their old pal without thinking about the underpinnings of cancer pain. These circumstances explain why cancer pain may be passed over in older pets when the pain is actually signaling cancer.

When cancer pain is superimposed on the comorbidities of the geriatric patient, it may be initially misinterpreted, greatly underestimated, passively accepted, or dismissed by the family and the attending doctor. See chapter 7 for more details regarding the recognition of pain and its management in geriatric cancer patients.

Older cats probably suffer more untreated pain than dogs due to their aloof, quiet nature. The warning signs of pain in cats appear as subtle behavior changes such as decreased self-grooming; increased sleeping; avoidance of food, water, and petting; withdrawal from normal interactions; change in sleeping places; litter box indiscretions; postural changes; hissing or growling when touched; purring; salivation; dysphagia; and so forth (Smith 2005).

Client Education

Use Table 3.2 ("Warning Signs of Cancer and Illness in Pets") at the end of this chapter in a monthly newsletter or in a client education handout for clients in your waiting room or exam rooms. This list is regrouped and reworded for the public from the routinely used list of cancer warning signs for the veterinarian (Table 3.1).



Figure 3.18. This 12-year-old Pit Bull (a) had advanced osteosarcoma of the left proximal tibia, which caused severe swelling and pain. Maggie, a 13-year-old German Shorthaired Pointer (b), with radiographs consistent with osteosarcoma in her right distal femur (c). Following amputation, Maggie had a wonderful quality of life for 5 months.

Table 3.1. Problems That Early Warning Signs May Signal

Warning Signs of Illness or Cancer	What or Where the Problem May Be	Type of Cancer to Rule Out
Sores that do not heal	Skin, face, abdomen	Skin cancer, squamous cell
Abnormal swellings on any part of the body surface that continue to grow	Infections or tumors of skin, lymph glands, mouth, nipples, testicles, anus	Skin cancer, lymphoma Breast, testicular cancer Oral, anal cancer
Weight loss, loss of appetite, loss of energy, pale gums	Illness, fever, cancer, abdominal mass	Visceral (internal) cancer Hemangiosarcoma
Bad breath, loose teeth, offensive odor, chronic sneezing, or runny nose/eyes	Dental disease, infection, nasal passage infection, tonsillitis	Oral cancer, nasal cancer, tonsillar cancer
Difficulty eating or swallowing, salivation, vomiting, regurgitation	Dental disease, foreign body ingestion, inflammation, ulcers	Oral, esophageal cancer, stomach cancer, intestinal cancer
Difficulty breathing, urinating, or defecating, prolonged elimination effort, change in shape of stools	Asthma, bronchitis, pneumonia, bladder, prostate, colon problems, constipation	Lung cancer, bladder cancer, prostate cancer, intestinal cancer, anal sac cancer
Trouble walking, or rising, hesitation to exercise, distended abdomen, reluctance to jump	Arthritis, hip dysplasia, orthopedic problems, misalignment, bloat, overeating	Bone cancer, joint capsule cancer, abdominal mass
Persistent lameness or stiffness, holding up a leg	Injury, fracture, arthritis	Bone cancer, nail bed cancer
Bleeding or discharge from any body-opening, bloody nose, diarrhea, blood in the urine or feces	Bleeding disorders, uterine infection (pyometra), infections, inflammations, colitis, inflammatory bowel	Oral, nasal, urinary, rectal, auricular (ear), eye cancer, intestinal cancer, uterine cancer, multiple myeloma
Increased water intake or urine output, change in color of membranes to pale or yellow jaundice	Kidney disease Liver disease, anemia Diabetes Hormonal imbalance	Liver cancer Pituitary tumor Neuroendocrine tumor Abdominal mass
Behavior changes, fainting Change in routine	Behavior problem	Benign brain tumor (meningioma)
Head pressing, seizures	Epilepsy	Brain cancer
Unequal size of pupils	Meningitis, liver disease	Liver cancer
Pain	Try to localize the pain	Bone, spinal cord tumor, oral tumor, abdominal mass Ulcerated skin tumor

Use a digital camera to take pictures of patients with enlarged lymph nodes, breast tumors before and after surgery, oral tumors, and skin tumors. Put together a picture album, digital photo collection, or a PowerPoint slide show. Develop a personalized talk to have with clients when their pet is having a senior wellness exam, about the various tumor types and the warning signs of cancer. Show your slides and be sure to educate clients to look for masses at vaccination and injection sites. You may also want to give them the AVMA brochures on the warning signs of cancer.

Table 3.2. Warning Signs of Cancer and Illness in Pets

Clinicians have permission to copy this table for distribution to pet caregivers.

The warning signs of cancer are easy to confuse with the warning signs of other illness. Cancer mimics other diseases. Use this checklist to recognize cancer's warning signs. Know what those signs indicate. If you see any of these physical changes in your pet, inform your veterinarian immediately and schedule a checkup.

Changes you can feel:

1. Abnormal swellings that continue to grow in the skin, especially enlarged lymph nodes.
2. Abnormal lumps in the mouth, mammary glands, testicles, vaccine sites, abdomen.
3. Sores or ulcers that do not heal in 2 weeks on the nose, ear tips, and face, particularly of white cats and in the white underside skin of dogs, particularly Italian Greyhounds, Whippets, and Bulldog breeds.

Physiological changes you can see:

4. Weight loss (use a baby scale to weigh cats and small dogs once every 2–4 weeks).
5. Pale gums and mucous membranes, yellow (jaundice) membranes, bruising.
6. Bad breath (halitosis) or more than one loose tooth at the same location.
7. Distended abdomen, fluid in the abdomen, blood in the abdomen.
8. Small red spots or red discoloration of the skin due to leaky capillaries, bleeding at any location, especially body openings.

Behavioral changes:

9. Appetite loss.
10. Difficulty eating, excessive salivation, spitting up (regurgitation), vomiting food or bile.
11. Chronic sneezing, discharge from the eyes, unilateral nasal discharge, noisy breathing.
12. Difficulty urinating, blood in the urine that persists after therapy.
13. Excessive urine output, increased water drinking (kidney, liver problems, diabetes, etc.).
14. Loose stools (diarrhea), straining to defecate, constipation, blood or mucus in the stool.
15. Reduced energy or exercise intolerance, trouble breathing, coughing, gagging.
16. Lameness, painful movement, painful joints, hesitation to exercise.
17. Weakness, disorientation, dizziness, paralysis, pain.
18. Fainting, muffled heart beat, breathlessness, increased panting, anxiety.

Where are my pet's lymph nodes?

There are five major external lymph nodes on either side of a dog or cat.

From Bullet's nose to his tail:

- 1 Submandibular
- 2 Prescapular
- 3 Axillary
- 4 Inguinal
- 5 Popliteal

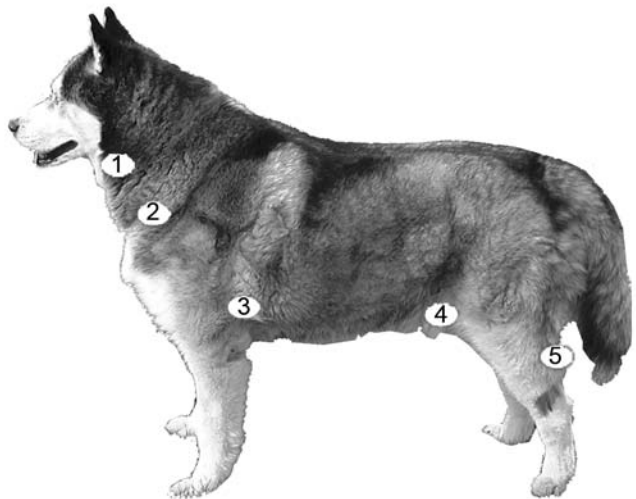


Figure 3.19. Lymph node location from "Help Your Dog Fight Cancer" by Laurie Kaplan. Printed with permission from JanGen Press.

The contemporary veterinarian also finds opportunities to reach out to the local community of pet owners with topics that favor health and longevity for the family pet. Over the years, I have enjoyed speaking to dog clubs; agility clubs; pet store clientele; Rotary, Kiwanis, and Lion's Clubs; women's clubs; garden clubs; and schoolrooms to familiarize people with the early warning signs of cancer and illness in their companion pets. I also educate people about cancer in humans. People are amazed to hear that cats living with smokers are at higher risk for oral and GI neoplasia. They need to know what to look for at vaccine and injection sites. They appreciate learning that lawn chemicals can cause bladder cancer and lymphoma in dogs. Talks with a comparative aspect geared toward the audience, young or old, may help save a life.

An interesting slide show, presented by you at a Rotary or Kiwanis Club meeting, promotes community awareness for pet health. It shows that you are a caring veterinarian, and it is a very good practice builder.

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Chapter 4

Basic Types of Cancer and Their Biological Behavior

When you have chosen your part, abide by it, and do not weakly try to reconcile yourself with the world. . . . If you would serve your brother because it is fit for you to serve him, do not take back your words when you find that prudent people do not commend you.

Ralph Waldo Emerson

Introduction

Cancer is the all-encompassing name given to over a hundred various types of neoplasia and related syndromes. A good working definition for neoplasia, proposed in *Tumors in Domestic Animals*, is: “A Neoplasm is a mass of tissue generated by cells capable of division which have acquired either permanent expressible heritable change or stable epigenetic change so that the cells no longer respond appropriately to one or more normal tissue-organizing stimuli, chemical or physical, intracellular or extracellular, in the organism in which it occurs” (Cullen, Page, and Misdorp 2002).

Neoplastic cell types are categorized either as mesenchymal or epidermal. A binomial system categorizes all forms of neoplasia according to benign or malignant behavior and their mesenchymal or epithelial cell type of origin. Mesenchymal refers to connective tissue, muscle, blood, and all endothelial cells, including mesothelium, synovium, and meninges. Epidermal refers to squamous cells of the skin, all glands, all cells lining tubular tracts and cells of neuroectodermal origin, including melanocytes (Cullen, Page, and Misdorp 2002).

Practicing veterinarians can more readily address oncology on a clinical basis by placing tumors within five major group divisions. By understanding cancer cell types within the construct of these major group divisions, the diagnosis, management, supportive care, and chemoprevention for geriatric patients may be more approachable. The clinician may also address cancer according to its location in the body, such as head and neck tumors vs. abdominal tumors. This approach often employs specific shared treatments.

Some malignant tumors grow so rapidly that they are difficult for the pathologist to classify. They may be reported as undifferentiated. Think of these as renegade cells that grow so fast that they have no time to pick up the morphological characteristics of their cell of origin. We can consider these cells to be “dedifferentiated.” When pathologists cannot identify the cell of origin, they may describe the tumor as “anaplastic carcinoma.” New diagnostic tests using molecular profiling (see chapter 5) will add to our ability to classify anaplastic cells in the future. Ask your pathologist if these differentiation tests are available.

The attending doctor needs to have a basic understanding of the origin of a particular tumor and its biological behavior, because the geriatric cancer patient's welfare is at stake. For clinical purposes, we can consider grouping cancer into the following five major categories:

1. **Carcinomas:** Cancer that arises from skin cells, mucous membranes, cells from glands and internal organs, or cells that form the lining of body cavities. Cancer arising from glandular tissue is often referred to as adenocarcinoma (AC).
2. **Sarcomas:** Cancer arising from connective tissues such as bone, muscle, and fibrous connective tissue and from various types of cells that reside in the body, such as mast cells, melanocytes, plasma cells, and dendritic cells.
3. **Blood cancer:** Cancer arising from hematopoietic tissues and lymph nodes or other lymphatic tissue, causing leukemias and lymphomas, respectively. Hemangiosarcoma may be included in this category.
4. **Nervous system cancer:** Cancer arising within the brain, in the spinal cord, or in nerve cells.
5. **Miscellaneous and uncertain cell types:** Histiocytic tumors, difficult-to-classify malignancies, and tumors of uncertain origin.

Carcinomas

Carcinomas arising from epidermal cells in the skin, from cells that form the lining of cavities, or from cells forming the inner surface of an organ. Many carcinomas, especially mammary tumors, testicular tumors, and perianal and sweat gland tumors, appear on the surface of the body and are initially noticed by the pet owner, whereas carcinomas that arise in the viscera remain insidious and occult until the pet becomes symptomatic.

Squamous cell carcinoma (SCC) arises in non-pigmented facial skin of older white cats and in the ventrum of light-skinned dogs due to chronic solar irradiation. Non-actinic SCC may arise anywhere in the oral cavity affecting the tongue, tonsils, and esophagus. Non-actinic SCC may also arise in the nasal sinuses, respiratory tract, and nail beds of both dogs and cats. Some reports have associated SCC of the tonsils in dogs with environmental pollution. Cats exposed to environmental tobacco smoke for five or more years are at an increased risk of developing oral SCC and GI lymphoma (Snyder, Bertone, and Moore 2001).

Carcinomas may arise from nasal respiratory epithelium at any location in the nasal passages and may involve the sinuses, extend between the eyes, involve ethmoid plate, and invade into the calvarium and brain. They cause turbinate destruction, unilateral nasal discharge, epistaxis, and facial deformity.

Carcinomas arising in the thorax in older dogs and cats include aortic body (heart-based) tumors, esophageal carcinoma, and respiratory and bronchogenic carcinoma. Primary lung tumors are rare in old cats but SCC is the most common cell type. In the feline, malignant cells may metastasize to the digits as a final event. Primary lung tumors generally appear as a solitary round mass in the caudal lung lobes in both dogs and cats.

Adenocarcinomas

The term "adenocarcinoma" applies more specifically to tumors that arise in glandular tissues of the skin and viscera and form glands within the neoplasm. Adenomas are benign tumors of glandular cells. Over time, some adenomas may transition into malignant tumors. The skin and mucous

membranes commonly give rise to carcinomas in dogs and cats as they age. AC may arise in the ciliary body of the eye and occasionally in the glands of the eyelids. Dogs are prone to develop sebaceous, mammary, anal sac, perianal, salivary, and sweat gland tumors. Cats are prone to develop squamous cell carcinomas, basal cell tumors, and mammary tumors. Perianal tumors in male dogs and mammary tumors in female dogs and cats are sex-hormone related.

Mammary tumors are encountered in 25% of older intact female dogs or in older dogs with OVH after 2½ years of age. Half of canine mammary tumors are malignant and 50% of this group dies within 1 year. Mammary tumors are less common in cats; however, more than 90% are malignant with a high rate of fatality if greater than 3 cm in size. Cats that had OVH late in life are more prone to develop mammary AC.

ACs may originate from glands in the abdomen, such as liver, colon, intestine, stomach, kidney, bladder, pancreas, prostate, and the adrenal glands. Widespread dissemination of cancer in the abdomen and throughout the body is given the term “carcinomatosis,” but this term may also include other tissue types.

ACs may also originate from any gland in the neuroendocrine or reproductive system, such as the thyroid glands, pancreas, adrenal glands, pituitary gland, ovaries, uterus, testicles, and prostate. This type of tumor often causes paraneoplastic syndromes related to their particular cell products. Sertoli cell, interstitial (Leydig) cell, and seminoma of the testicle may produce estrogen, causing feminizing syndrome and anemia.

Anal sac AC is the most common carcinoma associated with malignant hypercalcemia. (Lymphoma is the most common cause of malignant hypercalcemia, but a number of other malignancies may also cause this potentially life-threatening syndrome.)

Most mesotheliomas are classified as ACs although they have mesenchymal elements. They are rarely found in geriatric dogs and cats. Mesotheliomas arise from the serosal lining of the thorax, pericardium, and peritoneum, causing malignant effusions. In humans, mesotheliomas are associated with mining and working with asbestos.

Behavior of Carcinomas and Adenocarcinomas

Most ACs have an aggressive biological behavior with a persistent tendency for local and distant metastasis. Local recurrence following surgery is common. Local and regional lymph node invasion is common, followed by widespread dissemination. Most ACs expand to a detectable size by accumulation of cells and outward exponential growth. Various proliferative mechanisms drive tumor growth, especially angiogenesis. Mechanisms that promote cell membrane dissolution cause direct extension of neoplastic cells into local tissues, lymphatic vessels, and capillaries, setting the stage for dissemination.

Metastatic lesions are not detected in veterinary medicine until they can be seen or imaged. Lesions generally appear as nodular cell clones in the lungs, liver, spleen, abdomen, brain, or eyes and may further (but less commonly) metastasize to bone and skin.

Symptoms of metastatic disease may be sub-acute or chronic. Affected pets may develop coughing, gagging, exercise intolerance, dyspnea, ascites, or abdominal distention. Primary tumors of the lung and metastatic lesions may cause hypertrophic osteopathy (HO), a painful swelling of the legs due to periosteal new bone growth along the long bones of the limbs. Pulmonary metastases often demonstrate a “cannon ball” appearance or a patchy interstitial pattern on radiographs of the lung fields. Pulmonary and/or abdominal effusion is a common sequel of end stage metastatic carcinomas and adenocarcinomas.

Sarcomas

Sarcomas are malignancies that include all mesenchymal connective tissues, all endothelial cells, muscle tissue, bone, bone marrow, blood, mast cells, melanocytes, and miscellaneous cells. Sarcomas have a variable clinical appearance and have been subdivided into their palpable texture as soft tissue sarcomas vs. sarcomas of bone (firm) and blood (hematopoietic), which includes the leukemias and lymphomas. Various mesenchymal cell types give rise to distinctive neoplasms such as mast cell tumors, malignant melanoma, plasma cell tumors, and histiocytic (dendritic) cell tumors. These are also soft tissue sarcomas by definition. Sarcomas are so variable that they are often regarded as clinically distinct and comprise four of the five major cancer groupings as discussed in this book.

Soft Tissue Sarcomas

STSs arise in the connective tissues of the body, such as the skin, muscle, blood vessels, and fibrous tissue. Most STSs form a mass that is palpable on the surface of the body. However, some STSs that may originate from pluripotent stem cells of the bone marrow, such as hemangiosarcoma, may arise anywhere in the body (Modiano and Helfand 2005).

Sarcomas of Bone

Osteosarcoma is the most commonly found bone tumor in dogs and cats. The other sarcomas of bone are chondrosarcoma, synovial cell sarcoma, and malignancies arising from any other bone constituent. Large and giant breed dogs are more prone to osteosarcoma at growth plates than are medium and small breed dogs. Bone tumors are relatively rare and less aggressive in cats, affecting them in their senior to geriatric years.

Bone may be secondarily infiltrated by metastatic carcinomas and other sarcomas. However, dogs and cats do not experience the high rate of bone invasion from metastatic cancer that is seen in humans. There may be a protective mechanism that spares bone from metastatic disease in dogs and cats, or perhaps they simply don't survive long enough for this to occur. As animal cancer patients survive longer, we may see more late metastases to the bones. Metastases to bone are recognized in canine osteosarcoma patients previously treated with chemotherapy. It seems that chemotherapy may have protected patients from lung metastasis but left them vulnerable to bone metastasis.

Osteosarcoma exhibits an aggressive biologic behavior in dogs. Radiographs show lysis and destruction of normal bone architecture and cortex at the primary site. Elevation of the periosteum to form Codman's triangle is considered pathognomonic for osteosarcoma. Tumor growth, inflammation, and expansion cause invasion through the cortex into surrounding tissues. Lytic lesions and stretching of the periosteum cause intense pain.

Dogs may develop pathological fractures at the tumor site due to stress on the weakened bone. Micrometastasis to the lungs occurs early in the course of disease, resulting in pulmonary lesions that compromise respiratory function within 4 to 6 months in most cases. Cats rarely develop pathological fractures and metastasis to the lungs is slow to develop. Therefore, amputation may be curative in cats.

Vaccine-Associated Feline Sarcoma

Some cats have a genetic tendency toward developing STS at vaccine sites. Chronic inflammation at the vaccine site creates inflammatory tissue, which promotes and initiates malignant sarcoma cells

via mechanisms including genetic alterations of the tumor suppressor gene, p53. The situation was illuminated in 1991 by a letter to the editor in *JAVMA* by Dr. Mattie Hendrick, a pathologist at the University of Pennsylvania. She noted an increase in the number of cats with interscapular feline sarcomas and theorized that aluminum hydroxide adjuvant, observed as a blue staining substance at vaccine sites, may play a role in creating the inflammatory response leading to malignant soft tissue sarcomas (Hendrick and Goldschmidt 1991).

This tumorigenic phenomenon was given the name “feline vaccine-associated sarcoma” (FVAS). It has a bimodal appearance with the second peak affecting senior and geriatric cats. If a cat develops a mass at a vaccination site that persists over 3 months, it should be highly suspected as FVAS and treated as such (Moore 2004). The Vaccine Associated Feline Sarcoma Task Force (VAFSTF) was organized to unify the profession’s efforts at understanding the carcinogenesis, pathogenesis, therapy, and prevention of FVAS. The VAFSTF reached a consensus to review protocols and rationale for vaccination of cats.

FVAS behaves aggressively and has a high rate of recurrence and fatality. The neoplasm has tentacles that infiltrate deeply below the mass and along facial planes, resulting in incomplete surgical resections. In addition, macrophages that engulf the aluminum hydroxide adjuvant may travel and create new foci of inflammation that may transition into new malignant sarcomas.

Unfortunately, the recurrence rate is greater than 90% within 6–12 months following routine surgery. When a board certified surgeon performs excision, the tumor-free interval is greater because wider and deeper margins are attained. When surgery is followed by radiation therapy, the rate of recurrence is reduced to 50% within 1 year. Approximately 25% of long-term survivors develop metastases to the lungs. FVAS can be prevented via a personalized lifestyle vaccine program that minimizes over-vaccination. Using non-adjuvanted vaccines for cats may eliminate tumor formation (Macy 2005).

Biological Behavior of Sarcomas

The biological behavior of STS is variable. Some tumors tend to remain in the local site of origin, while others metastasize. Tumors that remain localized still have the potential to kill because they recur after surgery and often become quite large and debilitating over time.

Geriatric pets are good candidates for treatment of STS if the patient is considered to be in good health and condition at the time of diagnosis. If the patient has concurrent illness, the overall survival time may be limited. Geriatric patients are more easily stressed from multiple surgeries or from the rigors of radiation therapy, chemotherapy, recurrence, and tumor burden.

The STSs that tend to remain localized fall into a large group that may be treated with a similar strategy. Aggressive surgery is generally required. If STS is approached casually without a good strategic plan prior to surgery, inadequate removal and recurrence is likely. The morphologic shape of STS may be imagined as an octopus with tentacles extending laterally into facial planes and deeply into structures below the mass.

A well thought out plan for total removal of STS is required. Unfortunately, many STSs are incompletely or inadequately removed. Well-intended clinicians who lack the surgical oncology skills for enblock definitive surgery attempt to “debulk” a mass that could be completely excised by a board certified or qualified surgeon. It is important for the client to understand that if residual cancer cells remain in the body after the initial surgery, the cancer has *not* been removed. It has only been debulked, despite the good intention of the attending doctor and the healthy appearance of the surgery site.

Tumor removal can be a very humbling process, due to the high rate of failure in specific tumor types, especially STS. The surgeon’s goal in surgical oncology is to gain complete removal of the

mass with adequate margins of 2 to 3 cm beyond the extensions of the mass. Many surgeons feel and state with confidence that they “got it all.” An excision may appear complete even when the microscopic examination finds narrow margins or dirty margins (Figures 1.1 and 5.7). However, all remaining cancer cells are immortal and are committed to grow into a recurrent tumor and metastasize.

An incomplete first surgery may cause an interruption in the normal tissue planes. Additionally, growth factors involved in the wound healing process at the surgery site may allow residual cancer cells to behave more aggressively. Some sarcomas, such as hemangiopericytoma, seem to select a more aggressive cell line to grow back after successive surgeries and may transition toward fibrosarcomas.

Blood (Hematopoietic) Cancer

Malignancies of hematopoietic cells and lymphoid tissue are commonly referred to as blood cancer and include the leukemias, myeloproliferative disorders, and lymphomas. The leukemias are further classified according to the cell of origin, such as lymphoblastic, chronic lymphocytic, myelogenous, acute myelogenous, granulocytic, multiple myeloma (plasma cell), erythroleukemia, and so forth. Lymphomas are commonly diagnosed in dogs and cats. There is a retroviral etiology in cats but not in dogs.

Blood Cancer in Dogs

Lymphomas are described in dogs as large cell, blastic, cleaved cell, small cell, T-cell, B-cell, mantle cell, and cutaneous T-cell lymphoma (which includes mycosis fungoides). For prognostic information, clinicians may pursue immunophenotyping to differentiate T-cell vs. B-cell lymphomas in dogs. Canine T-cell lymphoma is less responsive than B-cell lymphoma. Boxers were found to have more T-cell lymphomas than most other breeds (Lurie et al. 2004), while geriatric dogs over 14 years of age were found to have more B-cell lymphomas (Modiano and Helfand 2005). This knowledge enables the attending clinician to more confidently determine an individual patient’s prognosis and predict patient response to combination chemotherapy. Geriatric lymphoma patients benefit from induction chemotherapy as soon as an FNA diagnosis of lymphoma is established. Delaying treatment while waiting for histopathology and immunophenotyping results may allow the disease to advance and compromise the chances of treatment success.

At this writing, there is an effort to create international acceptance of a single nomenclature and criteria of recognition and classification for hematopoietic neoplasms in dogs. Through an ongoing study, Dr. Ted Valli and members of the American College of Veterinary Pathologists hope to determine the value and ease of application of the WHO’s system. This classification of canine nodal and extranodal lymphoma was published in the *WHO International Histological Classification of Tumours of Domestic Animals* in 2002. Each category and subtype in this system constitutes a well-described and documented disease entity rather than a general cell type or morphology. Immunophenotype, disease topography, and signalment will be evaluated.

The study hopes to enroll six hundred cases from North America and Europe from oncology practices, pathology services, private practices, and colleges of veterinary medicine. An agreement form must be signed by the clinic and the animal caregiver to permit use of tissues for research purposes. The client will finance examinations, staging, nodal excision, and diagnostic procedures (including pathology and immunohistochemistry) to determine phenotype. Selected clinics may receive collection

supplies for harvesting fresh frozen tissue to study mRNA. Patients will be treated by their local oncologist/clinician within the philosophy and financial means of the pet's owners.

When this study is completed, it may provide a prognostic index to compare treatment protocols used in canine lymphoma subtypes. To contribute cases or for updates, contact Dr. Valli at the e-mail address v-valli@uiuc.edu (Valli 2005).

Blood Cancer in Cats

Retroviral infection with FeLV and FIV increases the risk for affected cats to develop lymphoma, leukemia, myeloproliferative disorders, and immunosuppression. Historically, over one-third of all feline cancer deaths were FeLV related (Cotter, Hardy, and Essex 1975). In addition, deaths occur from anemia and infections due to viral injury of the immune system. The current prevalence of FeLV in healthy U.S. pet cats is less than 1%, down from 5% during the 1970s and 1980s. This decrease is mostly due to test and isolation/removal programs.

The type of lymphoma diagnosed in cats has changed over the past 30 years. In the past, 50% of cats with hematopoietic malignancy had acute leukemia and 50% had lymphoma. The mediastinal form of lymphoma was most common and appeared in young cats. Seventy percent of cats with lymphoma tested positive for FeLV or were positive with virus isolation.

Today, we see more FeLV-negative lymphomas, 70% of which are the alimentary form of the disease (Cotter, Hardy, and Essex 2005). Variations in the viral subtypes and other causes for lymphoma, such as exposure to environmental carcinogens and tobacco smoke, may explain this. Chronic exposure to cigarette smoke has been associated with the occurrence of lymphoma of the gastrointestinal tract in cats (Snyder, Bertone, and Moore 2001). Since 24% of adults smoke cigarettes and many of them own cats, there is an enormous population of cats at risk as they age.

Many cats have a history of inflammatory bowel disease and weight loss prior to the diagnosis of GI lymphoma. Older cats with poorly differentiated GI lymphoma do poorly if they are debilitated at the time of diagnosis. It is difficult to monitor these patients because signs of progressive disease often mimic chemotherapy toxicity. The T- or B-cell phenotype is fairly evenly distributed in feline lymphoma. Phenotyping is not prognostically significant in cats. Predictive factors remain elusive. An initial complete response to therapy was found to be the only significant factor affecting survival for a series of 38 lymphoma cats. The average age was 11 years and 47% achieved complete remission with a median survival of 654 days (Milner et al. 2005).

The attending clinician should avoid stressful diagnostic surgery in sick cats in preference to non-invasive diagnostic techniques such as FNA or Tru-cut biopsy. Many of these older cats have concurrent conditions such as cancer cachexia, chronic renal failure, heart disease, hyperthyroidism, diabetes, and so forth. Treatment and supportive care for these cats requires skill, patience, and initiative. It is imperative to address each one of the geriatric patient's comorbidities and balance effective chemotherapy in the face of other concurrent illnesses.

CNS Tumors

Tumors that arise in the brain, brainstem, and spinal cord are extremely difficult to manage in the veterinary patient. In part, this is due to typically late diagnosis. Many dog and cat patients tolerate the initial growth of CNS tumors without overt symptoms. The undiagnosed tumor progresses until compression by the calvarium or the spinal canal causes the animal to exhibit the signs of CNS neoplasia, such as behavior changes, seizures, circling head tilt, ataxia, blindness, or paresis.

A workup and complete neurologic examination may localize the lesion. For confirmation, imaging with MRI, CT, or PET scan can visualize the lesion. If a mass is localized, situated peripherally, and accessible by surgery, then the patient may benefit. Radiation therapy may be helpful to control some brain tumors and spinal tumors. One of my 19-year-old, geriatric feline patients now in Pawspice is a 5-year survivor, following two surgeries for a large meningioma that caused blindness and circling.

Choroid plexus tumors are classified as carcinomas although they arise in the brain stem. They are not amenable to surgery and they are resistant to radiation therapy. Tumors that arise from nerve cells, including neurofibroma, neurofibrosarcoma, and nerve sheath tumor (schwannoma), are best treated as locally invasive sarcomas with wide surgical excision followed by external beam radiation therapy when feasible.

Miscellaneous Tumors and Tumors of Unknown Origin

Histiocytes are cells that have tiny extensions or dendrites on the cell surface (dendritic cells) such as macrophages, monocytes, and Langerhans cells. When transformed into their neoplastic counterparts, they multiply rapidly and infiltrate viscera. The cells often accelerate their signaling to phagocytize red cells and sometimes other white cells and other “self-cells,” causing illness. Histiocytic tumors create a confusing set of syndromes.

Tumor cell markers are used to differentiate the cell of origin because these lesions can be confused with anaplastic carcinomas or diffuse large-cell lymphoma. The most advanced collection of tumor cell markers for dendritic cells has been developed in the laboratory of Dr. Peter Moore in the Department of Pathology at the University of California, Davis. Unfortunately, as of this writing, the knowledge for tumor makers has served for diagnostic purposes only. When immunohistochemical (IH) stains become more readily available, we may be able to run detailed analysis to identify the cell type more clearly and plan for more strategic therapy.

Bernese Mountain Dogs (BMDs) are genetically predisposed to malignant histiocytosis (MH). Other susceptible breeds are Rottweilers; Golden, Labrador, and Flat-Coated Retrievers; and Doberman Pinschers. MH is rare in cats. The malignant cells in MH originate from the pet's own immune system. There is controversy as to the cell type. MH may originate from a mutated clone of tissue macrophages but there is also a theory that BMDs genetically lack the ability to suppress tumor cell proliferation.

Another type of histiocytic tumor behaves as a somewhat localized but aggressive soft tissue sarcoma. Malignant fibrous histiocytoma (MFH) appears in middle aged and older dogs and cats. The tumors appear most often in Golden Retrievers and Rottweilers. These tumors may appear on the limbs and skin or in the spleen as a solitary growth but in this case they also have a multi-organ variant. MFH may also arise at vaccine sites in cats. These localized tumors need to be aggressively excised. With follow-up radiation therapy or chemotherapy, some patients may have a variable tumor-free interval that may extend from a few months to years.

The tumors discussed in the following section are the most common histiocytic tumors encountered in general practice. Patients with these tumors need a thorough work with histology and staging to distinguish cutaneous from systemic histiocytosis and MH.

Histiocytic Tumors

1. MH is the most aggressive histiocytic syndrome. MH most commonly affects the lymph nodes, viscera, eyes, CNS, and skin of older male BMDs and Rottweilers but can appear in Golden

Retrievers, Miniature Schnauzers, Tibetan Terriers, and cats. The cells of origin are malignant tissue macrophages that show erythrophagocytosis and simultaneously infiltrate multiple organs and skin. MH is rapidly fatal. Some tumors may be misdiagnosed as granulomatous inflammation. Any clinician examining a sick BMD with CNS or ocular signs should be very suspicious and request special IH stains on cytology or tissue sample to rule out MH.

2. Systemic histiocytosis (SH) arises in the skin of younger BMDs and spreads to lymph nodes and viscera. The cells do not look malignant on cytology but show erythrophagocytosis. The disease runs its course over a longer period of time than MH but eventually causes the patient's death. Leflunomide (an orphan drug) has been proposed as somewhat helpful in both MH and SH but it causes GI toxicity when used with prednisone. Azathioprine and cyclosporine may also be of help.
3. Cutaneous histiocytosis (CH) is a multifocal proliferative variant of solitary cutaneous histiocytoma that remains restricted to the skin. This condition affects the nose, nasal mucosa, muzzle, and dorsum skin of BMDs, Briards, Collie breeds, and Golden Retrievers. The cells of origin for CH are dermal dendritic cells (positive for lysozyme marker on IH stains), whereas dermal Langerhans cells give rise to solitary histiocytomas found in young dogs. Lesions wax and wane over time but do not involve lymph nodes or viscera. Most pathologists do not classify these tumors as malignant but they do proliferate due to lack of tumor suppressor gene function. Some tumors may regress spontaneously. The tumors generally respond to steroids, surgery, or cryotherapy. L-asparaginase and azathioprine may also be used to achieve remissions.
4. MFH, formally known as giant cell tumor, behaves like a very aggressive soft tissue sarcoma in both dogs and cats. The cell of origin is often undetermined but may come from pleomorphic fibroblast-like cells that exhibit cartwheel patterns or an inflammatory variant with bizarre histiocyte-like cells that arise in the spleen. These tumors contain spindle and round cells. Because they can be confused with carcinomas, fibrosarcomas, or osteosarcomas, special stains are in order. The behavior of MFH is variable but most often fatal. The solitary cutaneous/subcutaneous masses can be excised with some success. The multicentric form of MFH is very resistant to all attempts at treatment.

Miscellaneous Tumors

1. Plasma cell tumors have many names, including plasmacytoma, reticulum cell sarcoma, Merkel cell tumor of neuroendocrine origin, atypical histiocytoma, and cutaneous plasma cell tumor. They can also be misdiagnosed as MH. They are rare in cats. What pulls all these misnomers together is testing for the presence of immunoglobulin (IgG or lambda light chains) in the cytoplasm of the cells with immunofluorescence or immunoperoxidase stains. Plasma cell tumors appear as fleshy solitary or multiple cutaneous or oral neoplasms. They typically have a benign behavior (despite their wild cellular pleomorphism) when completely removed and they respond to radiation and chemotherapy. They do not cause monoclonal gammopathy and do not metastasize to bone. If you see widespread lesions, they are more likely to be metastatic from a primary multiple myeloma in the bone marrow. Both multiple myeloma and IgM macroglobulinemia are responsive to chemotherapy with chlorambucil and prednisone.
2. Pulmonary lymphomatoid granulomatosis is rare. It appears as large masses in the lungs of dogs. The cell of origin is a pleomorphic population of atypical lymphoid infiltrates around and invading vessels. The majority of cases respond to chemotherapy protocols used for lymphoma and patients have similar median survival times as lymphoma dogs.

Rocky's Case (Systemic Histiocytosis Is Mean)

Rocky Racinto, a 10-year-old M/N Boxer, developed multiple, raised erythematous dermal lesions on his face, eyelids, and dorsum along with interdigital hyperemia and pruritis. The pathologist could not distinguish the cell type as cutaneous vs. systemic histiocytosis. Rocky's clinical appearance warranted a poor prognosis. Mr. Racinto, who worked night shifts as an orderly in a hospital, wanted to save Rocky but he had a limited budget. We recommended IH stains CD3 and CD79a to confirm systemic histiocytosis, but he was satisfied with my clinical impression and elected to spend his money on therapy. Rocky had a short regression of his tumors following induction with vincristine, L-asparaginase, and prednisone. His facial and cutaneous lesions cleared up. Following the first treatment of Adriamycin, Rocky experienced nausea and vomiting. Two weeks later, he had an acute onset of severe upper airway dyspnea for 24 hours. On exam, he had pharyngeal edema and a firm swelling in the neck with parasympathetic paralysis. Radiographs identified a mass that deviated his trachea at the larynx and megaesophagus. We presumed that Rocky had progressive disease. His cutaneous lesions remained reduced with some crusting, despite the internal devastation caused by the malignancy.

Bingo's Case (Have Optimism—Cancer Can Be Cured!)

Bingo, a 9-year-old male Bernese Mountain Dog, was adopted by the Snyder family after retiring from the show ring. Bingo developed a rapidly growing $8 \times 5 \times 5$ cm subcutaneous mass in the area of the fourth mammary gland. The biopsy report was MFH. No other lesions were found on a complete workup. The Snyders had a strong bond with Bingo and knew that his line had longevity until 10 to 12 years of age. The family had some financial constraints and asked me to recommend the most valuable and cost-effective procedure that could be done. They elected our multimodality protocol with wide, deep surgical excision, intralesional chemotherapy, and intraoperative radiation therapy for curative intent. They declined postoperative external beam radiation and chemotherapy due to the costs. Bingo lived cancer free for 3 more years, until age 12, when he developed fulminant MH.

Letty's Case (Plasma Cell Tumors Are Not All Bad)

Letty Klint, a 10-year-old F/S King Charles Spaniel–mix, developed a 1 cm mass in the gum tissue of her right caudal maxilla. Plain radiographs showed some bone loss. The mass was excised by her local veterinarian with narrow margins. During our consultation, the family told me that they had spoken to several other doctors: a holistic doctor, a family friend, and two veterinarians from their local practice. They also needed specific quotes for procedures and told me that they had financial constraints. I recommended either maxillectomy or radiation therapy for this generally localized oral tumor. The Klints declined invasive surgery. We referred them for a radiation therapy consultation. A CT scan was recommended to assess for bone invasion before the radiation therapy or surgical maxillectomy. The scan showed no abnormalities and the Klints declined treatment for Letty. Their reasoning was, “Since there was nothing about the CT scan that was abnormal, we are having doubts about the diagnosis from the pathologist. Since there was no evidence of local recurrence, we decided that there was no evidence that would make us put Letty through either option at this time.” The Klints made a

follow-up plan with their local doctor to have oral x-rays every 3 months. They said that they would not consider a follow-up CT scan at the cost of \$750.00. On a follow-up call four months later, Letty remained tumor free.

Fluffy's Case (She Outlived the Prognosis)

Fluffy Lockett, a 10-year-old F/S DSH, belonged to Liz Lockart, who lived and worked at Jones Veterinary Hospital in Santa Monica. Fluffy developed a $5 \times 5 \times 6$ cm solitary histiocytic lymphoma on her right hind leg. The pathologist gave a poor prognosis of 90% mortality within 6 months. Liz declined amputation and elected debulking surgery with intraoperative radiation therapy (RTx) followed by 12 fractions of external beam RTx to the field and chemotherapy. Fluffy was in remission for 10 months, at which time she developed popliteal and inguinal lymph node enlargement. The recurrence was resistant to treatment and within 30 days she developed fulminant disease involving the spleen, liver, and lungs. Liz was satisfied and proud that Fluffy had outlived her prognosis.

Approaching Cancer According to Location

Another way to manage the complexity of oncology cases encountered in geriatric patients would be to approach them by location (Figure 4.1). You may find this clinical approach more appealing as the tumors, by virtue of their location, have many management features in common. Once the tumor is localized, it can be approached as a carcinoma or a sarcoma at that particular site. Clinicians can factor in the geriatric patient's comorbidities, body condition, and performance assessment as they view tumors from a location perspective. Weighing all these factors helps the clinician with decision making for management of the most common malignancies in geriatric oncology patients.

Malignant skin and subcutaneous tumors

Carcinomas: Squamous cell, sebaceous, mammary, testicular, anal sac, perianal, salivary, sweat gland, basal cell, nail bed SCC, etc.

Sarcomas: Mast cell tumors, fibrosarcoma, liposarcoma, neurofibrosarcoma (nerve sheath tumor), myxofibrosarcoma, hemangiopericytoma, cutaneous actinic hemangiosarcoma, cutaneous non-actinic hemangiosarcoma, malignant melanoma, nail bed melanoma, rhabdomyosarcoma, leiomyosarcoma, transmissible venereal tumor (TVT), cutaneous plasmacytomas, etc.

Malignant head and neck tumors

Carcinomas: Oral SCC and thyroid, salivary, ceruminous gland (otic), and ciliary body (ocular) carcinomas, etc.

Sarcomas: Oral and facial fibrosarcoma, mast cell tumor, oral and facial malignant melanoma, etc.

Oral tumors: SCC, fibrosarcoma, malignant melanoma, osteosarcoma, acanthomatous epulis, etc.

Nasal tumors: Nasal planum SCC, nasal respiratory carcinoma, chondrosarcoma, etc.

Brain tumors: Glial tumors (more common in older, brachycephalic dogs), ependymoma, choroid plexus tumors, meningiomas (more common in old cats), etc.

Cancer Can be Named By Its Location

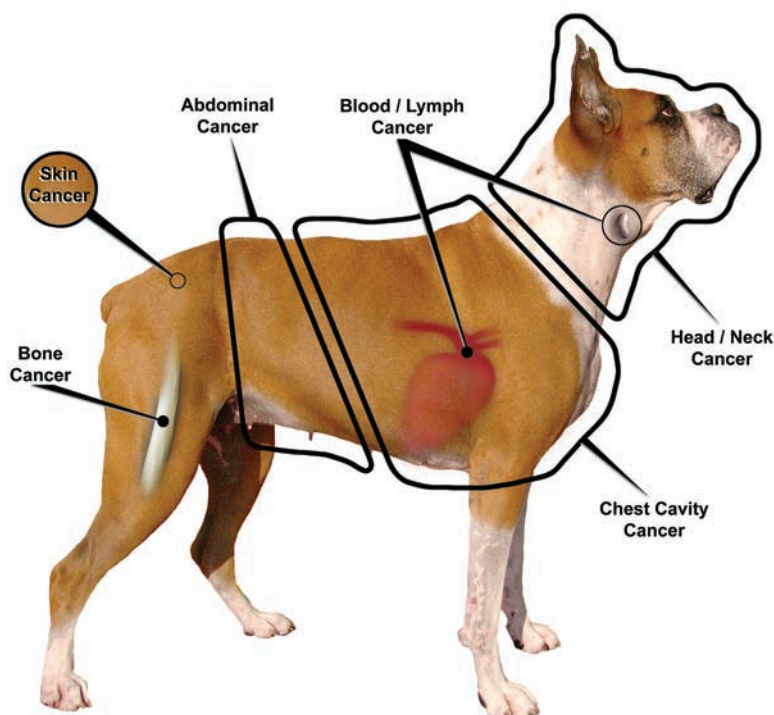


Figure 4.1. Cancer can be named by its location. Approaching cancer according to its location helps to manage the complexity of oncology treatments.

Malignant chest cavity tumors

Secondary: Metastatic pulmonary disease may be from either mesenchymal or epidermal origin malignancy.

Carcinoma: Bronchogenic carcinoma, squamous cell carcinoma, esophageal carcinoma, heart base (aortic body), cardiac tumors, mesothelioma, etc.

Sarcoma: Thymoma, thymic (mediastinal) lymphoma, hemangiosarcoma of myocardium, malignant histiocytosis, and lymphomatoid granulomatosis.

Malignant abdominal cavity tumors

Carcinomas: Gastrointestinal, splenic, hepatic, pancreatic, adrenal (pheochromocytoma), renal, bladder (transitional cell carcinoma), prostatic, gonadal cancer (ovarian, uterine, and retained testicular tumors), mesothelioma, carcinomatosis, etc.

Sarcomas: Hemangiosarcoma, lymphoma, leiomyosarcoma, mast cell tumor, malignant histiocytosis, extramedullary plasmacytomas, miscellaneous, etc.

Bone cancer

Osteosarcoma, chondrosarcoma, fibrosarcoma, giant cell, synovial cell sarcoma, secondary metastases, etc.

Blood cancer

Lymphomas, leukemias, multiple myeloma, myeloproliferative disorders, hemangiosarcoma, etc.

Summary

Cancer is prevalent in companion animals as they age. Clinicians may categorize neoplasia according to its benign or malignant behavior and according to its mesenchymal or epithelial origin to help in decision making for geriatric pets. Grouping cancer into the five major categories such as carcinoma, sarcoma, blood cancer, nervous system cancer, and miscellaneous cell types helps to understand its behavior. Tumors may also be clinically approached by location (Figure 4.1). Many tumors share similar management features due to their location. This information may allow the attending doctor to make early recommendations for the caregiver to consider as options for the geriatric cancer pet.

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Chapter 5

Generating the Diagnosis and Prognosis of Cancer in Geriatric Pets

If you were this patient, are these the diagnostics and treatments that you would like to have your doctor choose?

Carl A. Osborne, DVM, ACVIM

Principles and Perspective for Diagnosis in Geriatric Patients

It is essential to establish a working and definitive diagnosis to properly manage cancer in geriatric patients. However, by their very nature, geriatric oncology patients pose more diagnostic dilemmas due to age-related changes, which reduce the patient's tolerance to stress (Table 2.2). We must also document the geriatric patient's clinical condition and functional performance (see chapter 8). Each geriatric patient is unique and should be evaluated with the concept that age itself is not a disease but a physiologic condition in which cancer is more commonly found. Cancer is currently a more treatable disease in dogs and cats, but the first doctor consulted often determines the fate of the geriatric pet with cancer. This emphasizes the importance of education in geriatric oncology so that we can meet our clients' expectation for expertise and professional help when cancer strikes their aging pets.

If a biopsy or diagnostic procedure places the geriatric patient at risk or if the procedure is as stressful as the treatment, you are completely justified in getting the biopsy along the way. There are many instances where having the definitive diagnosis of a suspected cancer would not alter your immediate recommendation or the caretaker's decision for palliative or curative clinical control. Exemptions from the academic pursuit of a definitive diagnosis are justified especially for geriatric oncology patients when making recommendations for splenectomy for suspected hemangiosarcoma; amputations for suspected osteosarcoma; lobectomy for a solitary lung mass; mandibulectomy for a suspected fibrosarcoma, melanoma, or squamous cell carcinoma (SCC); and craniotomy for brain tumor.

The diagnosis and treatment of cancer places a negative burden on the geriatric oncology patient. Cancer and related interventions interact with the geriatric patient's concurrent illnesses and onboard medications for chronic conditions. All these considerations have a direct impact on the methods we choose to establish the diagnosis and staging of cancer. Caregivers of geriatric pets appreciate your efforts to provide a rapid cost-effective diagnosis for decision making.

Diagnostic Tools and Techniques Used for Diagnosis and Staging Cancer

Basic tools and techniques essential for diagnosis of cancer in geriatric patients include:

1. Calipers and cartoon body maps to measure and document location of tumors in chart.
2. Point of service laboratory tests (including complete blood count (CBC), chemistries, and electrolytes).
3. FNA cytology with direct microscopic examinations and laboratory confirmation.
4. New methylene blue stain for cytology and impression smears.
5. Punch biopsy and Tru-cut (Travenol Labs Inc., Deerfield, IL) needle core biopsy instruments, scalpel blade/handle, iris scissors, suture scissors, suture, skin glue, clips.
6. Imaging machines: diagnostic x-ray and ultrasound (if possible).
7. Local anesthetic, safe sedation, and anesthesia protocols for minor and major diagnostic procedures.
8. Ten percent formalin solution in a capped bottle, lab request form with history and map.

Utilization of sophisticated diagnostic tools and techniques involving ultrasound, endoscopy, CT, MRI, and positron emission tomography (PET) scanning or nuclear medicine requires collaboration with colleagues in specialty services. The most important goal for the practitioner to keep in mind is to gather as much information as possible with the least amount of stress to the geriatric cancer patient. Actively involve your clients in the diagnostic quest every step of the way so they feel satisfied that you are keeping them informed. This partnership enables the family to make good choices. When thorough and continuous involvement through good communication with the caregiver fails to occur, misunderstandings and dissatisfaction issues regarding cost of care and ultimate outcome of therapy are much more likely to happen.

Fine Needle Aspiration Cytology: A Very Handy but Underutilized Tool

In-house FNA cytology examination is a very inexpensive and rewarding diagnostic tool that is a consistent favorable practice builder. FNA helps to characterize skin tumors, lymph nodes, thoracic and abdominal masses, and effusions. It is definitely worth your while to gain confidence and some expertise in performing in-house cytology. My preference is to look at FNA cytology slides under the microscope immediately to get an idea of what type of tumor we are dealing with. Clinicians who read their cytology slides in house offer a tremendous point of service value that translates into an immediate medical and therapeutic advantage for their geriatric oncology patients.

FNA cells fall into these general categories: lipid, sebum, inflammation, infection, normal benign, hyperplastic, or abnormal cells. Abnormal cells appear bizarre and may exhibit one or more characteristics of malignancy. Characteristics that are easy to detect on cytologic examination that would suggest malignancy are macrocytosis, anisocytosis (variable cell sizes), pleomorphism (variable cell forms), and anisokaryosis (variable nuclear sizes). In addition, the cells may manifest high nuclear-to-cytoplasmic ratio, variable staining intensity of cytoplasm, variable sizes and shapes of nucleoli, and increased or abnormal mitotic figures (Meyer 2001; Cowell 2003).

It is easy and clinically very important to distinguish mast cell tumors (MCTs) from lipomas, wide-based warts, and masses that arise in the dermis and SQ tissues of geriatric pets. After screening for the granules in MCTs and melanomas, your job is to recognize the bizarre spindle cells of sarcomas and secretory vacuoles or epithelial appearance of carcinoma cells. Never postpone FNA of enlarged lymph nodes in geriatric oncology patients. They have a much higher cancer risk than

younger animals. Lymph node cytology is quick, easy, and rewarding. What is most important with in-house cytology is that you can generally start a plan of action using it as a point of service information source while laboratory confirmation is pending (Cowell 2003).

It is essential for clinicians working with geriatric cancer patients to use a reliable reference laboratory staffed with veterinary pathologists or clinical pathologists to read their cytology samples. There is a 15% variation between interpretations for cancer in human pathology vs. veterinary pathology. We have enough variations with pathologists in our own profession without asking for more variables. Identify which pathologist specializes in reading cytology slides and direct your slide specimens and questions to that individual. Turnaround time for samples submitted to your diagnostic laboratory should be within 24–48 hours to expedite patient management. Clients should not have to wait more than a few working days for results.

Lady's Case (Client Satisfaction Is Very Important)

Lady White, a 10-year-old Great Dane belonging to Dr. Angel White, a physician and researcher working at UCLA, developed a large swelling at the right distal radius. Dr. White, who breeds and rescues Great Danes, noticed the mass a week before presentation. I listened carefully to her issues and sensed her distress. She wanted to confirm her own presumptive clinical diagnosis of bone cancer without subjecting Lady's already painful leg to the recommended core biopsies. She had declined thoracic and limb x-rays due to reluctance to submit Lady to sedation or anesthesia.

After a supportive consultation, our staff was able to lift Lady onto the x-ray table and take an AP view of her right distal radius. The lesion appeared radiographically consistent with osteosarcoma. Using a local anesthetic injection of lidocaine and using the x-ray to identify the most lytic area of the lesion, I performed FNA with a 20-gauge needle. The cytology sample was stained with new methylene blue and immediately examined. It revealed osteoclasts and wild sarcomatous cells.

I invited Dr. White to view the cells at the microscope. She took a long look at the cells and then turned toward me with tears filling her eyes and said, "This was all that I needed to help me make my decision. Thank you for helping me to spare Lady from stress and pain." Dr. White has continued to use our oncology service for over 20 years.

If you suspect cancer upon viewing x-rays and FNA cytology, inform the pet owner of your suspicion and provide a short list of differential diagnoses to rule out. Pet owners appreciate a correct diagnosis when it is arrived at quickly, before their anxieties reach high levels. A prompt diagnosis also allows the clinician to advise clients regarding the next best step in the workup, staging, and subsequent discussion of the most suitable therapeutic options. The attending doctor should be the geriatric cancer patient's advocate in decision making. Your clinical judgment, common sense, compassion, and courage can help aging pets derive maximum benefit from diagnostic procedures with minimum morbidity.

Large Aspiration Needle Chop for Firm Tumors

There is a predictable glitch when it comes to FNAs of firm tumors. Be suspicious of firm masses because they are often sarcomas. Because these tumors do not exfoliate well and tend to yield non-diagnostic results, it is important to invest your time and energy into obtaining worthwhile cellular

samples from firm masses. Do not submit acellular samples from firm masses to the lab for cytology. This common failure to harvest cells from firm masses for cytology only wastes your time and your clients' time and money.

Harvesting cellular samples from firm masses is essential for an accurate diagnosis. To address this predictable problem, ratchet up your FNA technique by using a relatively large bore needle as an augur. Thrust an 18-gauge needle attached to a 6 cc syringe into the center of the tumor, and then briskly angle the needle off to one side. This will enable you to capture a tiny core of cells for aspiration. Repeat this procedure in two other directions using the same entry point until enough cells are harvested for cytology, always keeping the needle within the mass. This technique allows the end of the 18-gauge needle to chop off tiny cores of cells for retrieval and cytology. I call this version of fine needle aspiration "large aspiration needle chop" (LANC). The next step is to place a few drops of new methylene blue stain or diff quick stain and view the cells immediately. The LANC technique yields tissue for optimum diagnostic success. You will find that you get a higher rate of positive confirmations using LANC cytology on firm masses.

Many cases of feline vaccine-associated sarcomas (FVASs) experience delayed diagnosis due to the submission of acellular samples using routine FNA techniques.

Keno's Case (Don't Allow the Opportunity for Diagnosis to Slip Away)

Keri noticed a firm interscapular mass on her elderly cat, Keno. Her local veterinarian performed routine FNA, which was non-diagnostic. Keri, who was in the process of moving, drove cross-country with Keno under the incorrect assumption that the mass was benign or not of grave danger.

Three months later, the mass was much larger with extensions that delved toward the dorsal spinous processes. Keri's new doctor referred Keno to our service for consultation. We used the LANC technique and within a few minutes, confirmed that Keno had FVAS. If the LANC technique had been used for Keno's original FNA, it probably would have been diagnostic. Without a proper diagnosis, Keri felt that she lacked the information that she needed to treat Keno's mass quickly and appropriately. A review of the original records revealed that her doctor advised surgical biopsy if the mass did not regress. Keri felt that her doctor should have put her on high alert to rule out cancer without the intimidation of general anesthesia.

LANC would predictably increase the opportunities to establish initial diagnoses in numerous geriatric pets presenting with firm tissue masses. Estimates reveal that there could be as many as 22,000 cats developing vaccine-associated sarcomas every year in the United States, with no change in prevalence worldwide since 1993 (Ford 2004; Kass et al. 1993; Gobar and Kass 2002). Geriatric cats are prone due to the cumulative effect of vaccines over time. The LANC technique provides caregivers one more diagnostic option that may spare the pet from sedation or anesthesia.

FNA should be included in the routine physical exam for any geriatric patient with a mass since 33% of all tumors in dogs and 25% of all tumors in cats arise in the skin (Vail and Withrow 2001; Cowell 2003). My curiosity wants an instant answer and new methylene blue staining makes it easy to immediately view FNA slides under the microscope before submitting the rinsed slides to a clinical pathologist for confirmations as needed. Inform clients that your initial in-house cytology exam is a quality control procedure to locate significant cells. If the first set of FNA slides is not worthy for submission to the laboratory, it is convenient to approach the patient for more cells.

Use a body cartoon map to document the size, location, and FNA diagnosis of skin masses for the medical chart (Figure 5.1a). Be sure to review the basic cytology slides in this section. This collection

will help you to differentiate cells so that you can identify mast cells, leukemia, lymphoma, sarcoma, malignant melanoma, and carcinoma cells. You can offer basic cytology as a point of service test for your clients (Figures 5.1b through 5.6).

Characteristics of Cancer in Cytology

Neoplastic cells are often surrounded by inflammatory cells, cells undergoing apoptosis, areas of hypoxia, cell debris, and necrosis. This explains the heterogeneous nature of tumors and why FNA samples cannot be relied upon to rule out cancer entirely. The consortium of variable cells and

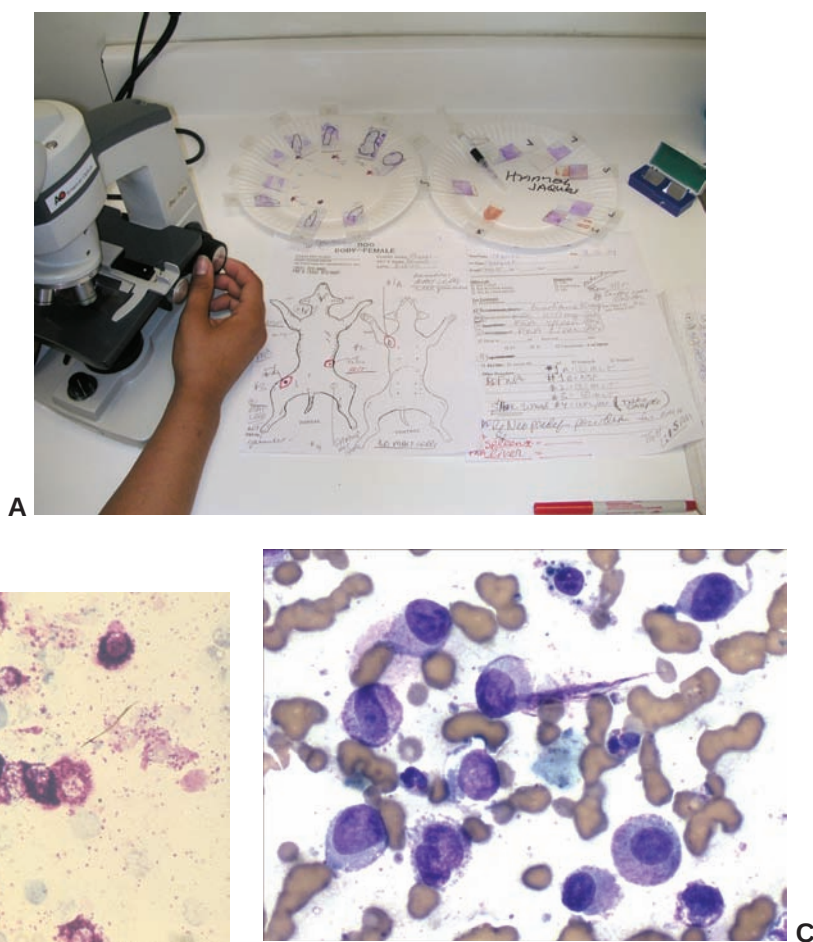


Figure 5.1. Basic features of common malignant cells. Use a body cartoon map to document the size, location, and FNA diagnosis of skin masses for the medical chart (a). Mast cells stained with new methylene blue (b), and with Romanowsky staining (c). Notice the cytoplasmic granules that may be released into the extracellular fluid. Figure 5.1b contributed by Deborah C. Bernreuter, DVM, MS, Veterinary Clinical Pathologist, IDEXX Labs. Figure 5.1c photographed specimens from the author's clinic by Dr. Lon Rich, DVM, ACVCP, Antech Labs.

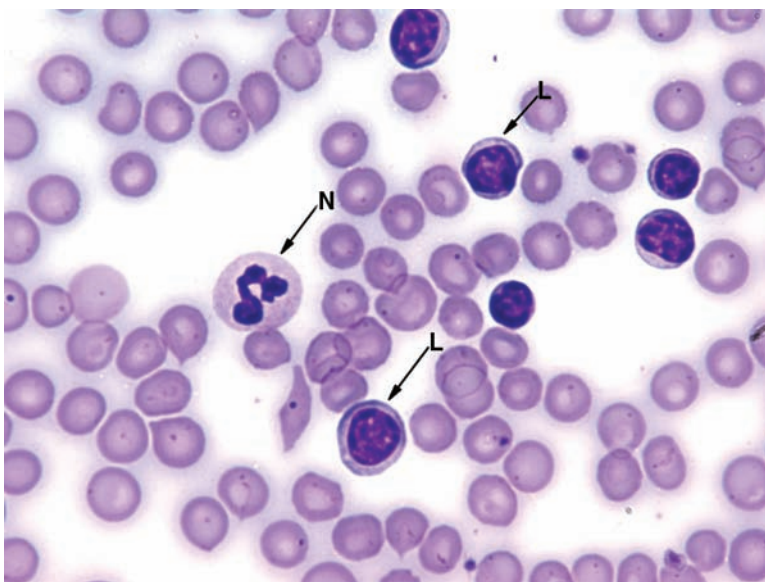


Figure 5.2. Leukemia: lymphoblasts (L), Neutrophil (N). Photographed specimens from the author's clinic by Dr. Lon Rich, DVM, ACVCP, Antech Labs.

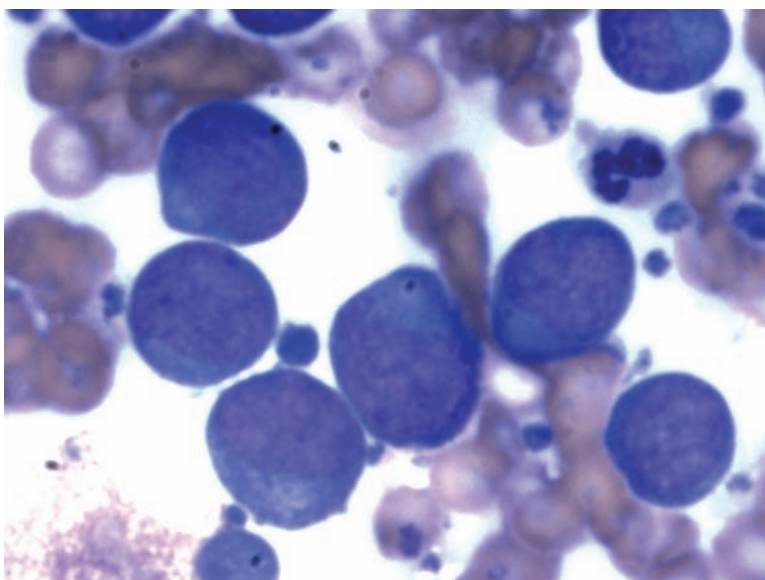


Figure 5.3. Lymphoblasts from an enlarged lymph node. Malignant lymphoma cells are large (blue staining) cells with large nuclei and nucleoli. Contributed by Deborah C. Bernreuter, DVM, MS, Veterinary Clinical Pathologist, IDEXX Labs.

areas inside malignant tumors causes an inherent error factor of 15% for cytology. On some occasions and with certain tumor types, such as feline abdominal masses, persistence is very important and rewarding. I often look at 15 to 20 slides before finding enough intact cells that are representative for diagnostic cytology. If you see 10 or more intact lymphoblasts on a cytology slide from a senior cat with an abdominal mass, you have a working diagnosis of lymphoma. Finding diag-

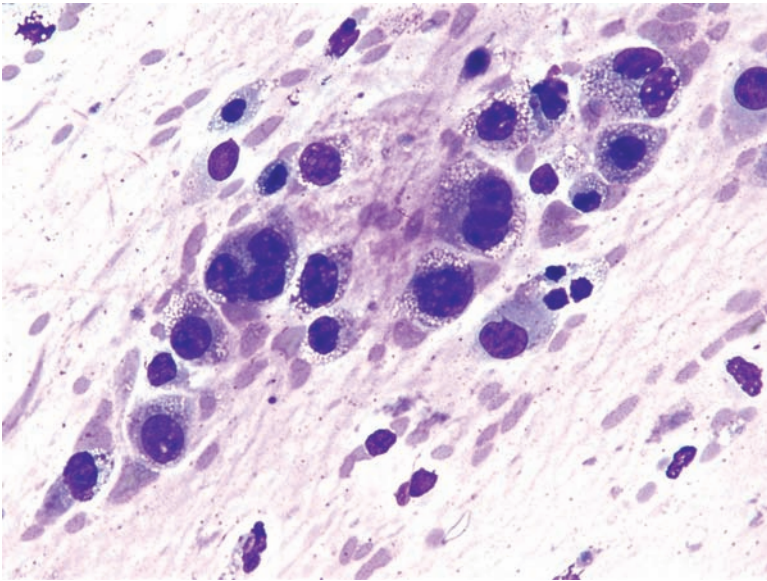


Figure 5.4. Sarcoma from FVAS: Notice the bizarre spindle-shaped cells. Photographed specimens from the author's clinic by Dr. Lon Rich, DVM, ACVCP, Antech Labs.

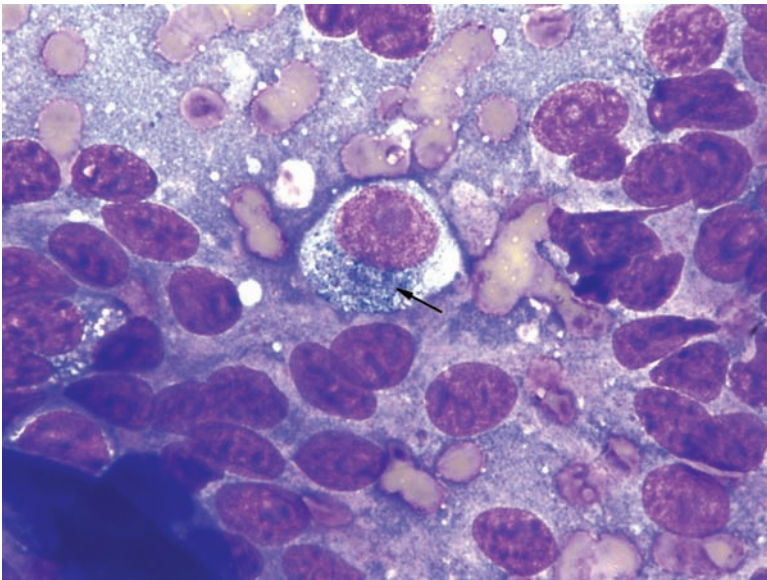


Figure 5.5. Malignant melanoma, showing cytoplasmic black granules. Photographed specimens from the author's clinic by Dr. Lon Rich, DVM, ACVCP, Antech Labs.

nostic cells is very rewarding, especially when it enables you to spare an elderly pet the rigors of exploratory laparotomy. When the cytology findings correlate with the clinical appearance of a mass, it negates the need and expense of sending the slides to the laboratory for further assessment. This saves both hospital and client added expense of using a professional laboratory to report the obvious.

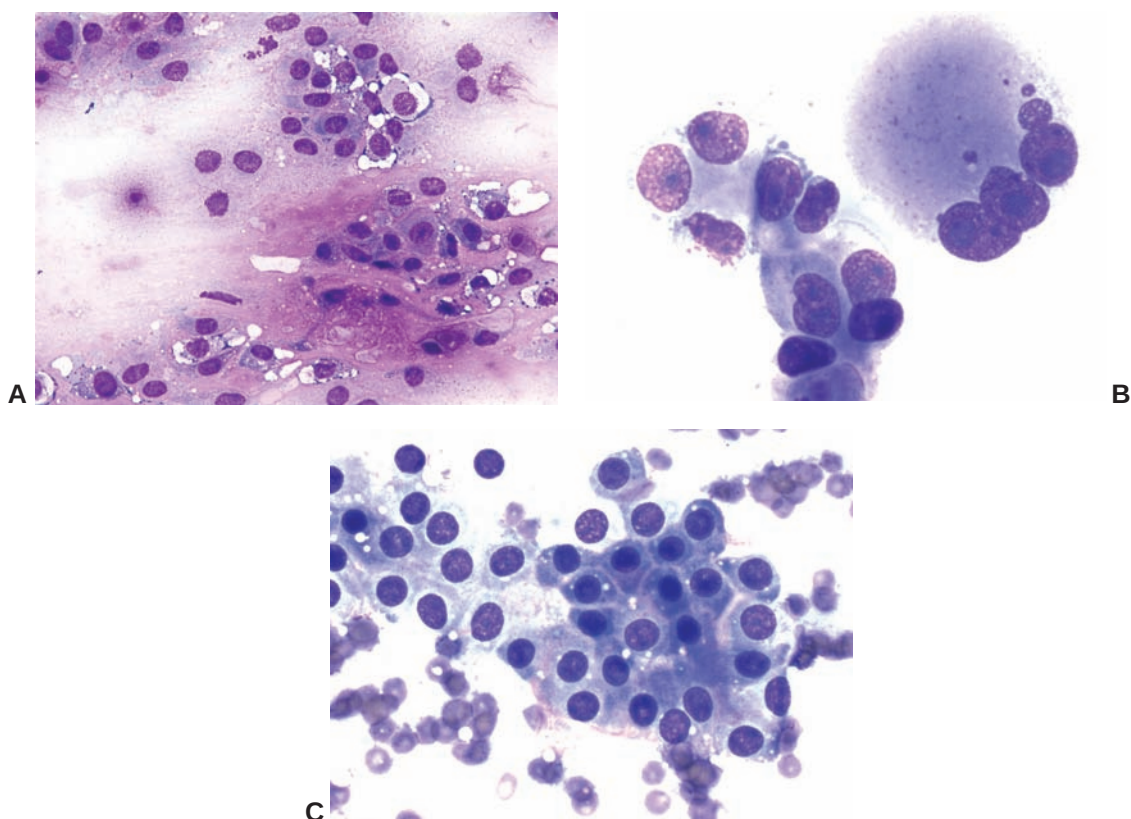


Figure 5.6. Carcinoma (a). Carcinoma showing secretory material (b). Thyroid carcinoma with pink secretory material representing colloid (c). Figure 5.1a photographed specimens from the author's clinic by Dr. Lon Rich, DVM, ACVCP, Antech Labs. Figure 5.6b and c contributed by Deborah C. Bernreuter, DVM, MS, Veterinary Clinical Pathologist, IDEXX Labs.

Nikki's Case (Don't Assume Mast Cell Recurrence until Proven)

Nikki Alvarez, a 12-year-old F/S Shar-Pei, presented with a firm, distended abdomen. Two and a half years previously, we had treated Nikki for MCT of the hard palate with external beam radiation therapy. Nikki was cancer free and on our cure list for MCT. Nikki presented to her local vet with a history of vomiting and reduced appetite. Her doctor palpated a huge abdominal mass on the left side of her abdomen, which he believed was an enlarged spleen. He found that Nikki also had greatly elevated liver enzymes. The referring doctor worried that the splenomegaly might be due to metastatic mast cell cancer.

Ms. Alvarez requested an evaluation for surgery. We performed abdominal ultrasound and FNA of the mass to rule out metastatic MCT. During the ultrasound study, we found moderate ascites and a normal spleen, which was displaced and compressed by a large hepatic mass. The left liver lobe was enormously enlarged and numerous hyper and hypoechoic lesions were imaged in the right liver lobes as well.

We used ultrasound for guided FNAs of the mass. The mass was firm and did not exfoliate cells for our initial cytology study, which did not contain mast cells. We performed another series of FNAs using 1½-inch long 22-gauge needles. By using our special version of FNA

using the LANC technique, we were able to aspirate representative cells for cytology. The cells were stained with new methylene blue and a cover slip was placed over them. The harvested cells had the appearance of hepatocytes and demonstrated several characteristics of malignancy. We also identified some cells that were spindle shaped. Ms. Alvarez wanted surgery for Nikki, if it would afford her a reasonable chance for 3 to 4 months of quality life afterward.

Based on the findings, we advised Ms. Alvarez to enter Nikki into our end of life care Pawspice program. We offered antiemetics and pain control medications and recommended feeding Nikki a liquid diet compatible with liver failure such as Hill's L/D canned food. We also placed Nikki on several supplements that were supportive of liver function. Nikki lived another 47 days in the comfort of her home in Pawspice care.

Punch and Tru-cut Core Biopsy Needle Techniques

Every veterinarian should have quick access to small gauge punch biopsy instruments and Tru-cut needles. The instruments should be handy in the exam rooms, treatment rooms, and in the ultrasound room. Diagnostic biopsies can be taken from most skin tumors of well-behaved geriatric pets simply with the use of local anesthesia and skin glue to control bleeding (Ogilvie and Moore 1995).

Nervous or stressed patients need relaxation and analgesia for many diagnostic procedures. We prefer to use a short-acting intramuscular sedation such as medetomidine (Domitor[®]) in healthy patients. It can be reversed with atipamezole (Antisedan[®]). The low dose combination of Domitor-butorphanol-atropine (DBA) (Table 5.1) delivers smooth sedation with analgesia, allowing most minor procedures. It has the advantage of reversal and smooth recovery. The three drugs are compatible in solution with one another and can be drawn into a 1 ml tuberculin (TB) syringe and administered intravenously via a butterfly catheter in place. This combination is safe for physiologically healthy patients with normal cardiac function. We seldom need the high dose DBA sedation.

For geriatric and frail patients and for patients with cardiac disease, the best choice for IM or IV sedation would be a short acting opioid such as fentanyl in combination with a short acting benzodiazepine such as midazolam.

Skin glue is very handy to seal small punctures and incisions if needed. Clips or sutures are also appropriate for skin apposition following punch biopsy. We often administer an injectable antibiotic at the time of the biopsy procedure if the tumor is infected or if the patient has concurrent UTI, dental disease, pyoderma, or any other antibiotic responsive condition that may affect the post-biopsy period.

Incisional vs. Excisional Surgical Biopsy for Diagnosis

If general anesthesia is required to harvest tissue for biopsy in a geriatric patient, a preliminary database including mucosal clotting time is essential prior to the procedure. It should include a thorough physical exam, a profile to determine organ function, a urinalysis, chest and abdominal x-rays, and abdominal ultrasound if indicated. Sterile surgical technique is employed to prepare the site. When using a punch, Tru-cut biopsy needle, or a scalpel, make sure that the incision penetrates into the tumor without traumatizing the tissue. Take deep samples at several sites in larger masses. Blot blood from the sample and place it on cardboard or wood tongue depressor with an orientation mark. Provide the pathologist with a drawing or digital picture that describes the lesion (Kunkle and Akucewich 2005).

Table 5.1. DBA Sedation and Reversal* Dosage Table

Weight		Domitor (Medetomidine)		Buthorph.	Atropine
		Low	High		
#	kg	ml	ml	ml	ml
1	0.45	0.005	0.009	0.005	0.25
5	2.27	0.023	0.046	0.025	0.25
10	4.54	0.045	0.091	0.05	0.25
15	6.8	0.068	0.137	0.075	0.25
20	9.1	0.091	0.182	0.075	0.25
25	11.3	0.114	0.228	0.075	0.5
30	13.6	0.136	0.273	0.075	0.5
35	15.9	0.159	0.319	0.075	0.5
40	18.1	0.182	0.364	0.075	0.5
45	20.4	0.205	0.410	0.075	0.5
50	22.7	0.227	0.455	0.075	0.5
55	24.9	0.250	0.501	0.075	1
60	27.2	0.273	0.546	0.075	1
65	24.9	0.295	0.592	0.075	1
70	31.8	0.318	0.637	0.075	1
75	34.0	0.341	0.683	0.075	1
80	36.3	0.355	0.710	0.075	1
85	38.6	0.386	0.774	0.075	1
90	40.8	0.409	0.819	0.075	1
95	43.1	0.432	0.865	0.075	1
100	45.4	0.455	0.910	0.075	1
105	47.7	0.477	0.956	0.075	1
110	50.0	0.500	1.001	0.075	1
115	52.3	0.523	1.047	0.075	1
120	54.5	0.545	1.092	0.075	1
125	56.8	0.568	1.138	0.075	1

Source: Adapted from Grimm, J.B., L.P. de Lorimier, and K.A. Grimm, 2006, Medetomidine-butorphanol-glycopyrrolate sedation for radiation therapy: An eight year study of 6,329 sedations in dogs and 1,862 sedations in cats for radiation therapy at the University of Illinois, Urbana, as presented in several meetings, quoted on VIN message boards, and pending publication; Grimm, J.B., K.A. Grimm, S.K. Kneller, W.J. Tranquilli, S.S. Crochik, M.G. Bischoff, and J.L. Podolski, 2001, The effect of a combination of medetomidine-butorphanol and medetomidine, butorphanol, atropine on glomerular filtration rate in dogs, *Vet Radiol Ultrasound* 42 (5):458–462.

*Reversal with Antisedan (atipamezole) using same ml as Domitor IV, IM.

Inflammation, necrosis, and tumor heterogeneity may obscure the diagnosis; therefore, it is best to take several samples along different tracts. Tissue samples taken at the periphery of the mass often have more viable cells and yield more information regarding invasiveness. The needle track used to harvest the biopsy must be recorded or marked on a map or directly on the skin with ink or sutures. If and when the tumor is excised or irradiated, the biopsy track(s) must also be included in excision or in the radiation therapy field. For bone marrow aspirations and biopsy of lytic bone lesions, be sure needle placement is accurate so that a representative sample may be harvested (Friedrichs and Young 2005; Withrow 2001).

It is quite easy to insert a Tru-cut needle instrument into a lymph node or tumor for diagnostic histopathology and tumor grade. Tru-cut biopsy is especially useful before attempting surgical excision

of any mass scheduled for surgery. An unknown excised mass has the potential to be a malignant tumor such as a MCT or a soft tissue sarcoma. Most well-behaved geriatric patients only require a topical or locally injected anesthetic for Tru-cut biopsy, as it is a minor procedure. Taking a punch biopsy even with the smallest gauge instrument requires an injection of local anesthetic and mild sedation.

Some doctors prefer the rapid induction and rapid recovery achieved using inhalant sevoflurane as a “sedative” technique. Geriatric cats can be conveniently given inhalant anesthetics in an anesthetic chamber and maintained with mask delivery. During sedation, look for other minor procedures that can be done to enhance the geriatric oncology patient’s quality of life, such as trimming overgrown nails, dental and ear cleaning, coat care, and so forth. This added care is especially important for older cats with oral tumors. These patients drool on their legs and paws, so their coats are generally unkempt and require constant cleaning.

Gunter’s Case (The First Surgery Can Be More Effective with FNA)

Gunter Fillmore, an 8-year-old, 98-pound M/N Weimaraner, developed a mass that appeared suddenly in the medial aspect of his right elbow. We treated him for a soft tissue sarcoma in the footpad of his left front leg the previous year. Gunter’s attending doctor removed the mass immediately and submitted it for histopathology. Ms. Fillmore called me in despair after learning that the mass was a grade I–II MCT excised with narrow margins. She felt that Gunter had lost his battle against cancer. I explained that the two tumors were unrelated and recommended a consultation to review the biopsy report and discuss options for dealing with the new tumor. The report described it as well differentiated with a low mitotic index. The margins were complete but inadequate for MCT. Gunter was referred to a board certified surgeon for excisional biopsy of the entire tumor bed. In my opinion, the second surgery could have been avoided for Gunter if his attending doctor performed FNA prior to surgery or used the rule of thumb principle of acquiring margins at least the size of the mass.

Some clinicians prefer to remove a suspicious mass quickly and get it over with. They often feel confident that their margins are seemingly complete at the first attempt. They submit the tissue to the pathologist and feel satisfied that they are serving their clients well by this approach. Their intent may be to avoid problems associated with biopsy of potentially “excitable” tumors or to avoid problems following the incisional biopsy procedure itself. But this approach may not be the best procedure for the patient. Attending doctors must think clearly and analytically about gathering more information on tumors prior to excisional surgery. At the very least, the clinician should determine if the mass is an MCT so as to plan for adequate 2–3 cm margins. If the surgeon knows preoperatively that a mass is a sarcoma or carcinoma, the patient is more likely to benefit with a wider, deeper excision and a true cut or wedge biopsy of the local and regional lymph nodes for staging purposes.

When excising a mass without the precaution of FNA cytology, it is best to acquire wide, deep margins around the mass that are at least the same size as the mass itself. This extra measure at surgery may achieve adequate margins around the tumor and save the patient a second surgery in the event that the mass is subsequently found to be a malignancy.

Histopathology Terms: Adequate or Complete Margins

The terms “complete margins” and “adequate margins” are often used by pathologists. They may seem interchangeable, but the distinction is of great significance to the patient’s survival. When

veterinarians read the word “complete” in the report, they want to believe that they “got it all” and that the surgery was complete enough for the case. In reality, “complete” indicates only that the tumor was removed in its entirety and does not indicate that the margins around the tumor are adequate for decreased recurrence or increased survival time.

The achievement of “adequate margins” occurs when the margins around the completely removed mass are wide enough to expect a lowered recurrence rate and an increased tumor-free interval. Complete margins are not as good as adequate margins, although the literal interpretations of these words in pathology reports have been misleading clinicians for years. Be very clear about the clinical significance of terminology and the definition of the words that your pathologist uses (Figure 5.7).

Intraoperative Cytology

A quick and inexpensive way to determine clean margins during surgery can be achieved by using intraoperative cytology. This is an underutilized diagnostic procedure that can make a big difference in the efficacy of surgical excisions. Intraoperative cytology has the potential to dramatically decrease recurrence rates and increase the tumor-free interval as well as patient survival times. We use intraoperative cytology most often when dealing with known MCTs, SCC, and soft tissue sarcomas.

When an undiagnosed mass is removed, use intraoperative cytology to determine the nature of the mass. Before placing the mass in the specimen jar for histopathology, make impression smears from a cut surface of the mass and look for mast cells or sarcoma cells. This information gives the surgeon the opportunity to excise the mass more aggressively, and perhaps to spare the patient a second surgery.

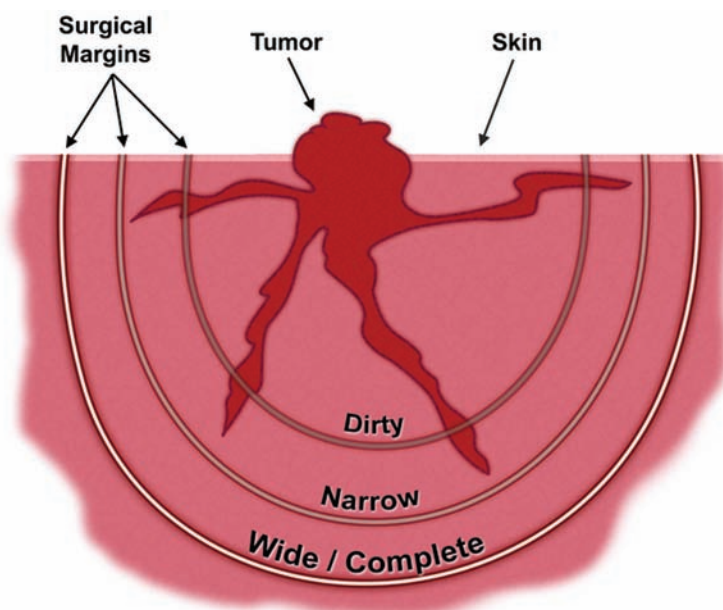


Figure 5.7. The octopus-shaped malignancy showing dirty, narrow, and adequate surgical margins.

To examine margins, make impression smears of the anterior, posterior, lateral, medial, and deep margins. Place the marked slides on a paper plate and examine them immediately under the microscope. If malignant cells are found on one or two of the slides, the surgeon knows where to cut more deeply to gain clean margins before closure. This requires cooperation between the surgeon and the person reading the slides and patience on the surgeon's part to wait for a go ahead before closure. It also extends anesthesia time for the patient, but with practiced teamwork between the surgeon and the reader, this time can be kept to a minimum.

I tell pet owners that this technique is the closest thing to Moh's surgery that we can offer our cancer patients. Moh's surgery involves the luxury of having frozen sections analyzed by a pathologist during surgery with immediate feedback to the surgeon to guide the adequacy of the excision. Intraoperative cytology is a practical and rewarding procedure that adds direct value to the veterinary surgical oncology effort and success. We use this technique as margin studies for known tumors and it is a valuable adjunct in routine mass excisions as well.

Sunshine's Case (Intraoperative Cytology Saves Lives)

Sunshine Johnson, an 8-year-old Afghan Hound with SCC of the rostral maxilla, was on the surgery table. Repeated intraoperative cytology slides found tumor cells streaming upward from the mass. Cancer cells were identified along the intended dorsal incision and invaded into the base of her nasal frenulum. I guided our surgeon to expand the excision dorsally. He provided me with several margin samples containing cancer cells. After several more cuts, the samples became free of malignant cells. I called Ms. Johnson during surgery to explain that there would be an unanticipated cosmetic defect because we had to take some of Sunshine's frenulum to gain clean margins. Sunshine developed osteosarcoma at 11 years of age and lived three-legged to the ripe old age of 12. She remained cancer free at her rostral maxilla.

A Word About Unhelpful Diagnostic Abdominal Surgery

FNA is overlooked far too often as a reliable diagnostic tool in the assessment of abdominal masses, especially in the senior and geriatric feline. Veterinarians often recommend exploratory surgery without suggesting FNA or ultrasound to better characterize the pet's abdominal mass. All too often, the caregiver is referred exclusively for surgical consultation after initial palpation or imaging of an abdominal mass.

The same push for exploratory laparotomy may also come from the surgeon following ultrasonography that anatomically visualizes but does not diagnose the patient's mass. The surgeon should not be more focused on the priority of removing an abdominal mass over the discovery of what the mass is. Geriatric cats are better served when the surgeon first rules out lymphoma, the most common cause of abdominal masses in cats. For non-obstructed patients, medical management is better than surgery.

Being rushed into abdominal surgery for mass removal is a problem for cats everywhere, especially for debilitated cats. Many elderly cats with GI or abdominal lymphoma can be definitively diagnosed with diligent sampling via percutaneous FNA cytology or true cut needle biopsy of their abdominal masses without the systemic stress of exploratory surgery. In fact, abdominal surgery is often counterproductive and may be a major setback for the geriatric patient.

Tessa's Case (Splenectomy Is Not Always Needed)

Tessa was a F/S DSH brown senior cat around 14 to 16 years old. Tessa was lethargic around the house. Her attending doctor initially referred Tessa to an internist for abdominal ultrasound evaluation. She had palpated small kidneys and felt that Tessa needed a more thorough workup. The ultrasound study found a 2.5 cm, highly echogenic mass in the tail of the spleen. FNA was not performed at that time.

At discharge, the internist recommended splenectomy as the treatment of choice with no further diagnostic tests. Bonney, Tessa's caregiver, asked if there was a test that could be done to figure out if the mass needed to be removed. The internist told her that it was better to just remove it. Bonney declined the surgery, fearing that Tessa was too old. She shared this fear with the attending doctor, who then referred her to our service for FNA of the splenic mass and a second opinion.

We located the mass in the spleen on ultrasound and obtained an FNA from the mass using a 27-gauge needle for FNA. We were able to aspirate several slide samples for cytology. We diagnosed the mass as lymphocytic hyperplasia on FNA. Our professional laboratory confirmed the diagnosis. This condition in the spleen, mesenteric lymph nodes, or intestines may be a precursor to lymphoma. We discussed options with Bonney and she elected to place Tessa on conservative chemotherapy to see if there was a response. This option would address the problem and avoid the angst and the debilitation of surgery. Tessa started to feel better from the moment treatment with oral prednisone and Leukeran began. The mass reduced in size and, after 8 weeks of oral chemotherapy, Bonney elected to discontinue treatment because Tessa was feeling much better and resisted being medicated.

The trauma of cancer surgery, recovery, and hospitalization may stress a geriatric feline lymphoma patient into a downward spiral. Following exploratory surgery for the diagnosis of lymphoma, the surgeon and/or attending doctor often informs the owner that definitive chemotherapy must be postponed because it delays wound healing. This precaution is justified for recovery of geriatric patients with intestinal anastomosis. It is sound advice to delay definitive chemotherapy for these patients, but a 10–14 day delay may reduce the chances for survival. The patient may recover in the hospital under doctor's care but lack specific care needed to deal with the rampant lymphoma.

When asked to consult in such scenarios, I tell pet owners that oncologists think differently. The cancer does not arrest itself and wait on the sidelines while the patient is healing. Over the years, this has been my experience when dealing with abdominal (GI, renal, hepatic splenic) lymphoma in the feline. Oncologists work hard to finesse a diagnosis from a feline patient's heterogeneous abdominal tumors with diligent FNA cytology or Tru-cut needle biopsy and impression smears. Acquiring a relatively non-invasive diagnosis allows the safe and immediate use of induction chemotherapy and avoids subjecting geriatric cats to unhelpful or deleterious surgery.

Sweet's Case (Cytology Can Preclude Surgery)

Sweet, a 14-year-old F/S DSH, was in the arms of her high-strung, nervous caregiver, who paced the room repeating, "She is the love of my life." But the timing was horrible. The caregiver was getting married in a week, merging two families together, moving to a new home, and leaving for a 3-week honeymoon. Sweet was vomiting and had anorexia for 1 week. Her attending veterinarian palpated an abdominal mass and scheduled Sweet for ultrasound. The visiting radiologist, who performed the study, found a 1 cm thickened bowel loop extending 6 cm but did not do FNA for cytologic diagnosis.

A consultation with the staff surgeon was scheduled at the time of pickup. The surgeon advised immediate exploratory surgery with the intention of removing the affected bowel. Sweet's owner was overwhelmed and declined surgery. She wanted to take Sweet home for a few days to think about it and get a second opinion. During our consultation, we explained that the most common type of cancer in the feline abdomen was lymphoma and that we might be able to diagnose the tumor via FNA and treat it medically.

We located the mass with ultrasound and performed ultrasound-guided FNA. The cytology slides were clearly diagnostic for lymphoma. We advised chemotherapy to see if it might reduce the mass without surgical intervention. We were given permission to administer chemotherapy, antiemetics, and an esophageal feeding tube.

Since the family would be on honeymoon for 3 weeks, we used L-asparaginase for induction and Adriamycin for its 3-week activity against lymphoma. The family was relieved that we were able to make a diagnosis and start definitive treatment without surgery. Sweet's caregiver was tormented with the emotional and financial burden of continuing chemotherapy and supportive care. After a few days, the new family realized that they had no time for the rigors of feeding and medicating and could not budget for the estimated costs. The family was able to arrive at this difficult realization based upon the FNA diagnosis and initiation of therapy without surgery.

Wally's Case (Look for Pitting Defects)

Wally, a 12-year-old Old English Sheepdog, developed a right-sided nasal discharge. Wally's referring veterinarian was unable to find a foreign body or any lesions worthy of biopsy during routine rhinoscopy using an otoscope. At presentation, there was no facial deformity, but on careful palpation of Wally's muzzle, a pitting defect was found, located along the proximal right side of his dorsal muzzle. FNA through this 1 cm lesion identified numerous malignant SCC cells on cytological examination.

Cytology of Fresh Blood Smears

Being curious and accurate about the immediate health status of the geriatric oncology patient allows instant decision making that may be life saving. Point of service laboratory evaluations for cancer patients reduce the guesswork and the omission of potentially life-saving stat care and supportive services. The need is most evident when dealing with oncology patients that have profound leukopenia, hypercalcemia, renal damage, or sepsis. A certain percent of geriatric oncology patients will present in preclinical and or precritical functional compromise. Identifying these complicating conditions on a stat basis clearly saves lives. The benefits to the patient are obvious and enhance the rewards found in successful case management.

World-famous Dr. Oscar Schalm was my hematology instructor at the University of California, Davis. He stressed the importance of looking directly at a patient's blood. If you practice oncology, you will lose animals unless you are prepared to look at fresh blood smears. In certain instances, you need to know what the patient's blood cells look like on a stat basis in order to identify or verify morphologic abnormalities such as leukemia (Figure 5.2), leukopenia, thrombocytopenia, autoagglutination, poikilocytosis, reticulocytosis, nucleated red blood cells, and so forth. Only if you know what your patient's blood looks like will you know when to disagree with the machines.

Look at fresh blood smears alongside automated CBC results. At each recheck visit for cancer patients, especially for chemotherapy patients, we need to directly evaluate some of the abnormalities reported by automated CBC units. When the white blood cell count is high, we must verify that we are dealing with leukocytosis vs. leukemia. If there is a low white blood cell count or a low platelet count, look at a fresh blood smear to verify the findings. Sometimes there are plenty of platelets, but they are clumped and will not read accurately on the automated units. If the white blood cell (WBC) is extremely low, the machine won't register any results and you must look at the smear directly to assess the presence or absence of white cells.

Leukopenia should be determined on a stat basis at your clinic for urgent care decision making. The sample can be sent to a professional laboratory for an exact count, but if you depend on an outside lab for this value, the patient may be in crisis before the lab results are in. If the clinic's lab equipment is unreliable or breaks down, you will need to look directly at the cells to expedite a decision. If in doubt, hold off on chemotherapy and provide supportive care until you get the results back from the lab.

It is convenient to use point-of-service (in-house) CBC equipment and chemistry machines to immediately assess the patient's hematology and organ function status. This information is required for on-the-spot decision making and dose adjustment before writing up orders for a patient's chemotherapy. Some of our referral clinicians do not have point-of-service laboratory equipment and they are unprepared or reluctant to examine fresh blood smears. They ask their clients to bring the pet in for blood work 1 or 2 days in advance of the chemotherapy date. This is acceptable but certainly places one more time-consuming burden on the client.

We often get a call from an attending clinician when a cancer patient presents with signs of chemotherapy toxicity or an adverse reaction. I always ask the doctor to take a CBC and examine a fresh blood smear. I ask the clinician to prepare the slides properly with special attention to the feathered edges and to assess white blood cells and platelets to see if they are present in normal or high numbers or absent. As a rule of thumb, if there are less than one to four white blood cells per high power field, we are dealing with leukopenia. If the patient is not febrile and has between two and four white blood cells per high power field, supportive care with outpatient antibiotics and symptomatic care may be all that is needed.

This clinical assessment is easily accomplished with an outpatient visit. The pet may be discharged with instructions for the pet owner to monitor the temperature twice daily, SQ fluids, oral antibiotics, and so forth. If there are less than or only zero to two white blood cells per high power field and the patient is febrile or sick, then immediate hospitalization is needed for IV fluids, antibiotics, and neupogen along with intense supportive care (see the section "Adverse Effects of Cancer Therapy in Geriatric Pets" in chapter 6). Immediate and direct assessment of the fresh blood smear, electrolytes, and blood chemistries is essential in providing the best care for the ongoing needs of geriatric cancer patients, especially those receiving chemotherapy.

Clinical Pathology and the Geriatric Cancer Patient

Elder pets are referred to our oncology service with a smorgasbord of concurrent conditions and diagnostic dilemmas. Geriatric cancer patients may have halitosis, polyarthritis, and/or endocarditis related to their advanced dental disease. Older dogs often have mild to severe arthritis, chronic heart disease, hypothyroidism, Cushing's disease, diabetes, or other ailments. Always ask the family if the pet is on any over-the-counter drugs, such as aspirin for arthritis.

Geriatric cats may also have concurrent hyperthyroidism, heart murmurs, inflammatory bowel disease (IBD), feline triad disease, CRF, obesity, diabetes, dehydration, and cachexia, to name some of their more common problems. Chemistry profiles should be rechecked if the most recent panel is over 1 month old.

The new profile may restate the previous general organ function abnormalities such as elevated hepatic enzymes, alkaline phosphatase, renal disease, or endocrinopathy. The urine analysis may reveal a sub-clinical urinary tract infection or show low specific gravity or bilirubinuria or micro-albuminuria. If the BUN and creatinine are elevated preoperatively, then the patient's values must be monitored post-operatively. These pretreatment values must also be re-evaluated before starting chemotherapy and during the course of chemotherapy to make the proper dosage adjustments.

When treating senior and geriatric pets with cancer, concurrent organ compromise must be carefully diagnosed and kept in mind during the diagnostic workup. These patients will require dose reduction of at least 25% and up to 50%, depending on the degree of organ compromise. Precautions for pets with CRF may necessitate admitting the patient into the hospital the day before procedures such as surgery or drug administrations that are expected to compromise renal function. The CRF patient can be given IV fluids during the 12–24 hours before treatment or before surgery. After the procedure, the patient may require 24-hour follow-up on IV fluids for 1 or 2 days in recovery. You may need to adjust the CRF patient's diet and make recommendations for daily SQ fluids as home care maintenance.

If CRF patients are to receive chemotherapy, elevated renal values signal the need for a dose reduction, especially for those drugs that are excreted by the kidneys (cyclophosphamide, vincristine, carboplatin, etc.). For dogs with CRF or compromised GFR, cisplatin should *not* be used because it is extremely nephrotoxic and would invite disaster. Cats should *never* be given cisplatin because it is extremely toxic to felines, causing respiratory failure.

Geriatric animals with compromised renal and/or hepatic function do not eliminate chemotherapy drugs properly. They may become toxic and exhibit signs of overdose with vomiting, diarrhea, anorexia, fever, immunosuppression, and leukopenia. Some pets may develop sepsis or pancreatitis, which may be fatal if the problem is not identified early and treated vigorously. The trouble with treating debilitated cancer patients is that it can be difficult to determine if it is the patient's illness or the treatment that is causing a specific problem.

Elderly pets, especially those with compromised or marginal organ function, require reduction of the initial chemotherapy dose by 25–30%. When using Adriamycin in geriatric large and giant breed dogs or in dogs with heart disease, I sometimes use a split dose schedule. This technique involves administering a proper therapeutic dose of drug but divided over a longer time span of several days to 1 week. The split dose schedule has become my preferred method for administering Adriamycin to geriatric large and giant dogs. We administer 20 mg/M² on the initial treatment day and then another 20 mg/M² 6–8 days later, working it into the protocol.

The split dose method addresses the thinking that large breed dogs are under-dosed with the meter squared (M²) scale. It also addresses the need to use precautions to limit the cardio and GI toxicity of Adriamycin. If the patient is able to handle the initial dose of drug without significant adverse side effects, and CBC and blood chemistries remain normal, dose escalation at the following cycle would then be considered for that patient.

When clinicians commit to the philosophy of close observation of the CBC and organ function, at all stages of the workup and during all stages of treatment, the patient benefits and the clients will be pleased. If you can, on a preliminary basis, evaluate the cells of any mass in question, assess a fresh blood smear, and react quickly to adapt therapy to the geriatric patient's organ function and

needs, then you are practicing responsive medicine. It is exhilarating to know that you can provide great service for the geriatric cancer patient and to feel on top of your chosen profession.

Imaging Detectable Tumors

A mass must be at least 0.5–1 cm before it can be visualized by most anatomic imaging techniques used in veterinary medicine today. Newer functional imaging techniques may detect smaller nodules at 3–5 mm. A small mass contains up to a billion cells by the time it is detectable. The inherent problem with traditional anatomic imaging of tumors is that we are looking for a mass. Unfortunately, by the time enough cancer cells have accumulated to form a detectable mass, it may have already experienced up to 25 doubling times and released its athletic cells to metastasize under the radar of the geriatric oncology patient's immunosurveillance system.

The use of anatomic imaging in the management of cancer patients is essential, but it cannot definitively diagnose a mass as a malignancy. The differentials may be inflammation or infection. This domain belongs to pathology. The value of visualizing a few malignant cells in the microscope remains the final word in the diagnosis of cancer. Imaging is used to locate, to stage, to guide for FNA and biopsy, for follow-up assessments, to monitor for recurrence, and for guiding the delivery of therapeutic or ablative agents.

Imaging Tumors with Radiography

Imaging with radiographs is the cornerstone of anatomic imaging services in most veterinary practices. The field of diagnostic radiology offers excellent textbooks for positioning, exposing, and reading. The points I would like to stress are quality and quantity. For senior and geriatric pets, radiographs should be suggested more often, especially as part of their routine senior wellness exams.

All coughing, limping, vomiting, and straining elderly pets have a justifiable need for radiographs. The thorax is not fully evaluated for tumors unless three views are assessed (right and left lateral views as well as the ventro-dorsal [VD] view). Thoracic tumors that are not visible in usual two-view routine films may be found in the left lateral exposure. If you are restricted from taking three views of the thorax because of an owner's financial constraints, inform your client that the study will be limited. Tell your client that this limited approach is a "scout" study.

If your facility is inconvenient for radiology or if your staff members have objections to the restraining techniques for using the equipment, it is essential to make the necessary changes so that radiography is a welcome procedure. Establish safe protocols for mild sedation for geriatric patients. The proper size x-ray cassettes should be on hand and they should be cleaned routinely. The proper film for the job should be available, such as non-screen mammography film for high-detail open mouth radiographs of the nasal passages, maxilla, and mandible. Good technique is essential to get high-resolution films of the skull and nasal passages, especially if dental film and dental radiography are not set up in your practice. All x-ray films should be marked properly for easy identification of the dates to compare recheck radiographs as you follow the patient's progress.

Digital radiography offers tremendous advantages and versatility. The equipment is expensive but it makes sense for high-volume practices to make the investment. If your practice takes a lot of radiographs, the overall savings on staff time, film, processors, and maintenance fees for processors may offset the initial capital investment in the long run.

Imaging Tumors with Ultrasound

My personal favorite diagnostic imaging instrument is the ultrasound machine. During the 1960s and '70s, we used real-time fluoroscopic imaging at UCLA for placing catheters that ran from the femoral artery into the heart or from the carotid artery into a brain tumor.

My first ultrasound unit was purchased in 1982. We upgrade ultrasound machines every few years and are ever on the look out for a better unit. There is nothing more enjoyable for me than to invite the caretaker and patient into our ultrasound procedure room. We instruct them to verbally comfort their pet and to encourage the pet to stay in position in the v-cut boat while they witness the ultrasound study. It is easy to determine if a mass is solid, cystic, or cavitated. We use ultrasound imaging for anatomical detection of tumors, for staging, for guiding FNA and Tru-cut needles, for centesis, and for guiding the delivery of intralesional therapy.

One of the most frequent uses of ultrasound in my practice is to evaluate patients on a per-region basis and for routine periodic follow-up assessments. We check on the size of a bladder tumor to see if it has reduced after chemotherapy and we image the patient's kidneys to see whether or not hydronephrosis has developed. We may evaluate the progress of metastatic hepatic lesions and primary masses to evaluate their response to therapy. In cats with abdominal or anterior mediastinal masses, we use the ultrasound to guide us for centesis of effusions, to guide FNA, and to monitor progress.

It is very easy to teach a technical staff to collect urine from a small bladder using the ultrasound for guidance. Ultrasound also offers the ease of identifying structures in patients with ascites when x-rays provide poor resolution. You can assess PUPD in intact female patients for pyometra and you can check that Golden Retriever with weakness and muffled heart sounds to immediately rule out pericardial effusion from hemangiosarcoma. There is nothing like having an ultrasound machine at your beck and call to excite and enhance your practice.

The terminology used to describe structures during ultrasound evaluation employs lengthy words such as hypoechogenic and hyperechogenic, cavitations, granularity, transitional zones, artifacts, and nodularity. For this reason, I suggest using a special ultrasound report form with all of the appropriate words so that the description of each organ may be checked off to expedite reporting and record keeping. We take digital pictures of the images for storage. Ultrasound-guided FNAs and true cut biopsies of tumors in the abdomen are routinely used for diagnosis and staging. Peripherally located thoracic masses may also lend themselves for ultrasound guided FNA when accessible. Occasionally, thoracic masses are situated peripherally enough so that it is considered safe to proceed with ultrasound-guided Tru-cut biopsy.

Ali's Case (An Old Akita Struggled Before Thoracotomy)

Ali Dehener, a 12-year-old F/S Akita, had a long history of gagging episodes. She started with a mild cough that progressed for 2–3 months. Referral chest x-rays showed complete consolidation of the left lung lobe. In my opinion, Ali's pulmonary condition posed an anesthetic risk for diagnostic procedures. During consultation, we advised ultrasound-guided percutaneous FNA without sedation or anesthesia. We infiltrated a local anesthetic into the intercostal site selected for percutaneous FNA and inserted a 1½-inch 27-gauge needle through the involved lung lobe into the mass and aspirated gently. Our FNA cytology samples contained mucinous debris and an occasional cluster of round pleomorphic cells. The cells possessed several malignant characteristics consistent with carcinoma. Our working diagnosis was primary

bronchogenic adenocarcinoma and our clinical pathologist confirmed it. Chest x-rays showed no hilar adenopathy. Based on this information and normal blood values, I was ready to send Ali to surgery right away but our surgeon insisted on a CT scan prior to thoracotomy. Ali suffered a major setback following the anesthesia and positioning protocol for the CT. Mucus and debris spilled into her airways, causing fever of 106 degrees and pneumonia. She was hospitalized for 7 days on IV antibiotics. The CT confirmed that her cancer was localized in one lung lobe. Ali underwent lobectomy and survived an additional year with excellent quality of life until recurrence.

Note: A standing tracheal wash procedure may also be helpful in cases like this. When there is a history of coughing or if x-rays identify lesions close to the major bronchi, tracheal washing may yield material for culture and sensitivity tests and for cytology.

Screening Senior and Geriatric Patients with Imaging

It is easy and convenient to screen the abdomen and heart with ultrasound. My ideal would be to hold semi-annual ultrasound wellness exams to check the spleens and hearts of senior and geriatric Golden Retrievers and German Shepherd Dogs to rule out hemangiosarcoma. Until routine blood samples can detect cancer in pets, imaging exams are not overly cautious because as many as 2.5 million dogs are estimated to die of hemangiosarcoma in the United States each year (Lamerato-Kozicki, Helfand, and Modiano 2005). Proactive breed screening makes sense since one in six Golden Retrievers is diagnosed with hemangiosarcoma at the average age range of 7–9 years and one in seven get lymphoma at the average age range of 6–8 years. The Golden Retriever Club National Survey found that 67% of males and 57% of females die of cancer and that the largest males are more prone (Glickman, Glickman, and Thorpe 2000).

Since 50% of dogs and over 30% of cats over 10 years of age die of cancer, it makes sense to consider using available methods of inexpensive imaging for screening with x-rays and ultrasound as part of a complete wellness exam. Soon there may be reasonably priced laboratory and/or blood tests that can check for sarcoma, carcinoma, and lymphoma tumor markers in dogs and cats. Until then, we have to rely on the physical exam and manual methods of anatomical imaging for proactive screening of our highly valued geriatric patients.

Imaging Tumors with CT and MRI

Computed tomography and magnetic resonance imaging are very helpful non-invasive technologies that can be used in the workup and staging of the geriatric cancer patient. CT and MRI enable us to make better treatment decisions because we know more about the anatomic extent of the patient's tumor.

CT scans the body using ionizing radiation in the form of x-rays. Sir Godfrey Hounsfield, who made the first CT scan machine in the 1970s, developed practical CT. He shared the 1979 Nobel Prize in medicine with physicist Allan Cormack, who wrote the first theoretical papers on the CT-scan system.

Today, newer generation CT scanners yield excellent studies for bone, soft tissue, and vasculature with the use of enhancement agents that allow better contrast. Contrasted CT is very helpful for

selecting operable tumors, such as prostate tumors, in humans. CT is used to visualize whether neoplasia is confined within the prostatic capsule or if it involves the urethra. This technology can be used for dogs to determine if an early stage prostatic tumor is operable (Henderson 2004, 2005). In veterinary medicine, CT is currently the preferred method for anatomic imaging of tracheobronchial lymph nodes in patients with primary lung tumors prior to surgery. The prognosis for survival post-lobectomy exceeds 1 year for dogs with negative node studies vs. only 6 months for dogs with infiltrated or enlarged tracheobronchial nodes. CT imaging is also very helpful in evaluating the chest for the diagnosis of metastatic disease.

Ulla's Case (Always Offer Clients All the Options)

Ursula was passionate in her quest to do the right thing for her beloved Ulla, a 9-year-old F/S Rottweiler. She came to us for consultation following a rib resection for Ulla's osteosarcoma (OSA). A bone scan performed prior to the rib resection was negative for metastatic disease. Ulla's chemotherapy treatments went well. She received six treatments of carboplatin in rotation with two cycles of Adriamycin. Eight months later, Ulla started having petite mal seizure-like episodes. We were very suspicious of metastatic disease but unable to document it with routine three-view chest x-rays. FNA by our LANC technique, described previously in this chapter, found no significant cells. Ursula expressed anxiety about spending so much family money on Ulla. We discussed the value of further imaging. If the results of the study were not going to change Ulla's treatment, then it would be a pointless expense. I learned more about the power of the human-animal bond and the inquiring mind of Ursula when, a few weeks later, she opted to have a CT scan of Ulla's lungs. The CT scan revealed that Ulla had seven or eight small metastatic lesions of variable size, distributed in multiple lung lobes. These small metastatic lesions were not detected in her most recent radiographs.

Ursula came in for a heart-to-heart consultation about her options. She felt that she just had to know what was causing Ulla's seizure-like episodes and now that she knew, she could deal with the grief. Ulla was not a good candidate for metastatectomy. She could try to enter a study using inhalation therapy with liposome-encapsulated interleukin-2 conducted by Dr. Chand Khanna in Minnesota. We called Dr. Khanna only to discover that the study was over.

We learned from Ursula and Ulla not to allow an owner's verbalizations about expenses to preclude discussion of the best procedures, including initial diagnostics and follow-up studies, even when the anticipated results may not change the treatment. Always inform clients of all of the options. Ulla's seizure-like episodes may have been due to decreased oxygen flow or metastases to the brain. Ursula did not pursue an MRI of Ulla's brain to rule this out. She needed the information from the thoracic CT study to make her decision to stop further treatment and place Ulla in Pawspice care.

There will be more caregivers, like Ursula, who will want to use advanced imaging for follow-up and monitoring of their geriatric oncology patient's progress. We should suggest it more often.

MRI delivers pulsed radiofrequency waves into the patient. Signals from the radiofrequency waves are picked up by a special magnetic coil and then processed by a computer for anatomic imaging. Paul Lauterbur first generated MRI images in the 1970s. During the 1980s, MRI machines were installed in most major health care facilities because it was regarded as superior for imaging brain, spinal cord, and musculoskeletal regions. Contrast agents such as gadolinium enhance the visualization of tumors by detecting variations in vascular permeability.

Both CT and MRI studies are divided into image slices, spaced along the patient's body like slices from a loaf of bread. These slices can be sectioned in several planes: transverse, longitudinal, and dorsal. MRI technology can localize tumors that are not detectable by x-ray or ultrasonography. MRI has excellent sensitivity for the imaging and evaluation of tumors in soft tissues, especially the liver, spleen, and adrenal glands.

Contrast agents may be administered IV to enhance and distinguish tumors in soft tissues. All veterinary patients must be heavily sedated or anesthetized and placed in a stationary position on a table that moves the body within the strong magnetic field for scanning. Many owners of geriatric cancer pets are reluctant to subject their pet to anesthesia for the purpose of CT or MRI imaging, which restricts the clinician's ability to provide a definitive diagnosis.

Positron Emission Tomography

Positron Emission Tomography is a functional imaging technique that uses radionuclide tracers that target glycolysis. Increased glucose metabolism is a distinguishing metabolic and functional characteristic of all malignant cells. Therefore, glycolysis is the most practical functional target used in PET scanning today. PET scanning is rapidly replacing the use of strictly anatomical imaging prior to high-risk exploratory and therapeutic procedures.

Hybrid Imaging Technology

Improvements in non-invasive imaging technology will have great value for our geriatric cancer patients. Hybrid machines that fuse PET with CT or MRI can deliver more accurate images and detect smaller tumors in difficult locations such as the mediastinum and pulmonary parenchyma. This exciting combination of functional and anatomical imaging enables us to detect and locate very early metastatic disease.

This unprecedented detection of early metastatic disease has created the problem of stage migration. For example, patients with one or two 1–9 mm pulmonary metastases and patients with gross disease (multiple 1–5 cm nodules) will be stratified in the same stage. This is an important consideration in understanding the discrepancy between how cancer patients have been staged in the past and how they are now staged. The modern-day oncology workup will classify more cancer patients as being in a more advanced stage than in the past. These cases migrated from a lower to higher stage. We would expect these cases to have better survival times than their historical peer stage cases. Tumors detected by hybrid technology have much less volume than anatomically staged tumors. Therefore, interpreting survival data will be challenging because the PET/CT/MRI fusion scanned patients will appear to have more prolonged survivals than the anatomically scanned same stage patients.

Evaluation of therapeutic agents such as targeted therapies will be very difficult to interpret unless new sub-staging is established to address the issue of stage migration discrepancy. Taking this problem into account is an obvious necessity. The gridlock of scientific bureaucracy and marketing pressures (which may override ethical considerations) of some drug companies may allow some drugs to appear more efficacious than they actually would be with further scrutiny. When hybrid imaging technology becomes available to our veterinary patients, they will endure fewer

futile thoracotomies and laparotomies. They will also benefit from more accurate radiation therapy field analyses and follow-up assessments.

Nuclear Imaging with Radioisotopes

The terms “radiopharmaceutical,” “radiochemical,” and “radioisotope” are used interchangeably in nuclear imaging. Radiopharmaceuticals can assess the function of cells and provide images of organ system function. Radiopharmaceutical compounds are composed of a gamma radiation-emitting substance and a specific drug that functionally seeks or is taken up by a structure or organ. The emissions are picked up by a gamma camera as black dots on an image screen. Nuclear imaging can reveal occult disease, such as “hot spots” in bone. It can demonstrate the amount of uptake by the liver in patients with hepatic shunts.

Nuclear imaging and medicine are commonly used in veterinary medicine both diagnostically and therapeutically for the thyroid gland. They are also used to diagnose (and on a very limited basis, to treat) some bone tumors.

The most commonly used radioisotope for imaging the thyroid glands in geriatric cats is technetium-99 pertechnetate. This compound is readily taken up by the thyroid glands. It is short acting and inexpensive. Technetium-99 pertechnetate is used for pretreatment assessment of the size and location of hyperthyroid glands and can detect aberrant, ectopic tissue or nodules. Iodine 131 (I-131), a potent beta and gamma emitter, is used for treatment where indicated. It has a long half-life of 8 days and is used most commonly to ablate hyperthyroid adenomas in elder cats.

Bone Scans and Function Scans

Technetium-99 (Tc99) is commonly combined with methylene diphosphonate and used to detect metastatic “hot spots” in skeletal bone. As we search for metastatic disease in the workup for osteosarcoma patients and as we monitor our geriatric cancer patients for metastases, there is an increasing role for radioisotope bone scans. To assess lymph nodes, liver, and spleen, Tc99 is combined with sulfur colloid. When this compound is introduced to the body, it is taken up by phagocytosis into the monocyte-macrophage system and yields readable function scans.

Generally, patients are referred to facilities that have the permits and expertise in this specialized area of nuclear medicine. The information that is gained from the uptake studies is used for individualized patient treatment planning. For a more in-depth review of nuclear medicine, see Widmer’s chapter 16 in W.B. Morrison’s book *Cancer in Dogs and Cats: Medical and Surgical Management*, 2nd edition, and basic nuclear medicine texts.

Screening Strategy for Active Surveillance

Screening geriatric patients for cancer makes sense since they are at very high risk for developing it. There is an ongoing national campaign with the AVMA to educate pet owners to bring their senior and geriatric pets in twice a year for a complete physical examination. In addition to a comprehensive panel, the geriatric checkup should include CBC and urine analysis, chest and abdominal x-rays,

and, in large and giant breed dogs (especially Golden Retrievers and Rottweilers), an ultrasound of the abdomen.

The controversy against whole body screening for humans uses two basic arguments: lead bias and length bias. It is theorized that if slow-growing tumors are detected earlier, they may be more amenable to treatment and cure. Lead bias counters this theory because if there is no effect from treatment, a cancer retains its natural behavior and kills the patient in a given time period no matter when the diagnosis is made. Although the patient lives longer from the date of diagnosis, early detection and early treatment have made no difference in overall survival time.

Length bias gives us a good example when looking at canine hemangiosarcoma. Most affected patients survive less than 4 months post-diagnosis. The argument against whole body screening contends that it would be less likely that a “hot” tumor (such as hemangiosarcoma) would be detected by a screening procedure at 6–8 month intervals. If the diagnosis is made 1–2 months earlier, and the patient lives 5 or 6 months from diagnosis, it would appear that early detection has made a difference where in actuality, it did not (Balducci 2004).

The only comfort here is that post-operative survival for dogs with non-ruptured splenic hemangiosarcoma is longer than for ruptured cases. We need more survival information on dogs diagnosed at a preclinical stage in order to know if they are receiving a survival benefit.

Staging Cancer

At the very least, the diagnosis and workup of the geriatric cancer patient should provide the clinician and the pet owner with a preliminary clinical stage of the pet’s cancer. Staging uses all of the clinical data collected from a patient, including blood work, urine analysis, radiographs, ultrasound, cytology of locoregional nodes, spleen, liver and bone marrow, biopsy, immunophenotyping, CT, MRI, bone marrow aspirates, core biopsy, bone scan, and so forth. In addition, staging acknowledges if the patient is symptomatic and/or has paraneoplastic disease.

Full knowledge about the impact of staging on each type of cancer enables the clinician to provide accurate information and advice to help the pet owner with decision making. I have comforted clients who were under the impression that stage III lymphoma was a very bad indicator for their seemingly healthy dogs. In most other types of cancer, advanced stage III carries a much more negative prognosis than it does for lymphoma. Clients who are misinformed and jump to conclusions tend to make irreversible decisions that they may later regret and that may endanger their pet’s chances for treatment and survival.

Most solid tumors are staged using the straightforward tumor, node, metastasis (TNM) system (Table 5.2). Accurate staging helps everyone involved in the case to speak the same language and allows the clinician to give a more accurate prognosis. Low-stage patients generally live longer and have better survival rates than high-stage patients. Staging assists in treatment planning and is also used in follow-up evaluations to see if therapy has down-staged the tumor. Staging is also used in clinical research to distinguish cases from one another for meaningful interpretation of survival data. Newer, more sensitive and specific diagnostic hybrid technology will classify current patients into a later stage of disease than previously. This results in stage migration and will cause survival data to appear improved, as discussed above.

The World Health Organization (WHO) TNM staging system has been adapted for animals. The TNM system is commonly used for evaluating primary solid tumors, other than lymphoma, in dogs and cats for pre- and post-treatment evaluations. “T” refers to the size of the primary tumor: Adding

Table 5.2. TNM Table**Using TNM for Primary Tumor (T) Staging**

Skin	T1	T2	T3	T4
Skin	< 3 cm	3–5 cm	> 5 cm	
Skin	Minor involvement		Major involvement	
Fascia, muscle, and thoracic wall	With or without fascia or muscle		Thoracic or abdominal wall fixation	

T* Description of Primary Tumor

Tis	Pre-invasive carcinoma (carcinoma in situ)
T1	Tumor, 2 cm maximal diameter, superficial or exophytic
T2	Tumor 2–5 cm maximal diameter, or with minimal invasion irrespective of size
T3	Tumor > 5 cm, or with invasion of the subcutis irrespective of size
T4	Invasion of other structures, e.g. fascia, muscle, cartilage or bone.

*T is subclassified: (a) with (b) without bone involvement.

N Group Regional Lymph Nodes

N0	Regional lymph nodes not palpable
N1	Movable ipsilateral nodes
	N1a Nodes not considered to contain growth*
	N1b Nodes considered to contain growth*
N2	Movable contralateral or bilateral nodes
	N2a Nodes not considered to contain growth*
	N2b Nodes considered to contain growth*
N3	Fixed nodes

M Group Distant Metastasis

M0	No evidence of distant metastases
**M1	Distant metastases present—specify sites:

* (–) = histologically negative, (+) = histologically positive.

** Distant nodes to be included.

Source: Morrison, W.B. 2002. “Using TNM for primary tumor (T) staging.” In *Cancer in dogs and cats: Medical and surgical management*, 2nd ed., by W.B. Morrison. Jackson, WY: Teton New Media.

numbers after the letters indicates degrees of growth or extent of disease, a sort of shorthand notation. T0 is no tumor (this code can be used post-op as pT0), T1 is used for carcinoma in situ (superficial) tumors < 3 cm, T2 is 3–5 cm, T3 is > 5 cm, and T4 is very large. “N” refers to the local lymph node involvement: N0 is normal; N1 is local involvement and moveable; N2 is regional involvement and moveable; and N3 is fixed node involvement. “M” refers to metastases: Some oncologists use MX to indicate undetermined status for metastases. M0 indicates no metastases; M1 indicates metastases beyond regional nodes (Morrison 2002).

When general staging systems are applied to cats and toy breeds, we meet with some frustration. We find poor analogy, especially in oral, head, and neck tumors, due to the minimal size of the feline head. A 1 cm mass in a cat’s mouth is comparable to a 3 cm mass in a human or large dog. Most WHO staging schemes are applicable for medium, large, and giant breed dogs. The most important principle is to document the appearance, size, and extent of a neoplastic disorder and to make clinical

staging an integral part of your initial workup. More details can be added to the staging process as further diagnostic information is gathered.

Canine Lymphoma Staging System

The WHO lymphoma staging system commonly used for dogs and cats was set up in 1980. The scheme applies well for dogs, because 84% present with multicentric lymphadenomegaly. It has less application for cats. Cats are generally categorized into the anatomic forms of lymphoma such as alimentary, mediastinal, multicentric, extranodal (renal, hepatic, spinal, etc.). Feline lymphomas are also grouped histologically into low, intermediate, or high grade depending on mitotic index, T- or B-cell type, and involvement.

Dogs with lymphoma are staged with the WHO scheme according to nodal involvement and divided into stages I, II, III, IV. They are further sub-classified as (a) clinically well, asymptomatic, or (b) sick, followed by the letter designations: h = hepatic, s = splenic, and b = bone marrow, indicating organ involvement (Table 5.3). Well patients with generalized multicentric lymphadenomegaly may generally be considered to be in clinical stage IIIa. Patients that are sick, have organomegaly, enlarged sternal, hilar, and iliac nodes, anemia, or pulmonary involvement should be considered in clinically advanced stages.

Phenotyping Lymphoma for Prognosis

T- or B-cell phenotyping of canine lymphomas is helpful as a confirmation tool and as a valuable guide for prognosis. Immunophenotyping of tissue or cytology slides can be performed at most

Table 5.3. World Health Organization (WHO) Clinical Staging System for Lymphosarcoma in Domestic Animals

Anatomic Site

- A. Generalized
- B. Alimentary
- C. Thymic
- D. Skin
- E. Leukemia (true)^a
- F. Others (including solitary, renal)

Stage* (to include anatomic site: A, B, C, D, E, or F)

- I. Involvement limited to a single node or lymphoid tissue in a single organ.^b
- II. Involvement of many lymph nodes in a regional area (tonsils).
- III. Generalized lymph node involvement, liver and/or spleen involvement (stage III).
- IV. Manifestation in the blood and involvement of bone marrow and/or other organ.

Source: Vail, D.M., E.G. MacEwen, and K.M. Young. 2001. "Hematopoietic tumors, canine lymphoma and lymphoid leukemias." In *Small animal clinical oncology*, 3rd ed., S.J. Withrow and E.G. MacEwen, pp. 558–590, Table 28-4. Philadelphia: Saunders.

Each stage (I, II, III, IV) is subclassified: (a) without symptoms (b) with symptoms.

^aOnly blood and bone marrow involved.

^bExcluding bone marrow.

veterinary laboratories by using antibodies against lymphocyte cell markers. The CD3 marker is used for T lymphocyte, distinction and the CD79a marker is used for B lymphocyte. In general, one out of three lymphoma dogs has the more resistant T-cell subtype. An observational study of archived lymphoma tissue found that 82% of 50 Boxers, 50% of 22 Golden Retrievers, and 19% of 37 Rottweilers had T-cell lymphomas (Lurie, Lucroy, and Griffey 2004). Another study of 1,263 dogs with lymphoma representing 87 breeds had similar findings (Modiano et al. 2005).

T-cell subtype lymphomas are more likely to exhibit hypercalcemia and retain shorter first remission times and shorter survival times than B-cell patients.

Precise staging of an individual lymphoma patient is not considered reliable without x-rays and a core bone marrow biopsy. Bone marrow cytology is evaluated to rule out leukemic involvement. Hawkins, Morrison, and DeNicola (1993) found that 33% of 47 dogs with lymphoma had pulmonary parenchymal evidence of involvement on x-ray evaluation and could be further cytologically evaluated with bronchoalveolar lavage.

A client who is highly bonded to his or her lymphoma pet will probably elect the best combination chemotherapy no matter what stage or phenotype is determined. For this reason and for financial considerations, many veterinarians do not pursue absolutely thorough testing for precise staging.

A Proposed International Prognostic Index for Canine Lymphoma

Dr. V.E. Valli, a pathologist at the University of Illinois, is asking veterinarians and oncologists to participate in a global study to update the staging of lymphomas to relate to outcome. If you are interested in contributing cases to this important study, e-mail Dr. Valli at vevalli@uiuc.edu.

Link between Vector-Borne Pathogens and Lymphoma in Golden Retrievers

Researchers at North Carolina State University are looking for Golden Retrievers that have been newly diagnosed with lymphoma with no history of antibiotic use within 2 weeks. If you have such a dog, contact A. Duncan at awduncan@ncsu.edu.

Tumor Markers for Diagnosis of Cancer

The study of proteins (proteomics) has opened the molecular Pandora's box that is the cancer cell. Scientists have only identified a small fraction of the millions of proteins in the body. Certain proteins act as growth factors, enzymes, and signals and may be over-expressed on the surface and in the cytoplasm of cancer cells. Tests to identify specific proteins, or markers, are used to differentiate tumors on a molecular basis. As a group, tumor markers can identify a host of molecules that can be indicators of tumor cell type, function, growth factors, tumor presence, response, or recurrence.

There will be more useable and specific tumor markers and tests developed to identify, characterize, and target tumors in the future. Some markers are used to detect tumor activity or recurrence. Other markers will be used to tell us if a tumor contains sites that would be susceptible to targeted therapies, such as anti-apoptosis, anti-angiogenesis, and kinase, telomerase, or metalloproteinase inhibitors. These special marker tests may be run on cytology slides, serum, biopsy, or fresh tissue samples.

Tumor marker tests may employ immunohistochemical stain techniques, polymerase chain reaction (PCR) technology, spectrophotometry, gel electrophoresis, or some other intricate technology for identification of selected proteins or for gene mapping. For example, tumor markers may identify the presence of tumor suppressor genes such as the well-characterized p53 gene found in canine

osteosarcoma. Tumor markers may be used to follow tumors as they transition from their dormant stage into their more threatening proliferative stage as with Ki-67, the nuclear antigen found in proliferating mast cell sarcomas and proliferating mammary adenocarcinomas. The constitutive activation gene, C-kit (CD117), is a proto-oncogene that can be used both as a screening tool and as a target for treatment. C-kit undergoes mutations in several cancers and can be detected by PCR. C-kit may one day serve as a useful target for gene therapy to control recurrent or inoperable mast cell cancer in dogs.

In the field of proteonomics, tumors are not identified by morphology, grading, or staging. Instead, tumors are characterized as being positive or negative for a certain set of protein receptors. One important set of growth factor protein receptors to be familiar with belongs to the angiopoietin family of receptors: vascular endothelial growth factor receptor (VEGFR), platelet-derived growth factor receptor (PDGFR), fibroblastic growth factor receptor (FGFR), and Tie1/2. Information about the presence or absence of these receptors links investigators to the type of signaling pathways that a particular cancer uses. The angiopoietin family of receptors signals for endothelial cell migration, proliferation, and coordination for the process of angiogenesis that is vital for cancer cell proliferation and survival (Abeloff et al. 2004).

Gene Micro Arrays on a Slide

The day has come when veterinarians have access to and can use the technique of tissue micro arrays. This sophisticated technique surveys a special slide for diagnosis of immunoreactivity and genetic makeup of certain cancers. How can we use the information?

NSAIDs such as thalidomide, piroxicam, carprofen, deracoxib, and meloxicam have cyclooxygenase-2 (COX-2) inhibition activity. It is also understood that COX-2 inhibition confers some antitumor effects in bladder cancer and selected cancers that over-express COX-2. But what is the role of NSAIDs in OSA management?

If we learn from a diagnostic micro array test whether or not an OSA patient's tumors express COX-2 activity, then we know that an NSAID would be a helpful therapy. Unfortunately, only a low percentage of primary OSAs do express COX-2. Micro array assessments of OSA pulmonary metastases have found an upregulated expression of COX-2. Therefore, COX-2 inhibitors may be more helpful in the metastatic phase of OSA vs. the primary phase.

COX-2 inhibitors can be used in all OSA cases from day 1, whether or not the pet owner elects amputation. The primary purpose of selecting a COX-2 inhibitor for the management of OSA is that it offers pain control. The secondary purpose is that there is a 10% chance that the drug may inhibit the primary tumor. The overall purpose is to provide an additional therapeutic advantage against metastatic disease in the amputated patient.

Alternative Methods Used in the Diagnosis of Cancer

Alternative medicine involves diagnostic tests that assess blood, urine, feces, and tissues, as in conventional medicine, but it also includes the assessment of hair samples, muscle resistance testing, biofeedback, pulse palpation, tongue examination, iris reading, and more. Some of these tests are controversial and disputed, but they generally reveal the diagnosis of toxicity and immunosuppression. The fundamental toxicity comes from heavy metals and environmental carcinogens. Immunosuppression comes from the malignancy and stress reactions due to allergies to specific foods, antibiotics,

drugs, chemotherapy, steroids, and so forth. The patient is tested further and generally withdrawn from the offending agent and placed on a detoxification program and a rebalancing program to regain a stronger energy field.

If a client wants to pursue alternative diagnostics and therapy, it is an opportunity to counsel them. Recommend that they take advantage of modern technology and that they create an integrative program that dovetails the most effective treatments from each branch of medicine so that their geriatric cancer pet receives the maximum benefit. Since conventional western medicine modalities do not offer comprehensive treatment solutions for all patients and all tumors, many pet owners seek “alternative” therapies to integrate into their geriatric pet’s treatment plan.

Veterinarians will increasingly be challenged to remain open-minded and somewhat knowledgeable about alternative approaches. Regardless of personal biases against alternative therapies, the contemporary veterinarian refers clients seeking alternative care to local practitioners who provide alternative care. The nurturing aspect of alternative medicine, such as massage, acupuncture, and nutritional counseling, serves the geriatric patient in a very positive way.

Summary

Geriatric patients present many diagnostic challenges when they develop cancer. Geriatric patients present in all stages of cancer, from early to advanced, superimposed on all stages of organ system compromise. Many of these patients have been previously referred to specialists for cataract removal, orthopedic surgery, dental care, and internal medical issues. They come into the clinic with various degrees of information and history from one or several attending veterinarians. When the actual diagnosis and stage of disease has not been established, the challenge is to pinpoint the diagnosis and extent of the problem by staging the patient against the backdrop of its physical and health status.

For definitive diagnosis, it is necessary to biopsy all suspicious tissue and then use anatomic and/or functional imaging to accurately stage the patient. The process of decision making should be a partnership between the patient’s caregiver and the doctor. Offer the owner information and access to all available options for therapy and then support and treat the patient within the owner’s parameters. Be mindful that newer, more sensitive, and specific diagnostic technology will come available, such as the endothelial precursor cell (EPC) test for hemangiosarcoma. This new technology will detect cancer at its earlier stages, but will also cast more cases in more advanced stages of disease, resulting in stage migration issues. Therefore survival information may be difficult to interpret.

Thorough, compassionate communication is essential when delivering the diagnosis of cancer. Keep in mind that most caregivers love their geriatric pets and do not want their pet to die. Compassionate, high-touch communication with sincerity and concern for the care and management of the geriatric cancer patient is as important as our high-tech machines, drugs, and surgical skills.

Note: If you are interested in learning about ongoing studies conducted by the Veterinary Cooperative Oncology Group, check the VCS web site, <http://www.veterinarycancersociety.org>.

Scooter’s Case (Some Skinny Cats Can Respond)

Scooter Abrams, a 12½-year-old F/S DSH, was referred for management of nasal planum SCC. On physical exam, Scooter was emaciated, dehydrated, and had an elevated heart rate. She was hyperactive, very excitable, and impossible to handle without sedation. Scooter also had that wide-eyed, surprised look found in hyperthyroid cats. Her body weight was only 4.75

pounds from her normal 8 pounds. Scooter's referring veterinarian had recently diagnosed her with hyperthyroidism: T-4 (RIA) = 11.63 (normal = 0.8–4.0 ug/dl) and Free T-4 (RIA) = 8.36 (normal = 0.5–2.5). Mr. Abrams used fish-flavored compounded methimazole (tapazole) at 5 mg BID. The biopsy of two nasal planum lesions reported carcinoma in situ. Although Scooter's lesions would be responsive to cryotherapy, she had cachexia, was clinically hyperthyroid, fractious, and a very poor candidate for sedation. Mr. Abrams was apprised of the risk.

We used IM Domitor sedation, took a blood sample, and treated Scooter's SCC lesions with liquid nitrogen cryotherapy. Mr. Abrams was instructed to give SQ fluids at home, along with a calorie-dense diet, and to continue methimazole at 5 mg twice daily. On recheck, Scooter's T-4 by radioimmunoassay (RIA) climbed from 11.63 to 13.72 ug/dL on the compounded tapazole. Mr. Abrams was asked to discontinue the compounded tapazole and give Scooter the tablet form. One week later, her T-4 (RIA) rose to 15.06 ug/dL. The normal T-4 (RIA) range for our laboratory was 0.8–4.0 ug/dL.

We referred Scooter to Dr. John Amman, a radiologist, for nuclear imaging of her thyroid glands and a GFR scan to evaluate her renal function. Our intention was to see if iodine 131 treatment would normalize her T-4 level. Tc99m DTPA was used for the GFR study. The GFR value for her left kidney was 2.88 ml/min/kg and the right was 2.1 ml/min/kg (normal > 2.5 ml/min/kg). Her renal function was considered within normal limits. After 1 hour, Scooter was given Tc99 pertechnetate to image her thyroid glands. Scooter's right thyroid gland was enlarged and her left gland had increased uptake.

Iodine 131 was given but Scooter's T-4 levels remained elevated following two treatments. Her thyroid glands were imaged again on the gamma camera and there was no change over 2 months. Ultrasound exam revealed a large circumscribed mass with an intact capsule. Lack of response of the right thyroid to treatment is consistent with thyroid carcinoma (Amman 2002). Scooter had thyroidectomy and follow-up monitoring of her calcium levels.



Figure 5.8. Mr. Abrams and 18-year-old Scooter: treated for nasal planum SCC, malignant thyroid carcinoma, hyperthyroidism, and finally, presumptive pulmonary carcinoma.

Thyroidectomized patients may experience life-threatening hypocalcemia, due to accompanying inadvertent parathyroidectomy. Scooter required calcium gluconate only once during her 2-day post-thyroidectomy hospitalization period. Scooter's T-4 normalized following surgery and she gained weight. Her nasal SCC lesions resolved with cryotherapy.

One year later, Scooter presented with new SCC lesions on her opposite nostril. The lesions were treated with cryotherapy. Her T-4 remained normal and her nose remained cancer free for 3 more years. At age 16, Scooter presented weighing 4½ pounds and vomiting. She had slightly pale mucus membranes, fleas, an elevated heart rate of 160, and her T-4 was elevated to 11 (Figure 5.8). Scooter was placed on 2.5 mg Inderal® BID, oral tapazole, and a calorie-dense diet. This time, her T-4 value dropped quickly on oral tapazole. Her renal function remained unaffected but she did not gain weight. Chest x-rays found a mass in the caudal lung field. Scooter entered Pawspice care fluctuating between 4 and 5½ pounds. Surprisingly, she gained ½ pound in 2 weeks after an experimental injection with T-Cyte®, a thymic protein that stimulates helper CD4 T-cell function, IL-2 production, and erythropoiesis (Beardsley et al. 2005).

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Part Three

Chapter 6

Treating Cancer in Geriatric Pets

We must uphold the traditional value of sharing and caring by avoiding the contemporary code of making and taking, with indifference to the needs of others.

Dr. Carl A. Osborne, DVM, PhD, ACVIM (AVMA News 2005)

Chapter 6 has the following sections: Principles and Philosophic Perspective; The Role of Surgery in Cancer Management; Chemotherapy in the Management of Geriatric Cancer; Adverse Effects of Cancer Therapy in Geriatric Pets; The Role of Radiation Therapy in Cancer Management; Immunotherapy, Vaccine, and Gene Therapy; Chemoprevention and Immunonutrition; and Integrative and Alternative Medicine.

Principles and Philosophic Perspective

Veterinary medicine is one of the few professions that hold the keys to a person's heart. We have a wonderful opportunity to enter the eye of an emotional storm and provide a healing atmosphere for both the geriatric cancer patient and the caretaker of that pet. The goals of this section are to muster your enthusiasm, increase your knowledge, and hone your skills for treating cancer in geriatric patients. It takes a positive attitude and clinical courage to treat any pet cancer aggressively. Yet more skill and thoughtfulness are required to successfully treat and care for geriatric cancer patients. Just as importantly, it takes wisdom and courage to realize that a certain patient has passed the window of benefit from known conventional therapies at hand.

Because cancer can be insidious and resilient, it often wins the battle despite the noble effort that veterinarians and pet owners put forth. However, the rewards of treating and caring for geriatric cancer patients are well worth the effort. When geriatric pets are past the window of therapeutic benefit, palliative Pawspice care comes to the forefront. We can develop this aspect of practice into an expected and respected care program for patients with advanced cancer. One client, Roberta, wrote a thank you note that said it well: "If Mitzi could have lived on love, she would have lived forever."

This chapter discusses using a multimodality approach for treatment of general types of cancer, such as adenocarcinomas and sarcomas. An overview of the most common treatment protocols for the most common types of cancer is provided. As new information explodes on us every day, we must expect to change and improve our protocols constantly. New drugs will target different mechanisms and they may hold more options for our geriatric oncology patients. They may be able to target metastatic disease and transform cancer into another chronic disease. We must be aware of and be willing to incorporate innovative drugs, biotechnology, and supportive therapies and supplements into our existing protocols.

Furthermore, we must be willing to adapt mainstream therapies to individual client and patient needs, even if that means we enter some uncharted territory with some innovative yet logical adaptations of known therapies. The most important objective must always be to provide the greatest benefit for the patient while respecting the emotional, financial, and physical capabilities of the patient's caregivers. This ultimate consideration will provide the best quality of medicine for the individual patient and client situation.

In addition, there are no two oncologists who treat their geriatric cancer patients the very same way or with the same bedside manner. This explains why your clients will get different opinions and impressions from different consultants. For this book I was asked to share my personal perspectives and approach to geriatric oncology and tell you the way I treat my patients. This is not a "how to" but rather "a way to" approach cancer management in geriatric patients.

There is no secret or mystery about what I have been doing for the past 35 years. This book is a vehicle through which I can share with other practitioners decades of experience admixing geriatric oncology, Pawspice, and the human-animal bond. I hope that this book will help you minister a greater number of geriatric cancer patients into a longer and higher quality of life. If these pages provide insight and have a positive impact on practitioners to develop and practice the art of geriatric veterinary oncology, then the production of this book as a tool to advance the care given to geriatric cancer pets will have accomplished its goal.

Contemporary oncology reaches into the molecular frontier called proteonomics. The acronyms and codes for the language of proteonomics force the readers of oncology books to swim (or sink) in a cumbersome pool of alphabet soup. The field of proteonomics gives scientists the keys to unlock, inhibit, and rearrange the signals of cellular mechanisms that promote carcinogenesis, angiogenesis, and metastasis. This moment finds us at the crest of development for new types of targeted therapies that will help to curb cancer for patients of all ages and species. Targeted therapies bind to specific proteins and inhibit activity that is vital for tumor cell division and immortality. There will be many advances in conventional protocols for veterinary cancer treatment as researchers harness the enormous minutiae in the molecular alphabet soup recipe and unfold its powerful technology (Vail 2006a).

Veterinarians across the United States call me daily to fill in the gaps left between the lines in their textbooks. They feel intimidated by and uncertain about geriatric oncology, yet are motivated to learn more by their clients' pleas for help. The first and most useful principle of geriatric oncology is to practice with compassionate understanding while comprehending the whole patient. Since so many of my patients have done exceptionally well under my philosophy of care, this information is no longer mine to keep confined within the limited reach of my private oncology practices. This chapter offers a fresh and practical addition to the excellent literature already available in veterinary oncology.

Each geriatric cancer patient is unique and must be individualized by the stage of disease, concurrent conditions, comorbid illnesses, and the pet owner's economic situation, personal philosophy, time commitment, and logistics regarding treatment choices. Surgical oncology and radiation oncology are more complex than the administration of chemotherapy protocols used in medical oncology. Most difficult surgical oncology cases and all radiation therapy cases are referred to specialists.

Clinicians have recently become more interested in using chemotherapy in practice. You will find that chemotherapy protocols are plentiful and are often modified and adjusted by the attending doctor as needed. Variations in chemotherapy drug sequencing and doses are common because the recommended treatment plans must be adapted to the responses and needs of each individual geriatric cancer patient. Customizing protocols is not always easy to do while staying within the boundaries of the pet owner's wishes and financial resources. Clients will appreciate the integration of these

principles into your style of practice. Such flexibility shows pet caregivers that the well-being of their geriatric pet is important to you and that you respect their personal issues.

Consult with an oncologist for the latest chemotherapy options to assist your client in decision making. Make an attempt to check with at least two or three current sources to verify that the protocols described in this chapter are still the current and favored way to treat the particular neoplasia that affects your patient. The best local source to check would be your state's veterinary college, or any veterinary college with an oncology service.

Oncology information abounds on the Internet. Professors regularly provide class notes online, as illustrated by Dr. Neal Mauldin's notes viewable at the Web site www.vetmed.lsu.edu/oncology. Drs. Tony Moore and Angela Frimberger have an online private oncology consultation service for veterinarians at vetoncologyconsults.com. Free medical information is available at www.Medscape.com. The National Library of Medicine hosts www.pubmed.gov, with access to MEDLINE, its flagship database.

Veterinary Information Network offers members, "Vinnners," interactive consultation and information at your fingertips to verify the latest treatment protocols with specialists in chat rooms at www.VIN.com. You and your clients can also download and copy user-friendly client information at www.VeterinaryPartner.com. This is a free online service for your clients from VIN. Members of Vetstream, at www.vetstream.com, receive updated CDs on a quarterly basis that contain the *BSAVA Manual of Canine and Feline Oncology* text with updates by Dobson and Lascelles (2003). By searching for the latest online information, you will be aware of the most up-to-date cancer treatments for your geriatric patients. Use the Internet to keep up with new drugs and recommendations to add to existing protocols that may extend remission and survival times for geriatric patients. Expert advice and supplies are also available for nominal membership fees regarding chemotherapy protocols and dose adjustments for particular cases at www.oncurapartners.com.

Many pet owners are members of pet cancer support groups on the Internet. They share their experiences and feelings regarding their pet's cancer. Some groups focus on a particular cancer type in a dog or cat. Pet owners discuss treatments, side effects, and the care their pet is receiving. They offer support to each other and a safe haven for people to express their feelings without the common "It's just a dog!" or "It's just a cat!" response.

Because chemotherapy is thought to be immunosuppressive, many Internet users are convinced that it will harm their older pet. Veterinarians need to be able to discuss the issues and the myths that concern clients. We can assure clients that cancer itself is immunosuppressive. A recent study of 21 dogs on chemotherapy found that they responded to vaccination as well as normal dogs. Combination chemotherapy caused these dogs more immunosuppression than single-agent therapy. However, some tumor vaccines are given concurrently with certain chemotherapy agents such as Cytosan[®] to enhance the vaccine's antitumor activity. (Walter et al. 2006).

Many Internet group members become extensively educated about protocols and medical oncology. When an owner speaks knowledgeably about cancer treatment, rather than being offended or annoyed, always applaud his or her dedication to the pet's well-being.

When a cherished cancer pet passes away, the support group members are very helpful in providing validation and heartfelt compassion within a safe peer group. Pet caregivers often create touching e-mail tributes in honor of their pet to share with the group.

Be forewarned that Internet support group members chat candidly about their doctors! They post comments about their doctor's bedside manner and they share their assessment of the doctor's motivation level and competence in treating their pet. Simply by keeping an unconditionally positive attitude toward every client and focusing on the human-animal bond while serving the geriatric cancer patient, you will remain in the good graces of the Internet support group network.

I enjoy discovering unique features in the history of each geriatric pet that I treat. Cancer therapy almost always needs to be individualized to satisfy clients' special situations and considerations. One of the best ways to approach a geriatric oncology case is to assure pet caregivers that you will take the time to tailor a protocol for their geriatric pet's particular needs and stay within their financial ability, without ever making them feel guilty about financial constraints.

An Overview of the Three Musketeers of Cancer Therapy

The "Three Musketeers" used in conventional cancer treatment are surgery, chemotherapy, and radiation therapy. The coarse terms used for these techniques are cut, poison, and burn. Most clinicians make the decision to perform surgery on a cancer patient with the blessings of their clients. However, it is often in the geriatric pet's best interest to consult a medical oncologist at the initial stages of treatment, before engaging a surgeon. Oncologists think differently from surgeons, internists, or radiation therapists when it comes to treating geriatric cancer patients.

Oncologists generally attempt to obtain a diagnosis and staging information in an efficient, patient-sparing way. This is especially beneficial for the geriatric cancer patient that may be compromised with the effects of aging and other concurrent illnesses. Oncologists understand the behavior and growth rate of various cancers and will generally move more quickly toward definitive therapy following diagnostic procedures. Proper imaging and staging may conclude that interventions such as surgery would be unhelpful or useless for some patients (Hahn 2006).

Rather than putting off therapy for the sacred 2-week healing period following surgery, oncologists often use neoadjuvant chemotherapy, radiation therapy, or a combination of treatments before, during, or shortly after surgery. This may prevent the patient's cancer from robustly skipping to a higher stage. Postponing treatment until after the post-operative healing period allows the malignant cells time to recruit and recur. If the pet is not scheduled for chemotherapy until 2 weeks after surgery, the residual tumor has a window of opportunity to undergo further cell divisions.

I have witnessed the rapid recurrence of excised high-grade abdominal lymphomas. Some tumors return to presurgical dimensions within 10–20 days post-op. One 17-year-old cat with an enlarged kidney underwent a nephrectomy because an FNA was non-diagnostic. The histology report diagnosed renal lymphoma. This old cat was presented to our service for management 2 weeks post-nephrectomy. His remaining kidney was huge and the BUN and creatinine were elevated compared to presurgery levels. This scenario is undesirable for pet owners who readily consent in good faith to their doctor's recommendation for major surgery. It was unfortunate for this geriatric cat that many practitioners are reluctant to pursue renal biopsy in the clinical evaluation of their patients. A Tru-cut renal biopsy may have yielded a precise histologic diagnosis without the stress of nephrectomy (Vaden et al. 2005). Due to adherence to an unnecessary chemotherapy delay following unnecessary surgery and its conventional post-surgical "waiting period," this old cat's renal lymphoma was allowed to robustly move onward with its fatal agenda.

Weezie's Case (Exploratory Surgery May Delay Needed Therapy)

Weezie, a 12-year-old M/N DSH, started to decline and was taken to his local veterinarian for an exam. The doctor palpated an abdominal mass. Despite the fact that Weezie was eating and passing stool, the doctor recommended immediate exploratory surgery. The family requested more diagnostics. They were referred to a surgical specialist, who performed an abdominal

ultrasound to visualize the mass. The surgeon strongly recommended exploratory surgery to remove the mass, and biopsy even though Weezie was eating and passing stool. The owners felt that they were given no other choice and surgery seemed to them to be the best course of action at that time. At surgery, a 6 × 8 cm mass was removed from the mesenteric nodes and intestine. The diagnosis was lymphoma, present in the kidneys, intestines, and mesenteric nodes. The recommendation was to start chemotherapy after recovery. Recovery was uneventful and sutures were removed 2 weeks post-op.

One week later, Weezie started to decline again. That is when I received a desperate call and we fit Weezie into our schedule on the following day. A large abdominal mass was palpated along with an enlarged kidney with elevations of the BUN and creatinine.

An oncologist would have approached this case differently. A palpable mass in the abdomen of an FeLV negative geriatric cat can be presumed to be lymphoma until proven otherwise. Cells can be characterized via persistent, diligent, percutaneous FNA cytology or Tru-cut biopsy. This non-surgical evaluation technique can diagnose lymphoma and avoid unhelpful surgery in cases like Weezie's. With infiltrative, low-volume intestinal lymphoma, endoscopy may be successful for diagnosis; however, surgery is often required to harvest full thickness samples of intestine for definitive diagnosis.

In Weezie's case, surgery and the subsequent postponement of chemotherapy were not helpful. Chemotherapy for high-grade abdominal lymphoma in cats and dogs is helpful when administered post-operatively within hours or within the first few days following surgery. In the post-operative setting, it is best to omit prednisone for the first 7–10 days. We adjust the protocol to sequence the induction drugs over several days rather than administering them simultaneously in order to use the best window of therapeutic opportunity for the patient's sake. The anticipating clinician often feels caught in a medical dilemma. Most choose to wait until after healing of the surgical wounds rather than administer perioperative chemotherapy in time to halt the relentless spread of the lymphoma. What would you do if this was your cat?

Neoadjuvant and Perioperative Therapy

Neoadjuvant (prior to surgery) and/or perioperative chemotherapy (including intralesional or intracavitary administration) are valuable combination therapy tools that are underutilized in practice.

Tumors need to undergo only seven or eight doublings after clinical detection to be fatal. Some cancers such as hemangiosarcoma and osteosarcoma synchronize with bone marrow derived progenitor host cells. These host cells home to tumor-specific pre-metastatic sites and form cellular clusters that encourage metastasis and angiogenesis (Kaplan et al. 2005). Therefore, by the time we see cancer in our patients, time is running out.

When a lymphoma patient has recovered fully from anesthesia and is on IV fluids, I may administer an induction chemotherapy drug in divided doses over 24 hours. High-grade lymphoma has a relentless agenda of its own and does not wait idly for 2 weeks while the patient recovers from surgery. Therefore, we need to finesse the art of medicine in these cases as a matter of life and death.

We need to take courage and do what we can to safely control the neoplastic dynamics of the individual cancer patient. This may go against generalized textbook recommendations that depict healing times as sacrosanct. Viewing the surgery day as day 0, I give a 50% dose of vincristine on day 1. If the patient is doing well, the other 50% of vincristine may be given on day 2. L-asparaginase at

400 mg/m² on either day 1 or 2 is an excellent perioperative chemotherapy choice for lymphoma patients, depending on the case. We hold off the use of prednisone until day 6 or 7 post-op.

If a cancer patient is a candidate for RTx, consult with a radiation oncologist before surgery and before ordering expensive diagnostic tests. Early referral may save the client money because the preliminary imaging used for the workup may favor CT over MRI. The radiation oncologist can set up the geriatric pet with diagnostic and therapeutic step-savers from the start. For instance, instead of ordering an MRI for a suspected brain tumor, the medical oncologist would order a CT scan if the owner is considering RTx. CT is more readily used to interface with a computerized radiation and dosimetry treatment plan. RTx can be safely started within a few days after surgery.

The attending surgeon may be asked to mark the tumor field with clips so that the radiation oncologist has proper orientation. The oncologist may request intralesional or intracavitary chemotherapy administration into the tumor bed following excision. In many cases, RTx is started as soon as possible after surgery, bypassing the 2-week delay recommended by many surgeons. To ensure fewer oversights and more efficient and beneficial care for the geriatric cancer patient, the team approach is best. This approach requires that all doctors servicing the pet are in good communication with the oncologist in charge of the case.

Novel Approaches

Novel approaches for treating cancer in animals are on the horizon. These new therapies may include gene therapy using vaccines, targeted therapy using small molecules against certain cellular components, immunotherapy, intratumor injections using jet guns, and the use of anti-angiogenesis compounds. From the initial work being done in the field, it seems apparent that these new treatments will be added to the arsenal of currently used techniques in the near future.

Novel therapies are designed to attack basic mechanisms of tumorigenesis and metastasis by a variety of cancers. It may be that after we cut, zap, burn, freeze, and poison the primary tumor, we will be able to arrest cancer's recurrence using novel medications. These smart, small, and stealthy molecules target the mechanisms such as telomere-regulated apoptosis, angiogenesis, and micro-metastasis.

Smart Molecules

Tyrosine kinase is the enzyme target for "smart" and small molecule drugs. Gleevec[®] (Imatinib, Mesylate) is an example of a small molecule drug. It inhibits a kinase in the abnormal Philadelphia chromosome found in chronic myelogenous leukemia (CML) patients. Gleevec blocks the receptor tyrosine kinase (RTK) kit at its adenosine triphosphate (ATP)-binding site. Another small molecule drug, Erbitux[®], blocks the ability of cancer cells to absorb growth factors.

Avastin[®] is a small molecule drug that thwarts angiogenesis. Other small molecule inhibitors of kinases that are potentially useful against cancer are Tarceva[®], Iressa[®], Cetuximab[®], Astra[®], Erptinob[®], and Bevacizumab[®]. Be prepared to encounter and make good use of many other new products as they are released for clinical use.

SU11654 is a small molecule drug developed by Pfizer[®], specifically as a veterinary product. It is an intracellular competitive inhibitor of ATP at the RTK domain. SU11654 causes tumor regression and inhibition of cell growth by inducing cell cycle arrest and apoptosis. This drug has efficacy against various tumors. Dogs with mast cell tumors treated with SU11654 had response rates ranging

up to 55% (London 2004). The long-term efficacy, side effects, dose scheduling, and maintenance costs will affect how veterinarians incorporate these new smart drugs into the contemporary management of geriatric cancer patients.

Understanding proteomic technology is an esoteric endeavor. It requires an in-depth taste for the alphabet soup used to name the milieu of cellular proteins. Suffice it to say that breakthroughs in the aforementioned technologies may not be very far off for practical applications in veterinary oncology.

Your clients will soon be reading, in lifestyle magazines and on the Internet, about clinical trials using SU11654 and other small molecule drugs as they are developed for targeted therapy. They will know that this new class of drugs has broad efficacy against cancer, especially against mast cell tumors. If new drugs have tolerable side effects and are affordable, people will want them to be used for their older pets with cancer. Therefore, an understanding of the tools of molecular biology, the concept of dysregulated cell signaling by cancer cells, and targeted therapy by small molecules should be incorporated into the contemporary veterinarian's approach toward the treatment of cancer in the geriatric patient.

Multimodality Therapy

Multidisciplinary or multimodality therapy for the treatment of cancer means that more than one method is used to treat a malignancy. Generally, this refers to using combinations of conventional surgery, radiation, and chemotherapy. Proper sequencing of the various treatments may enhance the efficacy of multimodality therapy. For instance, some oncologists theorize that preoperative radiation therapy is more helpful than post-operative radiation therapy for large, aggressive sarcomas. Others, including myself, feel that intraoperative therapy is particularly effective. The advantages proposed for preoperative radiation therapy would be improved tumor control at surgery by shrinking the mass and destroying its tentacles and satellites. The advantages for intraoperative radiation therapy would be that the tumor bed is sterilized beyond the incision planes. In addition, chemotherapy may be added before surgery (neoadjuvant) or during surgery (intralesional/intracavitary).

Many caregivers want an aggressive surgical technique to address a malignant tumor on their geriatric pet but they do not want to subject their pet to repetitive follow-up treatments. The use of multimodality intraoperative techniques serves the wishes of these families well.

Integrative Therapy

There is a recent trend for conventional practitioners to acknowledge the benefits and use of nutritional supplements and some alternative medicine and therapy techniques. Conventional practice has expanded into the nutrition and supplement field by marketing the addition of nutraceuticals, antioxidants, and supplements in commercial diets. Specialized foods are formulated to treat chronic degenerative conditions associated with aging, such as arthritis, cognitive syndrome, hepatic and renal disease, cancer, and so forth. This concept opens a rational door into the field of chemoprevention, nutrigenomics, immunonutrition, and some aspects of complementary and alternative medicine.

Integrative therapy involves the simultaneous use of conventional therapy, including multimodality therapy, along with some techniques of alternative therapy that complement the treatment.

Complementary and alternative medicine (CAM) may include chemoprevention, immunonutrition, acupuncture, chiropractic, massage therapy, herbal medicine, and so on. Many veterinarians use, suggest, or condone selected holistic remedies or preparations to treat specific chronic unresponsive conditions in their geriatric cancer patients.

Overall, the most important therapeutic ingredient to offer in geriatric oncology is supportive care for both the patients and their people.

The Role of Surgery in Cancer Management

If we did the things we are capable of doing, we would literally astound ourselves.
Thomas Edison

Surgery is considered the most aggressive, hands-on approach for solid tumors. However, since the mechanisms of metastases often elude even the most aggressive surgeries, a multimodality or multidisciplinary approach is now being used to improve patient survival.

Surgery is the mainstay treatment used for management of localized invasive tumors. The very first surgery performed on a mass is the single procedure that may give the geriatric cancer patient the best chance of survival. Therefore, the principles of surgical oncology are an important set of rules to apply diligently at the very first surgery. The preoperative workup, the surgical plan, the perioperative support, and client advice are just as important as the anesthesia and the surgical procedure when dealing with geriatric cancer patients.

Surgery is widely used in cancer management as a diagnostic tool to biopsy and to stage cancer. Surgery is also used frequently to debulk tumors (cytoreduction), to palliate life-threatening conditions (as with splenectomy for ruptured splenic hemangiosarcoma), and to reduce pain (as with amputation for osteosarcoma [OSA]). Surgery is used in cancer patients to bypass lesions, to remove obstructions, to relieve pressure exerted by a tumor, to establish drainage, to clear airways, and to place vascular access catheters and stents. Biliary stenting is a less invasive alternative to biliary rerouting to palliate dogs with extrahepatic biliary obstruction caused by pancreatic adenocarcinoma or bile duct carcinoma (Mayhew et al. 2006).

Surgical reconstruction and graft techniques are used to repair defects created by large mass excisions and radiation necrosis. Surgery is used to debride necrotic tumor tissue and wounds and repair extravasation defects. Cytoreductive surgery may correct abnormalities such as malignant hypercalcemia generating from anal sac carcinoma and other PTHrp-productive tumors. Surgery may correct disease syndromes from other hormone-producing tumors such as insulinomas, gastrinomas, Sertoli cell tumors, seminomas, and adrenal tumors in dogs. Surgical lobectomy is helpful for dogs with solitary primary pulmonary masses, while metastatectomy may help in selected cases. Hepatocellular carcinomas localized to a single liver lobe also benefit from lobectomy.

Surgery may prevent cancer. Spay and neuter programs accomplish this end. Surgery to remove both mammary chains in feline breast cancer is considered the best preventative approach to extend survival when performed in early stage disease, prior to micrometastasis from the primary tumor.

Surgery is life saving when used to remove obstructions, to control splenic hemorrhage, to excise masses, and to keep lumens patent and functional. Surgery is also used in the management of cancer to place feeding tubes, vascular access ports, stents, and stomas, and to palliate painful lesions. Surgery is the best pain control for OSA. The alleviation of pain is one of the primary goals accomplished with amputation of an OSA limb.

Special Considerations for Surgery

Any and all surgical procedures performed on a geriatric cancer patient should be directed at improving the patient's well-being. In addition, the client's concept of well-being for his or her pet should be discussed and respected. When improper planning leaves the patient with no benefit from the procedure, surgery was clearly the wrong approach. It is easy to say "wrong approach" after the fact, but the veterinary surgeon must weigh the facts beforehand and operate when the risk-benefit ratio favors the geriatric oncology patient. Careful attention to perioperative supportive care of the geriatric patient creates a smooth recovery and minimal hospitalization period.

Surgery should never be recommended perfunctorily and prematurely. Surgery generally contributes added stress to the compromised geriatric patient and may cause more unintended harm than good. These cases should be managed with finesse to spare the patient the stress of surgery whenever possible. I am all for surgery when it is realistically expected to be helpful to the geriatric cancer patient.

Surgery should never be recommended as a single modality for debulking non-localized tumors. When used without follow-up modalities for overall tumor control, debulking surgery for metastatic tumors may be essentially unhelpful in winning prolonged longevity for the patient. Debulking surgery is especially stressful in geriatric and debilitated patients. In fact, surgery alone may actually hasten the patient's death. This effect was shown to be true for nasal passage cancer patients undergoing rhinotomy. Unfortunately, the best surgery and the best radiation therapy are still limited in their ability to cure cancer that is metastatic. Surgery and radiation therapy can be curative only for those patients that have completely localized tumors.

Every geriatric patient about to have surgery for a solid tumor would benefit from comprehensive preoperative diagnostics and thoughtful presurgical planning. Attention to the principles of surgical oncology and the aggressive pursuit of clean wide margins may successfully remove the entire mass. I like to use intraoperative cytology to assist the surgeon in pursuit of clean margins. With intraoperative cytology, for instance, a well-planned and successful maxillectomy or mandibulectomy in a dog may result in a cure for acanthomatous epulis and freedom from recurrence of local disease from fibrosarcoma or squamous cell carcinoma. The two latter cases often benefit with follow-up radiation therapy to increase the tumor-free interval.

For oral malignant melanoma, we can achieve excellent local control with surgical mandibulectomy. However, we must expect metastasis at 10 months post-surgery. It is important to educate the client about the biological behavior and prognosis in order to help with decision making for follow-up therapy. The malignant melanoma patient needs further therapy to deal with metastasis. Options include using chemotherapy with carboplatin and/or immunotherapy with one of the new deoxyribonucleic acid (DNA) vaccines available from the University of Wisconsin or at New York City's Animal Medical Center (AMC).

Amputations of limbs for locally aggressive sarcomas in dogs and cats may be curative for the majority of cases where the tumor is distal enough for wide clean margins. If the mass is located in the proximal part of the limb and surgical margins are inadequate, recurrence is likely. If amputation is performed for a primary bone malignancy in the dog, further systemic therapy, using chemotherapy, chemoprevention, or vaccine therapy, is indicated in order to extend time to metastases.

Scintigraphy uses radiomimetic chemicals to identify "hot spots" in bone. It is used prior to surgery, for staging, and to monitor progression of disease on follow-up. If chest x-rays and the bone scan are negative, surgery has the potential to cure the patient. The best x-rays, CT, MRI, and scintigraphy cannot identify a single malignant cell, or even cell clusters. Don't fail to educate clients

regarding our frustration with the potential for metastasis. Fusion or hybrid scanners that combine positron emission tomography (PET) with CT or MRI are more sensitive in their ability to detect small metastatic lesions than conventional imaging techniques.

With improved preoperative evaluation and staging of the mass using new and improved imaging techniques, more success is expected from surgery because the cases will be better selected. This is especially true with peripherally located brain tumors.

When a surgeon approaches the patient with the full intention to perform complete excisional biopsy of a sarcoma or carcinoma, the patient will have improved survival. The amputation of a limb for osteosarcoma generally does not prolong a dog's lifespan without follow-up chemotherapy. The use of innovative modalities such as inhaled liposome encapsulated IL-2, IV immunomodulators, specific anti-tumor vaccine, samarium, the bone-targeting radiopharmaceutical agent Quadramet®, or small molecule therapy targeting proliferative pathways may enhance survival times for OSA patients in addition to chemotherapy.

A General Rule of Thumb for Oncologic Surgery

There is a general rule of thumb that most general practice surgeons would do well to incorporate into their surgical plan when approaching an unknown mass. The strategic plan would be to remove a diameter of tissue laterally and ventrally around the primary tumor that is at least half of (optimally equal to) the size of the primary mass itself. If this plan were universally adopted, more pets could be spared second surgeries and recurrences, and more lives could be saved. For all mast cell tumors, the ideal margins are at least 2–3 cm laterally and ventrally. For tumors that lay across bone, ligament, nerves, and other vital structures, at least one fascial plane should be removed below the mass. Otherwise, the surgery will be incomplete.

Most general practice surgery is unhelpful for cats with feline vaccine-associated sarcoma (FVAS). Board certified surgeons and those surgeons who plan aggressively to achieve wider and deeper margins do create longer tumor-free intervals and potential cures for FVAS cases. Surgery performed by the local practitioner for this vicious malignancy is best used strictly as an incisional diagnostic tool prior to referral of the case to a specialist for definitive surgery. I consider general surgery to be the wrong approach for FVAS. This iatrogenic malignancy needs extreme measures with wide and deep margins at the very first excisional procedure in order to do the cat justice. Anything short of an early aggressive and definitive approach to the excision of a sarcoma is unjustified in today's knowledgeable atmosphere.

Excisional biopsy of a large anal sac tumor that involves over half of the anal sphincter may cause fecal incontinence. The use of laser or radiation therapy may be better options to cytoreduce these cases. Excision of the caudal rectal area to remove tumors may cause permanent fecal incontinence.

Multifocal mast cell cancer may be helped by surgery if the tumors are well differentiated, limited in number, and expected to be localized to no more than three areas. Surgery is unhelpful in widespread multifocal mast cell cancer. It is better to address all multifocal lesions with a systemic therapy than to attempt surgical removal.

Abdominal Surgery

The outcome for exploratory laparotomy has fewer surprises and is more successful if there has been appropriate presurgical evaluation. Abdominal x-rays are informative, but abdominal ultrasound and imaging with CT or MRI can reveal more information and make a big difference in decision making.

Cytoreductive surgery is very helpful in patients with hormone-producing tumors such as gastrinomas, insulinomas, adrenal tumors, and metastatic anal sac tumors associated with hypercalcemia in dogs. Dogs with massive hepatocellular carcinomas localized to the left liver lobe benefit more with lobectomy vs. conservative medical management (Liptak et al. 2004).

Hemangiosarcoma Surgery

Emergency surgery to remove a bleeding splenic hemangiosarcoma is very dramatic and can be immediately life saving. Hemangiosarcoma surgery does not spare the majority of geriatric oncology patients from the ravages of metastatic disease and death within 6–8 weeks. It is important for clients to be made aware of the prognosis prior to electing surgery. If the family declines surgery yet is reluctant to euthanize their pet, it is appropriate to allow the patient the opportunity to stabilize in the hope that the blood can be resorbed. Some dogs with hemoabdomen will stabilize within a few days with strict rest, a belly wrap, and supportive care. The family appreciates the opportunity to have a more extended farewell from their pet during these days of quiet rest. I have received heartfelt thank you letters from pet owners who were able to enjoy precious time with their dog following acute hemoabdomen.

A few breakthrough treatments may completely change the outlook of surgery for patients with non-cutaneous hemangiosarcoma and for patients with a variety of solid epithelial cancers. Thalidomide may provide some value in combating angiogenesis, although it is costly and not readily available (Woods, Mathews, and Binnington 2004). Interest has piqued for the potential use of suberoylanilide hydroxamic acid (SAHA), valproic acid, and other histone deacetylase inhibitors. SAHA can be given orally and has no reported side effects. Leonard Cohen, MD, reported that an 8-year-old Rhodesian Ridgeback named Molly survived hemangiosarcoma for 3 years due to SAHA (Cohen et al. 2004). SAHA was unable to help one of my patients, a 12-year-old intact Siberian Husky named Tushka with hepatic and splenic hemangiosarcoma, survive past 4 months. The AMC in New York City is evaluating the efficacy of SAHA in malignant disease. Researchers at Colorado State University (CSU) are evaluating the antiproliferative and chemosensitizing effects of valproic acid (Thamm et al. 2006).

New treatments that target marrow derived host cells and signaling mechanisms for angiogenesis and micrometastasis may help hemangiosarcoma and other vascular tumor patients survive longer after surgery. Small molecule inhibitors such as Gleevec or multiple kinase inhibitors such as SU165 may help increase survival times following surgery (London 2004).

Transitional Cell Carcinoma and Surgery

Transitional cell carcinoma (TCC) of the bladder mimics cystitis and UTI syndrome. TCC is generally seeded extensively in the mucosal lining of the bladder, causing hematuria and stranguria. Most TCCs are located in the trigone area and are too advanced at the time of diagnosis to expect surgery to be helpful. In fact, surgery is often unhelpful unless the mass is focal and located near the apex of the bladder. Because surgery may actually seed malignant transitional cells along the incision site, the surgeon must take great care to make a glove change and use new instruments to close the incision.

Tumors at the apex of the bladder may be operable. Some may be benign polyps but most often the masses are TCC infiltrating extensively into the bladder wall. On ultrasound examination, a thickened appearance of the bladder wall adjacent to a primary mass indicates tumor infiltration.

TCC patients that seem to be candidates for surgery would benefit from presurgical cystoscopy to verify the diagnosis and to determine whether the mass can be completely removed. Areas of

neovascularization can be sampled to determine the extent of TCC infiltration. It is very difficult for attending surgeons to determine the true extent of the TCC infiltration at the time of cystotomy. Selected TCC patients with tumors confined to the apex of the bladder may benefit from surgery.

Cystoscopy to examine the bladder wall may be the most useful tool following ultrasound to actually determine whether surgery would be the right or the wrong approach. Procedures that remove the bladder and route the ureters into the distal colon have not yielded satisfactory clinical results. This procedure has failed to increase overall survival times due to metastatic disease.

Creating a stoma for urine to exit the bladder has been helpful in selected cases with outflow obstruction of the urethral lumen from trigonal and urethral TCC. The procedure for use of low-profile cystostomy tubes was described in four dogs and one cat. The patients were more comfortable and had more mobility with the low-profile tubes (Stiffler et al. 2003). The pet owner evacuates urine on a regular basis. I believe that cystostomy is a viable palliative option to offer selected TCC patients because it provides relief and clearly solves a life-threatening dilemma.

Prostate Cancer and Surgery

Prostate surgery has been considered unhelpful in dogs because the canine prostate gland is intimately involved with the prostatic urethra. Prostatectomy can benefit selected cases where neoplastic tissue is confined within the capsule and there is minimal to no urethral involvement. Imaging technology and exploratory surgery are both required to determine if the patient has an operable prostatic tumor. The surgeon must use caution to avoid complications and incontinence (Henderson 2004).

Male cats have tiny prostate glands that rarely develop malignancy and are generally not operable. I have only cared for two cats with prostate cancer in 35 years of practicing oncology. For one 13-year-old DSH cat, Shakespeare Rapheal, a debulking surgery and open cystostomy was life saving. Chemotherapy with mitoxantrone and piroxicam cyto-reduced a 3 cm recurrence, allowing Shakespeare a 1-year survival. The second case was Boukie Cohen, a 16-year-old DSH with a heart murmur. Boukie developed urinary obstruction from a malignant prostate tumor. Urine outflow was re-established with urinary catheter placement. Surgery was not attempted. Chemotherapy with mitoxantrone every 21 days and piroxicam 1 mg daily reduced the prostatic mass and allowed normal urine outflow after 7 days. After 6 treatments, he was switched to carboplatin. Boukie developed splenomegaly, reactive lymphadenopathy, and extensive non-painful cutaneous metastases from his prostatic carcinoma during the last 6 months of his 1-year survival.

Detailed descriptions for surgical oncology excisions of various tumor types and locations are described elsewhere in numerous texts. Please refer to chapters 18, 19, and 20 by Dr. Kathleen Salisbury in W.B. Morrison's book *Cancer in Dogs and Cats: Medical and Surgical Management*, and to related texts for in-depth information.

Freddy's Case (Control Multifocal Mast Cell Tumors without Surgery)

Freddy, a 9-year-old M/N Golden Retriever–German Shepherd Dog mix, with a history of colitis and inflammatory bowel disease, suddenly developed multifocal skin tumors extending over his neck, shoulders, and back. His attending veterinarian removed most of the tumors. They ranged from 1 to 3 cm in size. Histology diagnosed the tumors to be moderately to poorly differentiated, multifocal mast cell tumors (MCTs) with moderate to marked mitotic activity (high grade). The lateral and deep margins were complete but narrowly excised at less than 0.1 cm, and therefore inadequate. The prognosis was fair to guarded. When Freddy came in for his

first oncology consultation, he had sprouted 20 new tumors and some were growing in between the sutures. Multiple cutaneous MCTs in dogs are generally associated with a low rate of metastasis and a good prognosis with adequate excision (Mullins et al. 2006).

All of Freddy's tumors regressed rapidly following one treatment with 2 mg/m² of vinblastine IV, oral prednisone at 40 mg/m² PO daily for 7 days, tapering to every other day. He also received chlorambucil 6 mg every other day PO. Freddy received weekly injections for 2 months, tapering to monthly maintenance. Freddy's caregivers elected to discontinue his maintenance protocol after he remained tumor free for 8 months. Freddy remained in complete remission for 1 year. At that time, he developed inoperable intestinal carcinoma.

Sage's Case (Aggressive Surgery and RTx Curative for Five-Time Recurrent Hemangiopericytoma)

Sage, a 12-year-old M/N Whippet, had five surgeries on his left front leg for hemangiopericytoma. Sage's owner was determined to save the leg due to chronic arthritis. We approached this as a three-step multimodality procedure. Step #1 was to surgically remove the recurrent mass with a deep wide excision, followed by intraoperative radiation therapy. The wound was wrapped with a wet-to-dry bandage daily and left as an open wound to await the histology report. The biopsy reported clean but narrow margins. Step #2 followed a week later, when the wound was debrided and closed with an axial pattern flap graft. Step #3 was provided as follow-up external beam radiation therapy delivered in 10 fractions. Sage had no further recurrence over a 3-year follow-up period.

A Letter to Every Surgeon (Please Read Before Recommending Surgery)

I have often thought of writing the ideal letter to members of our profession who are planning to remove a potentially malignant tumor from a geriatric patient. I will take this opportunity to realize that wish. I hope that every surgeon will heed the advice in the following letter.

Dear Colleague,

This geriatric cancer patient would benefit if you were actually able to completely excise the mass with your first surgery. If your intention is not to provide definitive surgery (such as mandibulectomy for an oral melanoma, or a wide and deep excisional biopsy for a mast cell tumor or vaccine-associated sarcoma), your client must be made aware of this.

Would this pet be better off if you perform an incisional biopsy of the primary mass and regional lymph nodes today as a diagnostic, grading, and staging procedure? If so, please do so at this time. Rather than upsetting the tissue planes infiltrated by the mass with an inadequate excisional procedure, please consult with an oncologist and refer the case to a board certified surgeon for definitive enblock excision. This plan is more likely to provide the patient a greater tumor-free interval.

If you decide to proceed, then do so with wide and deep margins around the mass. If you consider the following oncologic procedures, your patients may survive longer and your success rate in curing certain cancers may soar.

Please perform an FNA cytology or impression smear of the mass, stain it with new methylene blue, and examine the cells. This takes 2 minutes of your time, but it is worth it because you will then know if you are dealing with a mast cell tumor or a sarcoma. Draw a line around the mass with ink and pre-place deep sutures to keep your margins intact during the excision. Remove the mass and a cuff of normal tissue on all planes around it without cutting into the mass itself. Mark

the deep margin with India ink. For large masses, slice them at 1 cm intervals for fixation and place each margin in a separate well-marked biopsy bottle.

Provide the pathologist with information about the mass and the surgical margins. Illustrate the location and size of the mass on a cartoon map for the pathologist and for the medical record and also write down the size of the deep and lateral margin excision around the tumor. Leave metal clips in place to show the complete extent of the borders of your excision in the event the pet is referred for radiation therapy. This information is vital because the entire surgical field is considered to be potentially seeded with cancer cells if the mass is incompletely resected. This information will also help to determine shrinkage. Margins around the excised tumor may have been 2 cm on the gross cut, but they may be reported as a third to a half of the actual operative margin due to shrinkage in formalin.

A new gold standard for all veterinary surgeons might be to create, around a mass, surgical margins that are, at the very least, the same size as the tumor itself. This means a 2 cm diameter tumor would have 2 cm wide margins. If margins are questionable, and it is feasible to use open wound management, then do not perform wound closure/reconstruction until the pathology report is accessible. Once again, please be certain to clearly illustrate and document the extent of the operative margins in the medical chart as part of the surgery report. Send the pathologist a copy of the surgical report as well as a cartoon map indicating the location and size of the mass. Mark the tissue's cranial, caudal, dorsal, ventral, or deep margins with sutures or India ink to provide orientation and a marking code for the pathologist, especially with large tumors.

Please do not send your pathologist a large tissue section in a small bottle. Avoid placing samples that are over 1 cm in thickness into small formalin containers. Please slice large tissue samples as if you were cutting a loaf of bread into one cm slices. Use a larger bottle to send large tumor tissues to the lab in a 1:10 ratio of tissue to formalin.

If you prefer to use only the small formalin bottles provided from your diagnostic laboratory, then follow this margin evaluation method: Cut a rim of tissue from the periphery of the mass and wind it flat on a gauze pad like an onion or cinnamon roll, starting with the cranial end on the inside of the roll. Place this rolled sample in formalin and send it to the pathologist along with samples of the mass.

Another technique to satisfy the curious oncologist is to cut new strips of tissue from the peripheral and deep margin of the tumor bed following excision of the mass. Be sure to mark the strips well with suture or India ink for orientation markers as well. These extra steps provide an excellent method for your pathologist to survey the cutaneous and deep margins. Then, when an oncologist or radiation therapist is asked to consult for follow-up therapy on the case, he or she will be able to review the pathology report and understand the patient's exact situation.

If you don't want to prepare samples in this way, most pathologists will accept larger samples. Keep the entire specimen refrigerated and properly packaged in a chilled container. Arrange for same-day transport and arrival of the sample at the laboratory. Be sure to mark the medial and anterior edges of the sample for orientation.

Lymph Node Cytology

For assessment of the local lymph nodes, perform FNA cytology on the draining lymph nodes before surgery. The FNA may be performed during surgery (intraoperative cytology) as well. If the lymph node(s) cytology is positive, removal is indicated. If a lymph node is not enlarged and is FNA-negative, then it is recommended to leave it in place. Please remove the local draining lymph node for staging of all oral and lip malignant melanoma cases. If you are performing a radical mastectomy, please locate and remove the inguinal and axillary nodes. Remove these nodes if you are removing the fifth or first mammary glands in a partial chain mastectomy for staging and prognostic purposes.

Exploratory Celiotomy

During exploratory laparotomy, please take samples of the liver and other involved organs and of enlarged lymph nodes during surgery. If the patient is a lymphoma suspect, consider examining

or sending an impression smear for cytology for an immediate answer (intraoperative cytology). This may assist patient support while the confirmation from the biopsy specimen is pending.

As soon as the biopsy report comes in, especially if it is lymphoma, seek consultation from an advising veterinary oncologist to formulate a treatment plan. In some cases, especially with lymphoma, the patient will need immediate follow-up treatment to control and/or downstage the malignancy so that it will not skip to a higher stage. Make every attempt to prevent recurrence and deterioration of the patient during the post-operative recovery phase.

If a geriatric patient is sick from the effects of abdominal neoplasia, and if there is no access to ultrasound or if ultrasound is not affordable, the attending veterinarian is justified in making the recommendation for exploratory laparotomy. In cases like this, secure a written agreement with the family that allows euthanasia if the mass is considered inoperable. We do this in the geriatric patient's best interest to avoid struggling with recovery and to bypass the expected difficulties of recovery and poor quality of life for the geriatric oncology patient as the malignancy progresses.

Lola's Case (An Inoperable Abdominal Mass Was Tamed)

Lola, an 8-year-old F/S Bassett Hound, presented with weight loss, anorexia, and vomiting. On physical exam, a huge mesenteric mass was palpated. Radiographs showed no involvement with intestines and no other organomegaly. Initial FNAs were non-diagnostic and exploratory laparotomy was recommended. The attending surgeon felt the mass was inoperable due to endangerment of the mesenteric vasculature feeding a large section of intestine. There was no obstruction. Lola's owners did not want euthanasia.

Samples were taken for histopathology. Wound closure was routine and Lola recovered uneventfully with the exception of vomiting, treated symptomatically. The biopsy report diagnosed lymphoma. Lola received combination chemotherapy and lived 4 wonderful years in complete remission. Three years into her remission, Lola was featured as a cancer survivor in a local magazine article.

Reconstructive Surgery

Wide surgical margins are necessary to excise the tentacles of the neoplastic lesion (Figure 5.7). Due to improved anesthesia techniques and perioperative pain control, geriatric dogs and cats are able to better survive prolonged surgical procedures. The reconstructive procedure necessary to cover large defects may be as challenging as the primary excision itself. Radical, aggressive excisional surgery that employs reconstruction techniques is the most effective procedure for cure of localized and slow-to-metastasize neoplasms. Tension free wound closure using Z-plasty and staggered parallel incisions can be very helpful. Axial pattern flaps can be used to cover large areas left open by radical surgical excisions of large tumors. Full-thickness mesh grafts are excellent options to cover open wound beds located in difficult to close areas where the wound is uneven or requires movement (Tobias et al. 2004). The use of engineered tissue products such as extracellular matrix bioscaffold technology may be very helpful to stimulate healing for wound closure at difficult sites (Norsworthy 2005). The most important consideration for tumor removal in the geriatric oncology patient is for the surgeon to do the first surgery correctly. This approach requires knowledge of the tumor type, its anatomical extent, and careful presurgical planning with reconstruction techniques for viable wound closure.

Summary: The Role of Surgery in Cancer Management

Well-planned excisional surgery with careful hemostasis and gentle tissue handling is life saving for many geriatric cancer patients. Anesthesia recovery and healing may be prolonged in older animals due to paraneoplastic syndromes, reduced functional reserve, and comorbidities associated with aging and senescence. Surgical intervention leaves the geriatric cancer patient more challenged with the issues of recovery and tissue healing. Excellent perioperative support and decision making regarding adjuvant chemotherapy or radiation therapy is imperative so that the geriatric patient may continue to fight for life. The attending doctor must provide the timeliest options for follow-up management of high-grade neoplasia, especially high-grade lymphoma. For more information read “Thinking Surgeon or Cutting Surgeon: To Be or Not to Be?” by Dr. A. Carl Osborne.

Chemotherapy in the Management of Geriatric Cancer

Wisdom is a blend of many attributes in addition to knowledge. They include understanding, discernment, thinking ability, intelligence, experience, diligence, shrewdness and good judgment.

Dr. Carl A. Osborne, DVM, PhD, ACVIM

Chemotherapy is the use of agents with the intention to kill viable cancer cells to retain quality of life and increase survival. It is currently the standard treatment used for control of many types of cancers, especially those that constantly shed cells that contribute to the metastatic process. Aging is associated with the progressive decline of physiologic organ system reserves, total body water, circulating plasma proteins, and hemoglobin concentration. These factors affect the pharmacokinetics and pharmacodynamics of the various chemotherapy drugs used in older cancer patients. The attending doctor must be knowledgeable and flexible with the dosing and administration of chemotherapy drugs for all geriatric pets. The clinician must have a working diagnosis and staging information and be mindful of the variability and vulnerability of the individual geriatric dog or cat. An older animal's physiologic age, chronologic age, body condition, and overall performance and health status must be evaluated and stabilized to minimize drug toxicity.

Chemotherapy dose adjustments are recommended for older patients with concurrent renal disease, cardiac compromise, and/or severe hepatic insufficiency, since the liver is the main site of drug metabolism. Geriatric pets fare best with a strategy that is mindful of using drugs offering dose flexibility. If we spread the total dose of oral and IV chemotherapy over 4 to 8 days, we can maximize absorption and minimize toxicity for the geriatric patient (Cova and Balducci 2004).

Handling Chemotherapy Drugs Safely

In general, caution must be taken with staff and surroundings when chemotherapeutic agents are being used. Safety glasses, chemotherapy gloves, gowns, and masks must be worn by all personnel handling the preparations or holding the patient for administration of the drugs. Precautions to prevent aerosolization of chemotherapy drugs should be used. Place gauze at the neck of drug vials or use a special aspiration filter when aspirating chemotherapy agents into syringes. Laminar flow hoods are required in pharmacies that dispense large volumes of chemotherapeutic agents (Takada 2003).

Special containers are needed for disposal of used drug vials, needles, and syringes. A chemotherapy spill kit should be readily available to the entire staff. The drug material safety data (MSD) sheets must be available to all staff. Occupational Safety and Health Administration (OSHA) regulations and recommendations must be carefully observed when using chemotherapeutic agents. (See instructions for handling chemotherapy drugs in the “Suggested Reading for Medical Oncology” section at the end of this chapter.)

Classification of Chemotherapy Drugs

Chemotherapy drugs are classified as alkylating agents, antimetabolites (analogues), antibiotics, anthracyclines, enzymes, hormones, plant alkaloids, taxanes, Platinol[®]-containing drugs, topoisomerase inhibitors, metalloproteinase inhibitors, telomerase inhibitors, protein kinase inhibitors, angiogenesis inhibitors, small molecules, and so forth. NSAIDs and tamoxifen are considered to be chemoprevention drugs. A growing number of supplements, considered as immunonutrition agents, may also fall into the category of chemoprevention agents.

Terminology for Applied Chemotherapy

Clinicians should be familiar with the basic use and terminology for the various methods and routes in the application of chemotherapy.

The initial use of chemotherapy for responsive tumors such as lymphoma is called the induction phase. It generally requires more intense and more frequent dosing with the goal of achieving a complete remission (CR). The patient's response may be described as achieving CR, partial remission (PR), stable disease (SD), or progressive disease (PD).

Maintenance therapy is the use of lower doses at less frequent intervals to sustain remission. When the patient relapses, the original induction protocol is given as reinduction chemotherapy. Rescue or salvage chemotherapy employs different drugs and/or protocols after front line chemotherapy has failed the patient. The use of maintenance chemotherapy for lymphoma is controversial (Simon et al. 2005; Rosenthal 2001). Long-term chemotherapy has always been my preference for lymphoma management.

Each chemotherapy drug has a specific nadir, when it exerts its maximum myelosuppressive effect. The nadir is the time when we expect leukopenia and it may span for several days. The nadir starts at a certain point such as 7 or 10–12 days following administration of a specific drug (Chun, Garrett, and MacEwen 2001; Morrison 2002). Some cancer patients may develop a prolonged thrombocytopenia from drugs such as lomustine or carboplatin. When a cancer patient develops pancytopenia, it is important to determine if the marrow hypoplasia is caused by the chemotherapy or a neoplastic mechanism (Kearns and Ewing 2006).

Adverse events (AEs) are unfavorable and unintended problems or reactions associated with treatment. A consensus document describing common terminology for AEs is available in Vail et al. (2004). It employs a clinical grading scale of severity from 1 to 5. AEs are graded as mild (1), moderate (2), severe (3), life-threatening/disabling (4), or death related (5) within various categories such as GI, blood/bone marrow, cardiac, renal/genitourinary, metabolic, and so forth (Vail et al. 2004).

Combination Chemotherapy in Geriatric Pets

It is well understood that combination chemotherapy is more effective in gaining remission and cure than treatment with a single-agent protocol. Most geriatric pets are able to tolerate combination chemotherapy. The selection and sequencing interval of drugs involved in a particular combination protocol are designed to accomplish three goals that are not possible with single-agent therapy: (1) To maximize cell kill without toxicity to the host; (2) to provide a broader range of coverage to heterogeneous, mutant/resistant cells; and (3) to prevent and slow the emergence of resistant clones. The dose-toxicity relationship and the nadir of each drug selected for a protocol should be known by the administrator in order to anticipate and be prepared to offset adverse side effects. Geriatric patients generally benefit from combination chemotherapy. However, the protocols should be tailored to their specific body condition and functional reserves.

For Dogs

At best, chemotherapy has an 85–94% chance of creating remission in lymphoma and myeloma, and just over 50% efficacy in mast cell tumors. For most other tumor types, it yields only 20–33% response or is considered palliative. In spite of treatment with combination chemotherapy, high-grade malignancies such as hemangiosarcoma develop early resistance and metastasis with median survival from 3 to 6 months (Sorenmo et al. 2000).

Most dogs and cats handle chemotherapy very well. The veterinarian administering chemotherapy must be mindful of potential side effects and prepare pet owners to recognize them and treat them properly. Poodles, Scottish and other long hair Terriers, Maltese, and Shih Tzu breeds have a continuously growing (anagen phase) hair cycle and may develop alopecia (especially with the use of Adriamycin). The hair coat generally grows back 2 months after discontinuation of chemotherapy.

For Cats

At best, chemotherapy achieves remission in 87% of cats with lymphoma (Milner et al. 2005). Chemotherapy only provides 20–33% improvement in other types of cancer. In general, cats handle chemotherapy very well but they cannot tolerate cisplatin, 5-FU, or Xeloda[®]. Cats may have anorexia following chemotherapy but exhibit less nausea and vomiting than dogs, and they do not lose their fur. In shaved areas, the fur will grow back very slowly and may be a darker color. After 1 year of chemotherapy, cats have a velvety texture to their coat and their whiskers fall out. Whiskers will not grow back until chemotherapy is discontinued.

Neoadjuvant Chemotherapy

Neoadjuvant therapy is the use of chemotherapy at the earliest possible time in a treatment plan to cytoreduce a mass. It is most often used prior to surgery or perioperatively. In addition to cytoreduction, neoadjuvant therapy may reduce the metastatic potential of a tumor as it is manipulated during surgery. Neoadjuvant therapy given prior to surgery is difficult to justify in geriatric oncology. A major concern would be that the older patient might be overburdened with the stress of anesthesia, surgery, and immunosuppression from the drug, resulting in complications. It is very helpful and life saving in high-grade lymphoma following surgery.

Directed Chemotherapy

Special uses and delivery of chemotherapy are particularly appealing for geriatric patients. Directed chemotherapy, for example, is the delivery of drugs by one of the following methods: into the tumor (intralesional), into the tumor bed (intracavitary), intraperitoneal, intrathoracic, intrathecal, intraluminal, inhalational, organ-directed therapy such as liver-directed therapy, and so forth. Some chemotherapy drugs are encapsulated into STEALTH[®] liposomes such as Doxil[®]. It accumulates in tumor tissue and extravasates to deliver doxorubicin HCL into a leaky vascular tumor bed. Some liposomes will keep a drug active for a longer period of time. Liposome encapsulation may reduce the toxicity of some drugs.

Patients receiving intracavitary chemotherapy during surgery may receive follow-up external beam radiation therapy to the tumor field along with systemic chemotherapy, concurrently or in sequence, in a multimodality protocol. Some patients may receive intralesional chemotherapy prior to radiation therapy in a series of treatments to cytoreduce tumors, especially oral, head, and neck tumors. Dogs with carcinomatosis, sarcomatosis, or mesothelioma (with or without malignant effusion) that were given intraperitoneal or intrathoracic mitoxantrone and/or carboplatin survived 10 months longer than untreated cases (Charney et al. 2005).

Intralesional Chemotherapy

Many geriatric cancer patients will not be allowed to have general anesthesia for definitive surgery or receive systemic chemotherapy to control their tumors. However, their caregivers may be willing to try other convenient, less toxic options such as intralesional chemotherapy. We can use this technique to infiltrate surgical excision sites of incompletely resected masses. The most common tumors and tumor beds that we inject are mast cell tumors, hemangiopericytomas, fibrosarcomas, and squamous cell carcinoma (SCC).

Direct local delivery is accomplished with syringe injection to infiltrate chemotherapy along closely spaced gridlines to evenly infiltrate the mass and the area surrounding it. Jet guns, which use air pressure to drive the drug through the skin into the mass, are also feasible for intralesional delivery of chemotherapy at an estimated depth. Local hyperthermia may also be used to enhance the effect of intralesional or regional chemotherapy.

Chemotherapy agents are emulsified with various matrix vehicles to keep the drug in the tumor tissue. Matrix agents commonly used for intralesional injections of tumors include medical grade bovine collagen, sesame seed oil, safflower oil, and autologous serum. Intralesional chemotherapy is an excellent palliative option for geriatric cancer patients, although it yields variable results (Kitchell 1993; Theon 1990–1994; Weisse 2004; Goldstein 2004; Hahn 2005).

Carboplatin and 5-FU are the most common chemotherapy agents used for intralesional chemotherapy in our practice. In the past, we have used other agents such as BCG vaccine (for malignant melanoma), cisplatin, linoleic acid, inositol hexaphosphate (for fibrosarcomas), and more recently, Agaricus extract (from Agaricus blazei mushroom) for hemangiopericytoma, various other sarcomas, melanoma, and mammary carcinoma with some surprising successes. Intralesional delivery techniques may also be used to deliver gene therapy and vaccine into tumors.

Regional Chemotherapy

Interventional radiology (IR) is increasingly being used in veterinary medicine. It offers less invasive options that may deal with tumors that are difficult to access, holding promise for geriatric patients. IR uses fluoroscopy or ultrasound to guide the delivery of antitumor agents into the vasculature of non-resectable and metastatic tumors. The agents are designed or compounded to cause tumor embolization (embolotherapy) and localized cell death. With this growing sub-specialty, geriatric cancer patients have another option for tumor cell kill at lower overall systemic doses. Ultrasound imaging is also used to provide direct visualization of inoperable nodules that can be treated with percutaneous injections with various agents. The agents used with IR are creative and include ethanol, brachytherapy particles, magnetic particles, gene therapy, and so forth (Weisse 2004; Goldstein 2004).

Protocols for Various Tumor Types

There are literally hundreds of chemotherapy protocols used in cancer management. Each university teaches its favored protocols to resident students, who then modify them according to their preferences and their geriatric patients' needs. Every oncologist has his or her own favorite protocols and drugs. Appendix 1 has protocols that are currently used at my clinics to treat specific tumors in our geriatric oncology patients. Use good clinical judgment to select a working protocol and modify it to accommodate the individual geriatric oncology patient's requirements.

The drugs most commonly used for common tumors are presented in chart form (Table 6.1). When providing chemotherapy, it is important for the practitioner to check up-to-date information regularly, to learn of innovative protocols that improve patient survival. Look at a wide range of protocols to see which one fits your geriatric patient's unique set of concurrent conditions and polypharmacy to avoid interactions and side effects. Research the methods that other oncologists use for the particular malignancy and the issues that your geriatric patient is dealing with.

Since it is impossible to present all the protocols from the vast field of oncology in these pages, please refer to the specialty textbooks, proceedings, journal articles, www.Medscape.com, and membership sources through www.vin.com and www.vetstream.com. Veterinary Information Network (VIN) provides a free online information site for your clients, with helpful articles, at www.veterinarypartner.com. Lecture notes in oncology by Dr. Neal Mauldin show current protocols and clinical trials used at Louisiana State University, at www.vetmed.lsu.edu/oncology. A Web site hosted by Drs. Anthony Moore and Angela Frimberger, www.oncologypartners.com, contains insightful and up-to-date information for clinicians. www.Oncolink.com is run by the University of Pennsylvania Cancer Center for humans. It addresses animal cancer under the link Types of Cancer; Veterinary Oncology. Oncura Partners offers DVM consultations and case management suggestions for a fee at www.oncurapartners.com. In addition, most major clinical laboratories provide oncology consultations at no charge for clinicians who use their services.

Table 6.2 is a list of protocols used at Ohio State University Veterinary Oncology Service under the direction of Guillermo Couto, DVM, ACVIM (hematology-oncology). These protocols represent one of the most highly respected teaching hospitals that offer oncology services in this country. Chemotherapy protocols vary from one institution to the next and they are constantly changing. The protocol and drug doses that you select for your geriatric oncology patients should be verified as current through one of the given references and/or a consulting oncologist.

Table 6.1. Common Chemotherapy Drugs and the Animal Cancers in Which They Are Useful or Potentially Useful

Drug Name	Type of Cancer							Misc. Notes
	MCT	LSA	OSA	AC	MM	SA	CNS	
Prednisone (Hormone)	*	*	HO				*	Plasma cell, histiocytosis
COX-2 Inhibitors			*			*		Pain & palliation
Piroxicam, Meloxicam			*	*		*		TCC, SCC Anticancer effect
Deracoxib, Carprofen, etc.			*			*		Pain control Anticancer effect
Plant-Derived								
Vincristine (Oncovin [®])	*	*				*		TVT
Vinblastine (Velban [®])	*	*						Vasosclerotic
Taxol				*		*		Acute GI toxicity
Alkylating Agents								
Lomustine, carmustine	*	*					*	T-Cell LSA, histiocytosis
Cyclophosphamide (Cytoxan [®])		*		*	*	*		Hemorrhagic cystitis
Ifosfamide		*		*	*	*		Cystitis Must use Mensa
Chlorambucil (Leukeran [®])	*	*		*				M. Myeloma
Melphalan (Alkeran [®])		*r		*				M. Myeloma
Dacarbazine (DTIC-Dome [®])		*r			*			4–5 days
Procarbazine		*r					*	Lung cancer
Mechlorethamine		*r						T-Cell LSA
Antitumor Antibiotics								
Doxorubicin (Adriamycin), Epirubicin, Anthracyclines, Doxil, daunorubicin		*	*	*		*		Cardiotoxic, vasosclerotic hypersensitivity
Mitoxantrone		*r		*		*		RTx sensitizer
Actinomycin-D		*r						Vasosclerotic
Bleomycin		*r						SCC
Doxy/minocycline	*	*	*	*	*	*	*	Antiangiogenic
Antimetabolites								
Cytosine Arabinoside		*					*	4 hr. drip/SQ
Methotrexate		*					*	Folic acid *r

(continued)

Table 6.1. Common Chemotherapy Drugs and the Animal Cancers in Which They Are Useful or Potentially Useful (continued)

Drug Name	Type of Cancer							Misc. Notes
	MCT	LSA	OSA	AC	MM	SA	CNS	
Antimetabolites (continued)								
5-FU, Xeloda® (Never in cats)				*				Abdominal carcinomas, SCC
Hydroxyurea								Polycythemia
Gemcitabine (Gemzar®)				*				Pancreatic AC
L-asparaginase (Enzyme)		*						Potential allergic reactions
Heavy Metal Platinol								
Cisplatin (Never in cats)			*					Head/neck tumors Nephrotoxic Never use in cats
Carboplatin			*	*	*	*	*	Safe in cats
Anti-Angiogenesis Agents								
MMP Inhibitors	*	*	*	*	*	*	*	Investigational
Thalidomide	*	+/-	*	*	*	*	*	Birth defects
Tamoxifen (Hormone)				*	*	*		MGAC
NSAIDs, Avastin®, etc.			*	*	*	*		GI side effects
Targeted Therapy								
								Adjunctive Antisense therapy
Interferon		*		*	*	*	*	Retrovirus
Monoclonal Antibody		*						Target antigen
Gene Therapy		*		*	*	*		Investigational
Tyrosine Kinase Inhibitors	*	*	*	*				Small-molecules
Gleevec®, SAHA						*		Hemangiosarcoma
SU11654, small molecules, etc.	*							Miscellaneous To be announced

*r = Rescue drugs used in resistant lymphoma protocols.

Table 6.2. Protocols Used at the Ohio State University Veterinary Oncology Service**I. Lymphoma****A. Induction of remission****1. COAP protocol**

Cyclophosphamide (Cytoxan®): 50 mg/m² BSA, PO, every other day for 8 weeks in **dogs**; (200–300 mg/m², PO, every 3 weeks in **cats**).

Vincristine (Oncovin®): 0.5 mg/m² BSA, IV, once a week, for 8 weeks.

Cytosine arabinoside (Cytosar®): 100 mg/m² BSA, IV, or SQ, divided BID, for 4 days.

Prednisone: 40–50 mg/m² BSA, PO, SID for a week; then 20–25 mg/m² BSA, PO, every other day for 7 weeks.

In cats, cytosine arabinoside is used for only 2 days, and the remaining 3 drugs (cyclophosphamide, vincristine, prednisone) for 6 weeks rather than 8 weeks.

2. COP protocol

Cyclophosphamide (Cytoxan®): 50 mg/m² BSA, PO, every other day dogs; or 300 mg/m² BSA, PO, every 3 weeks (dogs or cats)*.

Vincristine (Oncovin®): 0.5 mg/m² BSA, IV, once a week.

Prednisone: 40–50 mg/m² BSA, PO, SID for a week; then 20–25 mg/m² BSA, PO, every other day.

*The duration of chemotherapy using this protocol is variable.

3. CLOP protocol

As in COP, but with the addition of L-asparaginase (Elspar®), at a dose of 10,000–20,000 IU/m² BSA, SQ, once every 4–6 weeks.

4. CHOP protocol (21-day cycle)

Cyclophosphamide (Cytoxan®): 200–300 mg/m² BSA, IV, day 10.

Doxorubicin (Adriamycin): 30 mg/m² BSA, IV, day 1.

Vincristine (Oncovin®): 0.75 mg/m² BSA, IV, days 8, 15.

Prednisone: 40–50 mg/m² BSA, PO, SID days 1–7; then 20–25 mg/m² BSA, PO, QOD, days 8–21.

Sulfa-trimethoprim: 15 mg/kg, PO, BID.

B. Maintenance**1. Chlorambucil (Leukeran®): 20 mg/m² BSA, PO, every other week;**

Prednisone: 20–25 mg/m² BSA, PO, every other day.

2. LMP protocol

Chlorambucil (Leukeran®) and prednisone as above, plus methotrexate 2.5–5 mg/m² BSA, PO, twice or 3 times a week.

3. LAP protocol

Chlorambucil (Leukeran®): 20 mg/m² BSA, PO, every other week.

Prednisone: 20–25 mg/m² BSA, PO, every other day.

Cytosine arabinoside (Cytosar®) 200–400 mg/m², SQ, every 2 weeks, alternating with Leukeran®.

4. COP protocol used every other week for 6 cycles; then every third week for 6 cycles; and once a month thereafter.**C. "Rescue"****DOGS****1. D-MAC protocol (repeat continuously for 10–16 weeks)**

Dexamethasone 0.5 mg/lb, PO or SQ on days 1 and 8.

Actinomycin D (Cosmegen®) 0.75 mg/m², IV push on day 1.

Cytosine arabinoside (Cytosar®) 200–300mg/m², IV drip over 4 hours, on day 1.

Melphalan (Alkeran®) 20 mg/m², PO, on day 8 (**AFTER 2–3 DOSES OF MELPHALAN, SUBSTITUTE IN LEUKERAN® AT THE SAME DOSE**)

(continued)

Table 6.2. Protocols Used at the Ohio State University Veterinary Oncology Service (continued)**I. Lymphoma (continued)****C. "Rescue" (continued)****DOGS (continued)****2. ADIC protocol**

Doxorubicin (Adriamycin) 30 mg/m² BSA IV, Q/3 weeks.

Dacarbazine (DTIC-Dome[®]) 1,000 mg/m² BSA, IV drip for 6–8 hours, once every 3 weeks.

3. L-asparaginase (Elspar[®]) 10,000–30,000 IU/m² BSA, IM, Q/2 or 3 weeks.

4. CHOP protocol if second relapse on COAP or if good response to Adriamycin was previously observed in the patient.

CATS

1. Cytosine arabinoside (Cytosar[®]): 100–200 mg/m² BSA/day, IV drip for 6–24 hours.

Mitoxantrone (Novantrone[®]) 4 mg/m², IV drip, mixed in the bag with the Cytosar[®].

Dexamethasone 0.5–1 mg/lb, PO, once a week.

Repeat every 3 weeks.

II. Acute lymphoid leukemia (ALL)

COAP, CLOP, or COP.

III. Chronic lymphocytic leukemia (CLL)

1. Chlorambucil (Leukeran[®]): 20 mg/m² BSA, PO, every other week (with or without prednisone 20 mg/m² BSA, PO, every other day).

2. Cyclophosphamide (Cytosan[®]): 50 mg/m² BSA, PO, 4 days a week.

Prednisone 20 mg/m² BSA, PO, every other day.

IV. Acute myelogenous leukemia (AML)

1. Cytosine arabinoside (Cytosar[®]): 100 mg/m² BSA/day, IV drip or SQ (divided BID) for 4 days.

6-Thioguanine (6-TG[®]) 40–50 mg/m² BSA, PO, SID, or QOD.

2. Cytosar[®] and 6-TG[®] plus Adriamycin (10 mg/m² BSA, IV, on days 2 and 4 of the cycle).

3. Cytosine arabinoside (Cytosar[®]): 100–200 mg/m² BSA/day, IV drip for 1–2 days.

Mitoxantrone (Novantrone[®]) 4 mg/m², IV drip, mixed in the bag with the Cytosar[®].

Repeat every 3 weeks.

V. Chronic myelogenous leukemia (CML)

1. Hydroxurea (Hydrea[®]): 50 mg/kg, PO, divided BID, daily or QOD until normal white blood count.

VI. Multiple myeloma

1. Melphalan (Alkeran[®]): 2 mg/m² BSA, PO, SID x 1 week; then QOD.

Prednisone: 40–50 mg/m² BSA, PO, SID x 1 week; then 20 mg/m² BSA, PO, QOD. Can also be used at 6–8 mg/m², PO, for 5 days, repeating every 21 days.

2. CHOP protocol.

VII. Mast cell tumors (systemic)

1. Prednisone: 40–50 mg/m² BSA, PO, SID for a week; then 20–25 mg/m² BSA, PO, QOD.

2. Prednisone: 40–50 mg/m² BSA, PO, SID for a week; then 20–25 mg/m² BSA, PO, QOD.

Cimetidine (Tagamet[®]): 10 mg/kg, PO, QID (optional).

3. Prednisone: 40–50 mg/m² BSA, PO, SID for a week; then 20–25 mg/m² BSA, PO, QOD.

CCNU (lomustine) 60–100 mg/m², PO, q/3–4 weeks

4. CVP protocol

Vinblastine (Velban[®]): 2 mg/m² BSA, IV, once a week.

Cyclophosphamide (Cytosan[®]): 50 mg/m² BSA, PO, QOD or 4 days a week.

Prednisone: 20–25 mg/m² BSA, PO, QOD.

VIII. Soft tissue sarcomas—Dog**1. ADIC protocol (for spindle cell sarcomas)**

Doxorubicin (Adriamycin): 30 mg/m² BSA, IV, Q/3 weeks.

DTIC-Dome[®] (Dacarbazine): 1,000 mg/m² BSA, IV drip for 6–8 hours; repeat Q/3 weeks.

Sulfa-trimethoprim: 15 mg/kg, PO, BID.

(continued)

Table 6.2. Protocols Used at the Ohio State University Veterinary Oncology Service (continued)**VIII. Soft tissue sarcomas—Dog (continued)**

2. VAC protocol (21-day cycle) [for other sarcomas]
 Vincristine (Oncovin®): 0.75 mg/m² BSA, IV, days 8, 15.
 Doxorubicin (Adriamycin): 30 mg/m² BSA, IV, day 1.
 Cyclophosphamide (Cytosan®): 200–300 mg/m² BSA, PO, day 10.
 Sulfa-trimethoprim: 15 mg/kg, PO, BID.

IX. Soft tissue sarcomas—Cat

1. Carboplatin (Paraplatin®) 200–280 mg/m², IV, every 3–4 weeks.
2. AC protocol (21-day cycle)
 Doxorubicin (Adriamycin): 1 mg/kg, IV day 1.
 Cyclophosphamide (Cytosan®): 100–150 mg/m² BSA on days 10 and 11.
3. VAC protocol (28-day cycle)
 Vincristine (Oncovin®): 0.5–0.75 mg/m² BSA, IV, days 8, 15, 22.
 Doxorubicin (adriamycin): 1 mg/kg, IV day 1.
 Cyclophosphamide (Cytosan®): 100–150 mg/m² BSA on days 10 and 11.
4. MiC protocol (21-day cycle)
 Mitoxantrone (Novantrone®): 4–6 mg/m², IV drip over 4 hours, on day 1.
 Cyclophosphamide (Cytosan®): 200–300 mg/m², PO, on day 10.
5. MiCO protocol (21-day cycle)
 Mitoxantrone (Novantrone®): 4–6 mg/m², IV drip over 4 hours, on day 1.
 Cyclophosphamide (Cytosan®): 200–300 mg/m², PO, on day 10.
 Vincristine (Oncovin®): 0.5 to 0.6 mg/m², IV, on days 8 and 15.

X. Osteosarcoma—Dog

1. Cisplatin (Platinol®): 50–70 mg/m² BSA, IV drip, Q/3 weeks. Prior intensive diuresis is required.
2. Carboplatin (Paraplatin®): 300 mg/m², IV, Q/3–4 weeks.
3. Doxorubicin (Adriamycin): 30 mg/m², IV, every 2 weeks, for 6 doses.

XI. Carcinomas—Dog

1. Carboplatin (Paraplatin®): 300 mg/m², IV, Q/3–4 weeks
2. CMF protocol
 Fluorouracil (5-FU): 150 mg/m² BSA, IV, once a week.
 Cyclophosphamide (Cytosan®): 50 mg/m² BSA, PO, 4 days a week or QOD.
 Methotrexate: 2.5 mg/m² BSA, PO, 2 or 3 times a week.
3. FAC protocol
 5-Fluorouracil (5-FU): 150 mg/m² BSA, IV, days 8 and 15.
 Doxorubicin (Adriamycin): 30 mg/m² BSA, IV, day 1.
 Cyclophosphamide (Cytosan®): 200–300 mg/m² BSA, PO, day 10.
 Sulfa-trimethoprim: 15 mg/kg, PO, BID.
4. Cisplatin (Platinol®): 60–70 mg/m² BSA, IV drip, Q/3 weeks. Prior intensive diuresis is required.
5. VAF protocol
 Vincristine (Oncovin®): 0.75 mg/m² BSA, IV, days 8, 15.
 Doxorubicin (Adriamycin): 30 mg/m² BSA, IV, day 1.
 5-Fluorouracil (5-FU): 150 mg/m² BSA, IV, days 1, 8, 15.
6. VAC protocol
7. 5-Fluorouracil (5-FU): 150 mg/m² BSA, IV, once a week.
 Cyclophosphamide (Cytosan®): 50 mg/m² BSA, PO, 4 days a week or QOD.

XII. Carcinomas—Cat

5-Fluorouracil is toxic for the cat, producing severe and often fatal CNS signs. Cisplatin is also extremely toxic, causing acute pulmonary toxicity in this species.

1. Carboplatin (Paraplatin®) 200–240 mg/m², IV, every 3–4 weeks.
2. AC protocol (28-day cycle)
 Doxorubicin (Adriamycin): 1 mg/kg, IV day 1.

(continued)

Table 6.2. Protocols Used at the Ohio State University Veterinary Oncology Service (continued)**XII. Carcinomas—Cat (continued)**

2. AC protocol (28-day cycle) (continued)
Cyclophosphamide (Cytoxan®): 100–150 mg/m² BSA on days 10 and 11.
3. VAC protocol (28-day cycle)
Vincristine (Oncovin®): 0.5–0.75 mg/m² BSA, IV, days 8, 15, 22.
Doxorubicin (Adriamycin): 1 mg/kg, IV day 1.
Cyclophosphamide (Cytoxan®): 100–150 mg/m² BSA on days 10 and 11.
4. Vincristine (Oncovin®): 0.5 mg/m² BSA, IV, once a week.
Cyclophosphamide (Cytoxan®): 50 mg/m² BSA, PO, 4 days a week or QOD.
5. MiC protocol (21-day cycle)
Mitoxantrone (Novantrone®) 4–6 mg/m², IV drip over 4 hours, on day 1.
Cyclophosphamide (Cytoxan®) 200–300 mg/m², PO, on day 10.
6. MiCO protocol (21-day cycle)
Mitoxantrone (Novantrone®) 4–6 mg/m², IV drip over 4 hours, on day 1.
Cyclophosphamide (Cytoxan®) 200–300 mg/m², PO, on day 10.
Vincristine (Oncovin®) 0.5–0.6 mg/m², IV, on days 8 and 15.

Precautions with Specific Chemotherapy Agents

You have the ultimate responsibility for your geriatric cancer patients. Conversions, calculations, and decimal placement for all dosages should be double-checked and confirmed prior to use, including chemotherapy drugs that are dispensed. Be sure to use an overweight patient's lean body mass for all calculations. Adjust all drug doses and selections for species-specific toxicity, obesity, chronic kidney disease, cardiac disease, liver disease, cancer cachexia, leukopenia, thrombocytopenia, anemia, and other concurrent medical conditions and polypharmacy that may affect each particular geriatric patient. Use the dose escalation system for geriatric cancer patients, starting with the lowest dose first and then increasing the dose to the known maximally tolerated dose (MTD) if the patient shows no adverse side effects.

An example of using specific precautions applies to the use of ifosfamide (Ifex®) for treating sarcomas. It is an alkylating agent that shares similar pathways with Cytoxan to produce metabolites that release acrolein, which causes hemorrhagic cystitis. A 6-hour Mesna-diuresis protocol is required to prevent the adverse effects of acrolein-induced damage to uroepithelium and nephrotoxicosis. The MTD dose for dogs is 375 mg/m², whereas cats tolerated dose escalations to an MTD of 900 mg/m² in a phase I study (Rassnick et al. 2006a). Ifex is not considered nephrotoxic in dogs but caused acute renal failure in 7% (2/27) of cats in a phase II study (Rassnick et al. 2006b).

The following precautions have become incorporated into our protocols to avoid toxicity for geriatric and frail patients:

1. Avoid Cytoxan-induced hemorrhagic cystitis: Advise clients to increase the pet's fluid intake when using Cytoxan. We give prednisone at 20 mg/m² on the days of oral Cytoxan and recommend feeding broth or soup. This strategy has reduced the incidence of Cytoxan-induced hemorrhagic cystitis in our practice to almost zero. We don't use Cytoxan IV in geriatric patients. Our preference is to spread out the dose PO over 2 or 3 days to avoid toxicity.
2. Avoid Adriamycin toxicity and under-dosing in large-breed dogs: Split the delivery of Adriamycin in large-breed dogs by giving 20 mg/m² and repeat in 4–8 days. This technique provides a higher overall total dose. It avoids using the MTD of 30 mg/m², which may cause adverse events yet is considered an under-dose in large dogs.

3. Avoid lomustine nadir: Divide the MTD of 50–90 mg/m² by three to four and give that dose over 4–8 days. Repeat every 21 days in dogs and every 30–42 days in cats, depending on CBC results.
4. Avoid toxicity in frail geriatric patients: Consider metronomic (low continuous dose) therapy. For example, instead of giving Xeloda in a pulse cycle PO twice a day for 10 days on and 10 days off, give it once a day or once every other day on a continuous basis. Never use Xeloda in cats.

The Treatment Calendar

Caretakers are often emotionally overwhelmed by the news that their pet has cancer. They are additionally overwhelmed by the list of treatments, medications, tests, and supplements that will be used to help their pet survive. A treatment calendar helps clients to get organized at home without forgetting to give medications and supplements on schedule.

When we give clients their treatment calendar, we explain the entire chemotherapy protocol as well as supportive drugs and supplements. The calendar includes recheck dates and the type of blood test needed for monitoring. Our technicians check the calendar and draw the patient's blood accordingly. They run the tests while the owner is waiting for the exam.

The top line of the treatment calendar reads: *“Always bring this calendar and your Rx bottles with you on your next appointment”* (Figure 6.1). We read this top line to the caregivers and remind them to bring the chemotherapy chart and their medication bottles for each visit.

Encourage clients to keep notes on the treatment calendar about how the pet seems to feel after each chemotherapy visit and any side effects that occur. We carefully review this calendar with the client at every recheck.

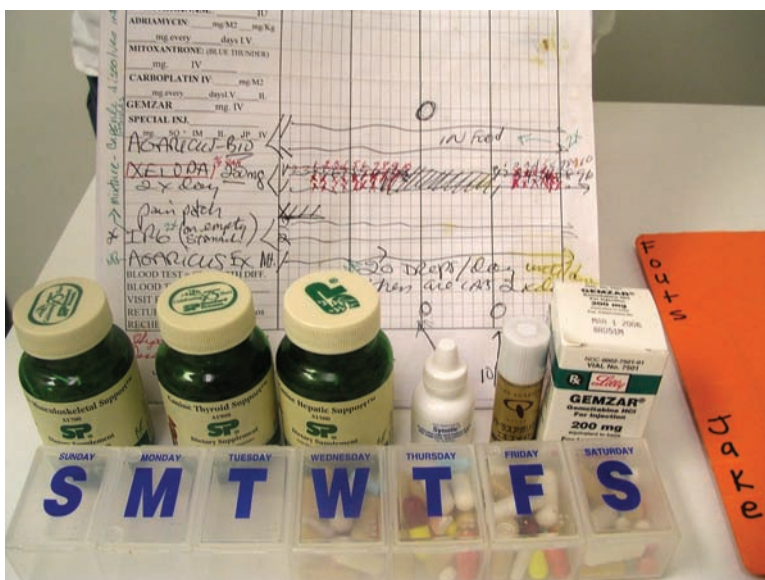


Figure 6.1. The treatment calendar and Rx bottles are reviewed at each visit.

This calendar is important as it quickly shows us what medications the patient has received and what drug is next. By taking the time to go over the previous month's chemotherapy calendar and outline the drugs for the new calendar, we can catch mistakes made by the pet owner and look for potential drug interactions.

Our nursing staff looks at the bottles and sometimes we count the tablets to see if they are being used properly. It is important to take these precautions, especially for senior citizen clients who may have some confusion. It is not unusual to discover something that needs to be adjusted. This inspection is a review for the client on the importance and purpose of the medications and to see if the pet is having any problems accepting them.

It is surprising how many people make mistakes. The May 2005 issue of *Veterinary Economics* focused on servicing a growing segment of senior clients. It quoted from the American Animal Hospital Association (AAHA) 2004 Pet Owner Survey that 7% of active clients are 65 or older and that this segment may increase to 35% by 2020. Some elderly people may have trouble understanding and remembering what they are told. Some forget instructions and get confused with the medications. Sometimes a mistake can be fatal, as in Pookie's case, which follows. Common sense is an ingredient that we are unable to add to our client's thinking. However, we must do the best we can to give clear written instructions and then carefully check the use of potent chemotherapy drugs in order to prevent mistakes.

Pookie's Case (A Senseless Senior Moment Overdose)

Pookie, a 12-year-old F/S Scottish Terrier-mix, belonged to a senior couple. She was referred for treatment of residual grade II-III mast cell cancer. The family elected to use oral alternate day prednisone and lomustine. Their instructions were to give one 10 mg capsule of lomustine once a day for 2 consecutive days only. We dispensed two capsules per visit. They were instructed to repeat the cycle for lomustine every 21 days after recheck blood tests to monitor platelets and liver enzymes. They wanted to save money and learned that their daughter could get the lomustine at a friend's pharmacy. The directions and dose were clearly outlined in the chemotherapy treatment calendar and the clients had used lomustine properly according to instructions for over 2 months. We issued a written prescription for the lomustine to be used as directed on the chemotherapy treatment calendar.

Three weeks later, Pookie was presented in very poor condition for a recheck. The CBC revealed profound neutropenia and thrombocytopenia. These low values were totally unexpected. We reviewed the chemotherapy treatment calendar with the couple and found no errors. I asked the family to show me their Rx bottles and show me exactly what pills they were giving on a daily basis. We found that the new prescription of lomustine was being given improperly at the rate of one 10 mg capsule once a day, every day! This represented a fatal overdose for poor Pookie.

We explained to the clients that Pookie needed to be hospitalized on an emergency basis and that she needed intense monitoring and nursing for over 6 weeks because lomustine has a prolonged effect. We offered options for treatment with Neupogen® and multiple transfusions to help restore red cells and white cells but we had no way to restore her platelet count. We explained that Pookie's platelets would most likely not regenerate following the magnitude of her lomustine toxicity. For these reasons, we knew that the damage to Pookie's bone marrow was most likely irreversible. She would probably die even with the best of supportive treatment even if the family could afford the expense.

Summary: Chemotherapy in the Management of Geriatric Cancer

Geriatric dogs and cats undergo a progressive decline in the functional reserve of their major organ systems. They may be less able to cope with chemotherapy following the stress of surgery and radiation in a multimodality protocol. The presence of comorbidities associated with aging necessitates modifications to the drug dosages and timing of standard chemotherapy protocols. Astute clinical and home monitoring of the geriatric patient is needed, as well as accessible, compassionate doctor-client communication.

Combination chemotherapy offers better efficacy for treating cancer; however, dose modification is important to minimize toxicity for geriatric patients. The attending doctor can research and offer other less toxic options such as intralesional and regional chemotherapy delivery or metronomic (low dose) therapy or pulse therapy. Successful pulse therapy was reported for 14 dogs with apocrine anal sac adenocarcinoma following surgery. They were given melphalan at 7 mg/m² orally over a 5-day period followed by 16 days off for life (Emms 2005).

In the coming years, cancer patients may routinely receive small molecule therapy and chemoprevention as part of a permanent maintenance program. This would add yet another maintenance modality of therapy, sequenced after the initial treatment.

Adverse Effects of Cancer Therapy in Geriatric Pets

We must never lose sight of the fact that there are some patients we cannot help; there are none we cannot harm.

Dr. Carl A. Osborne, DVM, PhD, ACVIM

The treatment of cancer in geriatric pets bears a risk-to-benefit ratio that includes the possibility of experiencing a wide range of AEs from the use of surgery, radiation, and chemotherapy. The adverse effects from surgery and radiation therapy are discussed in previous sections of this chapter. This section focuses mainly on the various adverse effects associated with chemotherapy and its multiple applications. The caregiver needs education regarding what and when to expect adverse effects. A user-friendly list of AEs may be very helpful to educate caregivers (Table 6.3).

The Veterinary Cancer Society has a clinical trials arm known as VCOG (Veterinary Co-operative Oncology Group). VCOG created a consensus document known as CTCAE (Common Terminology Criteria for Adverse Events), which parallels the National Cancer Institute (NCI) evaluation program, available at <http://ctep.cancer.gov>. The VCOG-CTCAE tables are adapted for dogs and cats and are intended to standardize the reporting of adverse effects for clinical trials using the grade 1–5 system described in the “Chemotherapy in the Management of Geriatric Cancer” section of this chapter. Some oncologists use the 0–4 grading system for chemotherapy-related toxicities (Table 6.4).

Chemotherapy agents, along with the support drugs used in cancer management, are well known for causing physical side effects such as polydipsia, polyuria, nausea, vomiting, colitis, and diarrhea. More insidiously, chemotherapy may cause bone marrow suppression with severe leukopenia, which may result in life-threatening sepsis. Thrombocytopenia may be induced by chemotherapy drugs, especially the platinum-based drugs and lomustine. Renal failure is notorious with nephrotoxic cisplatin. This agent is not used in my clinics. Cats are intolerant of certain chemotherapy drugs, specifically 5-FU and cisplatin. Cardiomyopathy is a well-known adverse effect in dogs receiving cardiotoxic doxorubicin (Adriamycin). Familiarize yourself to know what drugs can injure which susceptible tissues, resulting in the specific adverse effect (Table 6.5).

Table 6.3. Chemotherapy Agent Clearance and Adverse Events

Generic Name	Brand Name (®)	Cleared Via	Clearance Time	Route of Therapy	Side Effects
actinomycin-D	Cosmegen	Urine, feces	7 days	IV	Vessels, marrow, GI
doxorubicin	Adriamycin	Feces	7 days	IV infusion	Marrow, GI, heart, anaphylaxis, severe vesicant
asparaginase	Elspar			IM or SQ	Allergy, marrow
azathioprine	Imuran	Urine	8 hours	PO	Marrow, GI
carmustine	BCNU	Urine	4 days	IV	Marrow, lungs, GI, nephrotoxic
lomustine	CCNU	Degradation	1 day	PO, IV	GI, marrow, lungs, liver
carboplatin	Paraplatin	Urine	1 day	IV infusion	Marrow, GI, allergy
cisplatin	Platinol	Urine	1 day	IV, IV infusion	Nephrotoxic, GI, marrow, KILLS CATS
capecytabine	Xeloda (oral prodrug of 5-FU below)	Urine	1 day	PO	Marrow, GI, CNS, KILLS CATS
fluorouracil	5-FU	Urine	1 day	IV, IL	Marrow, GI, CNS, KILLS CATS
chlorambucil	Leukeran	Urine	1 day	PO	Marrow, GI
cyclophosphamide	Cytoxan	Urine	3 days	PO, IV	Marrow, nephrotoxic, GI
cytosine arabinoside	Cytosar-U	Urine	1 day	IV, SQ	Marrow, GI
etoposide/VP-16	VePesid	Urine	1 day	PO, IV	Marrow, GI
gemcytabine	Gemzar	Urine	3–4 days	IV	Marrow, GI, flu syndrome
ifosfamide	Ifex	Urine	7 days	IV infusion	Urotoxic without mesna, marrow, CNS
interferon	(many)	Urine	1 day	SQ, IM, PO	Lethargy, prostration
mechlorethamine	Mustargen	Urine	5 minutes	IV	Toxic contact, vesicant, amyloidosis
melphalan	Alkeran	Urine	7 days	PO, IV	Marrow
methotrexate	Trexsol	Urine	1 day	PO, IV	GI, marrow
mitoxantrone	Novantrone	Urine, feces	7 days	IV infusion	GI, marrow
paclitaxel	Taxol	Feces	5 days	IV	Marrow, GI, anaphylaxis
prednisone		Urine	12 hours	PO	PUPD, weakness, panting, Cushings
procarbazine	Matulane	Urine	1 day	PO	Marrow, GI, liver, CNS, drug interactions
small molecules	TBA	Variable	Variable	PO, IV, IL	Variable
vinblastine	Velban	Urine	3 days	IV	Vessels, marrow, GI
vincristine	Oncovin	Urine, feces	7 days	IV	Vessels, nerves, marrow, GI
vinorelbine	Navelbine	Urine	5–8 days	IV infusion	Marrow, vesicant

Source: Reprinted with permission of Laurie Kaplan from the book *Help Your Dog Fight Cancer*, and adapted by Alice Villalobos DVM.

Table 6.4. Toxic Effect and Grade for Chemotherapy-Related Toxicities, Adapted from the NCI Toxicity Table

Toxic effect and grade for chemotherapy-related toxicities adapted from the NCI toxicity table					
Grades	0	1	2	3	4
Effects					
Neutropenia	None	1,500–2,500	1,000–1,500	500–1,000	< 500
Diarrhea	None	Soft stools, response to diet change	< 2 days	2–5 days	> 5 days
Vomiting	None	Nausea	Sporadic, self-limiting	< 2 days	> 5 days or requires hospitalization
Anorexia	None	Inappetence	< 3 days	3–5 days	> 5 days

Source: *Veterinary and Comparative Oncology*, Volume 2, No. 3, September 2004 with permission of Blackwell Publishing.

Table 6.5. Common Adverse Effects from Various Chemotherapy Agents

Name of drug	Susceptible tissue	Adverse effects
Anthracyclines Doxorubicin (Adriamycin®) Daunorubicin Doxil (liposome compound)	Heart Bone marrow Gut, kidneys (in cats) Perivascular tissues (Vasoclerotic) Skin-hand-foot, axilla, groin	Arrhythmias, Cardiomyopathy, Congestive heart failure, death emesis, colitis, azotemia (cats) Myelosuppression Severe, deep, fungating necrosis if extravasated (read section)
Vincristine (Oncovin®) Vinblastine (Velban®) Vinorelbine tartarate (Navelbine®)	Bone marrow Peripheral nerves Ulcers if extravasated	Mild bone marrow suppression, Mild tingling of nerves, ileus Vomiting, colitis, constipation Peripheral neuropathy
Cyclophosphamide (Cytosan®) Ifosfamide (Ifex®)	Bladder mucosa Bone marrow Gonads Renotoxic (cats)	Low WBC, hematuria, chronic hemorrhagic cystitis, sterility, Bladder cancer (late onset) Mensa-diuretic protocol needed
Prednisone, prednisolone Dexamethasone (all steroids)	Hunger/thirst center Muscle Gut Skin and coat Endocrine	Increased water intake and urination, restlessness Muscle wasting, bleeding ulcers, obesity, thin skin Diabetes mellitus, hepatopathy
Chlorambucil (Leukeran®)	Bone marrow	Mild myelosuppressant
Carboplatin (Paraplatin®) Cisplatin (Platinol®) (I don't use this drug) Must be given during intense diuresis (25 ml/kg/hr)	Bone marrow, kidneys Nephrotoxic w/o IV fluids Bone marrow Gut, acoustic nerves (Lungs—KILLS CATS)	Myelosuppression Acute kidney failure and death Myelosuppression, colitis, hearing loss, Cats: Pulmonary edema, death

(continued)

Table 6.5. Common Adverse Effects from Various Chemotherapy Agents (continued)

Name of drug	Susceptible tissue	Adverse effects
Cytarabine (Cytosar [®])	Bone marrow (if given IV)	Low WBC
Dacarbazine (DTIC-Dome [®])	Gut, bone marrow	Low WBC, vomiting, seizures
Mitoxantrone (Novantrone [®])	Bone marrow	Low WBC
Fluorouracil (5-FU, Xeloda [®])	Gut, CNS (<i>Kills cats</i>)	Seizures, ataxia
Bleomycin	Lungs	Fibrosis, poor diffusion
Lomustine (CeeNu)	Bone marrow, liver, eyes	Low platelets/white cells
Methotrexate	Kidneys, liver	Vomiting
Mechlorethamine (Mustargen [®])	GI tract, vasosclerotic	Vomiting, myelosuppression
Piroxicam/thalidomide NSAIDs	Gut, liver Kidneys, coagulation system	Bleeding ulcers, vomiting Anemia, coagulation problems
Melphalan (Alkeran [®])	Bone marrow	Myelosuppression
Taxol [®] , Taxotere [®] , paclitaxel	GI tract	Myelosuppression, CNS, tingling Vomiting
Capecytabine (Gemzar [®])	GI tract, liver Bone marrow	Myelosuppression, vomiting, diarrhea
Imitinab (Gleevec [®])	Liver	Bone marrow suppression, GI
Anti-angiogenesis drugs	Gastrointestinal	Multiple pathways
Targeted therapy drugs	Specific proteins in cells	Multiple pathways
Gene therapy	Specific features in cells	Multiple pathways, Sense and antisense
Newly released drugs: To Be Announced (TBA)	TBA	TBA
Protocols: lymphoma-leukemias	Malignant blast cells	Tumor breakdown syndrome

Some multimodality treatment protocols call for the concurrent use of chemotherapy during the radiation therapy cycle (Table 6.6). Multimodality treatment may increase tumor kill but also places the geriatric oncology patient at greater risk for chemotherapy- and radiation-related acute toxicity (Gustafson et al. 2004). Radiation therapy predictably causes immediate and delayed effects with variable levels of toxicity. Acute effects from radiation therapy include erythema, pain, desquamation, mucositis, lethargy, and diarrhea (Table 6.7). Radiation toxicity is related to the dosimetry and fraction scheme. When evaluating chemotherapy-related radiation toxicity, use the grade 0–4 Radiation Morbidity Scoring Schema (Table 6.8).

Table 6.6. The Most Frequently Recommended Treatments for the Most Common Tumors

Type of Cancer	Type of Multimodality Treatment			
	Surgery	Chemotherapy	Radiation	Adjuvant Tx
Mast cell tumor	*	*	*	H-2 blockers
Skin cancer, SCC	*	+/-	*	Cryotherapy Laser therapy
Lymphoma	-/+	*	+/-	MoAb, vaccine
Breast cancer	*	*	+/-	Vaccine
Anal, sweat AC	*	*	*	Ck calcium
STS	*	*	*	Gene therapy
FVAS	*	*	*	Gene therapy
OSA	*	*	*samarium	Limb sparing
Head/neck	*	*	*	Brachytherapy
Malignant melanoma	*	*	*	Vaccines
Oral cancer	*	*	*	Brachytherapy
Nasal cancer		+/-	-/+	Post-RTx Sx for residual disease
Brain tumor	+/-	*	*	Steroids
Endocrine tumor	*	*	+/-	Iodine 131
Abdominal tumor	*	*		Second look Sx
Bladder/prostate cancer	-/+	*	+/-	Piroxicam
Hemangiosarcoma	*	*	-	Antiangiogenesis Tx
Liver cancer	+/-	*	-	Percutaneous ethanol inj. in selected tumors?
Intestinal AC Colorectal AC	*	+/-	-	Downstage with chemo/radiation before surgery
Primary lung cancer or metastatic disease	*	*	- /+	Nebulized liposomes containing IL-2

Some chemotherapy agents are synergistic or radiomimetic with radiation and may cause increased local tissue necrosis and discomfort. Radiation oncologists use this synergism to benefit the geriatric oncology patient. Mast cell tumors have the potential to release histamine during surgery or radiation therapy, causing localized inflammatory swelling and systemic effects. Clients must always be educated and informed about potential side effects so that they can be watchful and prepared.

Table 6.7. List of Typical Short- and Long-Term Side Effects and Risks of External Beam Radiation Therapy (Teletherapy) Directed at Specific Locations of the Body

Radiation Therapy Field (Tumor Bed)	Short-Term Side Effects	Long-Term Effects Late Onset Risks
Brain, cranium	Dermatitis, conjunctivitis Mucositis, acute otitis	Cataracts, hearing loss, mental dullness, necrosis
Nasal passage Frontal sinus	Mucositis, dermatitis Oral sensitivity	Dental problems, cataracts Skin necrosis over bone
Throat, oral cavity, mandible, maxilla	Mucositis, pain, (most severe if pet has not had dental prophy)	Hypothyroidism Dental problems, xerostomia Bone necrosis, sequestrum
Chest/thorax	Dermatitis, esophagitis	Fibrosis of lungs and heart
Skin Mast cell cancer Soft tissue sarcoma	Dermatitis, hair loss Local desquamation Degranulation reaction dermatitis, self-injury	Hair loss, scar formation, thin skin, later malignancy Scarring, permanent hair loss Need for skin graft
Legs/extremities, bone	Dermatitis, lameness Anemia, lymphocytopenia	Demineralization, necrosis, ligament failure, sequestrum
Abdomen and pelvic area	Colitis, indigestion	Liver, gut, kidney problems
Anus	Mucositis, colitis	Stricture, loss of function

Medications used for pain control, such as NSAIDs and narcotics, may cause GI ulceration, hemorrhage, constipation, and sedation. It is essential to teach caregivers how to take their pet’s temperature and to monitor, recognize, and be prepared to deal with any type of adverse side effects as soon as possible. This is particularly important for caretakers of older, more fragile patients.

Side Effects of Chemotherapy

The drugs used in cancer management may cause polydypsia, polyuria, panting, nausea, vomiting, diarrhea, anorexia, bone marrow suppression, alopecia, acute renal failure (cisplatin, ifosfamide), cardiac arrhythmias, heart failure (Adriamycin), hepatopathy, pancreatitis, urticaria, rash, anaphylaxis, blindness, neuropathy, erythema multiforme, toxic epidermal necrolysis, and so forth. Patients treated for advanced stage lymphoma-leukemia may experience acute tumor lysis syndrome. The list of adverse effects related to chemotherapy is extensive and must include the possibility of unforeseen death.

The degree of neutropenia, diarrhea, vomiting, and anorexia induced by chemotherapy can be more objectively evaluated using the grade 0–4 scale adapted from the NCI chemotherapy-related toxicity table (Table 6.4).

A unique ulcerative plantar-palmar rash called hand-foot syndrome occurs with Doxil, a liposome encapsulated Adriamycin preparation. The rash may also appear in the axilla and groin and cause

Table 6.8. Radiation Toxicity

Tissue	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Acute radiation morbidity scoring scheme (RTOG)					
Skin	No change over baseline	Follicular, faint or dull erythema, epilation, dry desquamation, decreased sweating	Tender or bright erythema, patchy moist desquamation, moderate edema	Confluent, moist desquamation other than skin fold, pitting edema	Ulceration, hemorrhage, or necrosis
Mucous membrane	No change over baseline	Injection may experience mild pain not requiring analgesic	Patchy mucositis, which may produce an inflammatory serosanguineous discharge, may experience moderate pain requiring analgesic	Confluent fibrinous mucositis, may include severe pain requiring narcotic	Ulceration, hemorrhage, or necrosis
Late radiation morbidity scoring scheme (EORTC/RTOG)					
Skin	No change over baseline change, some hair loss	Slight atrophy, pigmentation, total hair loss	Patchy atrophy, moderate teleangiectasis	Marked atrophy, gross teleangiectasis	Ulceration or necrosis

Source: Dobson, J., S. Cohen, and S. Gould. 2004. Treatment of canine mast cell tumors with prednisolone and radiotherapy. *Veterinary and Comparative Oncology* 2 (3):141. Blackwell Publishing Ltd.

Note: Radiation Morbidity Scoring Schema may be found on RTOG Web site, <http://www.rtog.org>.

*EORTC = European Organization for Research and Treatment of Cancer; RTOG = Radiation Therapy Oncology Group.

self-mutilation. Using pyridoxine (vitamin B₆) supplements helps to alleviate this rash as well as the rash associated with radiation sickness (Kisseberth and MacEwen 2001; Morrison 2002).

Iatrogenic Cushing's Disease and Polypharmacy

Long-term use of steroids, as in some lymphoma and mast cell cancer protocols, may cause iatrogenic Cushing's disease. Dogs are more prone to this effect than are cats. The use of immunosuppressive drugs may injure the function of and reduce the number of white cells and occasionally platelets as well. Many geriatric cancer patients are on polypharmacy for pre-existing problems. If these patients develop leukopenia and/or thrombocytopenia from chemotherapy, they are more prone to infection and hemorrhage. The concept of supporting the immune system is popular with pet caregivers and they are very interested in using supplements that may offset immunosuppression (see the "Chemoprevention and Immunonutrition" section of this chapter).

Bone Marrow Toxicity

Explain to pet owners that the bone marrow is made up of rapidly dividing cells, which are therefore highly susceptible to the effects of chemotherapy. For this reason, it is important to monitor the CBC before each chemotherapy treatment. Educate caregivers about the function of the bone marrow as the manufacturing plant for white blood cells, platelets, and red blood cells.

It is natural for the bone marrow to experience some suppression with chemotherapy. The suppression can be more dramatic in geriatric pets due to fibrosis and reduced stem cell function. Since the red cell count is often on the low side of normal in elderly animals, we must make every attempt to avoid severe myelosuppression.

Neutropenia

Neutropenia becomes the most common dose-limiting factor for most of the chemotherapy drugs used in animals. Instruct the client to expect that his or her pet's white cell count will be lowest during the drug's nadir, which generally occurs 7–10 days after administration. Teach the client to take the pet's temperature and to be alert for the signs of sepsis.

If the absolute neutrophil count drops below one thousand, the pet is at great risk for life-threatening sepsis, with signs including fever, anorexia, weakness, lethargy, general malaise, and collapse. Some dogs develop aspiration pneumonia from inhaling vomitus.

No matter how prepared we think clients are for a crisis, they still feel better if they have ready access to their oncologist for advice. They must be ready and able to admit their sick pet for urgent care at a local hospital or emergency clinic.

The treatment for sepsis is standard supportive care that includes IV fluids, broad-spectrum antibiotics, correction of electrolytes, Neupogen[®], and granulocyte colony stimulating factor (G-CSF) at 5 ug/kg SQ BID. The effect from Neupogen[®] is dramatic and this may only be needed for 1–2 days. Because we have access only to human recombinant G-CSF, it is expected that animals will mount a cross-reactive antibody response. Therefore, we use it when absolutely necessary rather than prophylactically.

Thrombocytopenia

Thrombocytopenia most commonly occurs with the Platinol drugs and lomustine but may be induced by any combination of chemotherapy drugs. The long-term effect of lomustine may cause a prolonged period before platelet rebound. Patients are usually asymptomatic until the platelet count falls

below twenty thousand. It is generally safe to continue the protocol in the face of thrombocytopenia, as long as the platelet count does not drop below sixty thousand.

Anemia

Some chemotherapy agents and protocols, especially when used for several weeks or more, may cause low-grade anemia. Chemotherapy may be responsible for a dip in the hematocrit as low as 20. It is important to establish anemia and other hematologic effects as having been caused either by the cancer or by the treatment (see the section “How Cancer Causes Anemia” in chapter 3).

Regardless of the cause, anemia creates weakness, decreased appetite, tachycardia, bounding pulses, and tachypnea in the geriatric oncology patient. It must be addressed with proper precautions. Withdrawal of chemotherapy or increasing the interval between treatments will often correct chemotherapy-related anemia but in the geriatric oncology patient this may increase the risk for coming out of remission. Help your clients to understand that you are walking a tightrope to find the very elusive line between treatment toxicity and maintaining remission. These clients will deeply appreciate your efforts.

Susceptible Tissues and Species Sensitivities

Organ toxicity is often related to a specific drug's characteristics and a specific pet's unique and unpredictable sensitivities. It is very important to know which drugs endanger which organs (Table 6.5). It is also important to know which drugs cannot be given to cats. For instance, cisplatin is nephrotoxic and should not be used in dogs with CRF and *NEVER* in cats. I would never use cisplatin in geriatric cancer patients because their aging kidneys have less functional reserve. The risk is just not worth it, in my book! I exclusively use carboplatin for geriatric animals, including cats that need a Platinol drug. Cats are unable to handle 5-FU in any form. It is also important to know that the therapeutic index and the maximum tolerated dose for a drug may be different between dogs vs. cats. Cats may require lower doses of a drug than dogs. Expect to find further variability linked to the individual geriatric oncology patient's health and hydration status.

If a geriatric cancer patient has pre-existing heart disease, or is a breed that is prone to dilated cardiomyopathy, such as the Doberman Pinscher, or is a geriatric cat with renal disease, such as CRF or glomerulonephritis, then it is best not to use Adriamycin and other anthracyclines. Cats and small dogs weighing less than 20 pounds should be dosed at 1 mg/kg. The meter squared (m^2) body surface area (BSA) graph is not appropriate for small patients because they often experience unacceptable toxicity. Large dogs over 80 pounds may be under-dosed using the BSA formula. I have found that splitting the dose for large dogs minimizes side effects without compromising efficacy. When we need to use Adriamycin for compromised or large canine geriatric patients, we divide it into two doses of 20 mg/m^2 each. We administer the first half, diluted in sterile saline to 1 ml/pound, and administer it as a 15-minute IV bolus and then give the second half the following week.

Splitting Adriamycin has spared our large canine geriatric patients from unwanted side effects while providing an overall higher therapeutic dose. We feel this method safely treats cardiomyopathy-prone breeds and geriatric cancer dogs with less risk for side effects, while remaining efficacious. Adriamycin-induced cardiomyopathy can occur at any dose but the risk is greater in dogs as they exceed a cumulative dose of 240 mg/m^2 .

Cats are resistant to clinical cardiotoxic effects of Adriamycin, but they develop adverse histologic changes in the myocardium. Some cats experience elevation of their creatinine and BUN levels. All cats developed histologic evidence of renal disease following administration at 30 mg/m^2 to a total cumulative dose of 300 mg/m^2 . Based on this information, the feline dose for Adriamycin has been

reduced to 1 mg/kg or 25 mg/m² (O’Keef et al. 1993). Adriamycin-induced cardiac and renal toxicity should be anticipated when treating cancer in geriatric cats with heart disease and/or pre-existing CRF.

Organs Sensitive to Chemotherapeutic Agents

Know your chemotherapy drugs backward and forward. Be familiar with how the drugs are metabolized and excreted by the body. Know which drugs cause fatal toxicity in cats vs. dogs. Be aware that Collies, Shelties, Australian Shepherds, and Long-Haired Whippets are at risk for toxicity from Adriamycin, vinca alkaloids, taxanes, dactinomycin, and etoposide. The following list will get you up to speed on this important issue. Also be sure to check these details with new drugs as they come on the market.

Bone marrow: Most chemotherapeutic drugs have the potential for myelosuppression.

GI tract: Most chemotherapeutic drugs at higher doses cause nausea, vomiting, and colitis. Steroids and NSAIDs cause ulceration, hemorrhage, and reduced gastric cytoprotection.

Heart: Adriamycin, daunorubicin, all anthracyclines (cumulative dose).

Lungs: Bleomycin causes fibrosis. *Cisplatin KILLS CATS* by causing pulmonary edema/effusion.

Liver: NSAIDs, steroids, lomustine, miscellaneous other drugs.

Kidneys: Cisplatin nephrotoxicity—requires intense diuresis, *KILLS CATS*, Adriamycin (cats).

Bladder: Cyclophosphamide (Cytoxan) and ifosfamide cause sterile hemorrhagic cystitis.

CNS: Vinca alkaloid induced neuropathy, cisplatin induced hearing loss, 5-FU may induce seizures in dogs and *KILLS CATS*.

Eyes: Cisplatin may cause blindness; one of my geriatric canine mast cell cancer patients developed blindness with lomustine.

Skin: Hypersensitivity (rash, angioedema, urticaria, facial edema) L-asparaginase, Adriamycin, paclitaxel. Palmar-plantar erythrodyesthesia syndrome (PPES) may appear in the axilla, groin, and footpads of dogs given Doxil and various other drugs. Using vitamin B₆ at 50 mg PO TID abates PPES.

Hair follicles: Delayed growth—most drugs, Adriamycin alopecia in Poodles, Old English Sheepdogs, and Terriers; cats develop a velvet-like coat after long-term chemotherapy.

Whiskers: Fall out with no replacement due to long-term chemotherapy in cats.

Collie breeds: Drugs that are actively transported by the p-glycoprotein pump induce toxicity due to a pharmacogenetic mutation of the MDR1 allele. Some Collies are adversely affected by Platinol-related drugs. To identify homozygous dogs at greatest risk, send cheek swabs for a special PCR assay c/o Dr. Katrina Mealey at Washington State University Veterinary School (Vail 2006b).

Cats: Some chemotherapeutics are fatal in cats. Do not use cisplatin or 5-FU by any route in cats.

Coaching Caregivers

We coach clients to be on patrol for side effects with a 25% expectation rate in healthy pets and 25–35% in geriatric pets. Instruct caregivers to use a strategic plan for detection and handling of the most common chemotherapy side effects: GI tract and bone marrow toxicity. Make sure that the family knows how to take their pet’s temperature and that they understand the significance of fever. Make sure that they know when the drug will typically nadir. At the slightest sign of anorexia or

lethargy, instruct clients to take their pet's temperature. If it is above 102.5 degrees, advise them to start oral antibiotics for a minimum of 5 days. If the pet is listless for 6–12 hours, advise the client to visit the doctor ASAP for a CBC and assessment for sepsis.

Medications used to control inflammation and pain also produce side effects. Steroids and all NSAIDs may cause vomiting, GI ulceration, and hemorrhage. I recommend oral Pepcid® on an empty stomach daily for geriatric cancer patients taking steroids and NSAIDs. This will reduce the potential for GI ulceration. Warn clients that narcotics, including all morphine-related pain control drugs, may cause sedation, disorientation, drooling, loss of appetite, and constipation.

Prepare a “cancer care package” for your clients, containing specific medications to manage anticipated side effects. Each medication bottle should be clearly labeled with the name of the medication, dosage, and its purpose. This enables the owner to immediately begin treating the adverse problem and possibly offset a visit to the emergency room. Explain to clients that if the problem persists or worsens, the geriatric cancer patient should be seen by a veterinarian for evaluation on an emergency basis.

Because we anticipate that the cancer patient may encounter some degree of nausea, vomiting, or diarrhea during treatment, we send two or three prescriptions home with the client after the very first visit. For control of nausea and vomiting, we send home metoclopramide (Reglan®). Metoclopramide is effective to offset nausea and emesis for most cases and most clients are willing to learn to give subcutaneous injections of it to help their pet feel better around chemotherapy treatment time. Some dogs may not respond to or tolerate metoclopramide and will need antiemetic therapy with oral ondansetron (Zofran®) or Anzemet® or Kytril®. These antiemetics are excellent for refractory vomiting and may also be used on a pre-emptive basis against nausea and vomiting. A good choice for treatment of colitis is Azulfidine or metronidazole (Flagyl®).

We also inform clients about the potential need for using oral Pepcid® or sucralfate (Carafate®) to help their pet avoid nausea and feel better during chemotherapy. If the pet experiences nausea and vomiting with metoclopramide tablets, we instruct the client to crush the pills and blend the powder with honey, then rub the compound onto the pet's lips. Clients can also crush tablets, mix the powder with butter, and then shape the compound into bullets. Instruct clients to put these “butter bullets” in the freezer until they are firm. Medicated butter bullets can be administered rectally as a suppository.

For colitis or diarrhea, we send home sulfamethoxine (Azulfidine® or Flagyl). We also recommend using oral Kaopectate® and Immodium to help control diarrhea when Azulfidine or Flagyl is not helpful.

Oncology clients must have access to their oncologist, attending doctor, or a good emergency clinic for after-hours advice. It is important that caregivers are properly educated to anticipate that an adverse reaction may escalate and lead to death if it is not reversed or if the pet fails to respond to treatment. Educate your clients to evaluate their geriatric pet for dehydration, fever, and sepsis. Remember to send the client home with antibiotics as part of the cancer care package for the client to keep on reserve to treat fevers at home.

The caretaker of a geriatric pet in chemotherapy with serious side effects should not wait 2–3 days before calling a veterinarian or going to an emergency clinic. If the pet is taken to the hospital, evaluation and treatment for leukopenia, sepsis, and GI disease is empirical. The attending doctor must use antibiotics aggressively to deal with sepsis. Neupogen® may be life saving for patients with severe leukopenia where the WBC is below one thousand.

A Word of Caution About Vesicants

Some of the most important chemotherapy drugs routinely administered as intravenous injections are vesicants. This means that the drug may cause a variable degree of localized tissue injury if there is

a perivascular leak. The problem is compounded if the extravasation goes undetected and untreated. The most notorious vesicants are drugs in the anthracycline family, of which Adriamycin is the most commonly used. In my opinion, there is no equal to the damage that even small amounts of this extremely potent vesicant can cause to a patient's limb.

Adriamycin and vincristine, the most commonly used vinca alkaloid in dogs and cats, rank as severe and moderate vesicants, respectively. Actinomycin D ranks with the anthracyclines as a severe vesicant. Vinblastine, vinorelbine, and mechlorethamine (Mustargen[®]) are moderate vesicants. Cisplatin, mitoxantrone, dacarbazine (DTIC), 5-fluorouracil, mithramycin, etoposide, streptozotocin, and bleomycin are considered mild vesicants. They pale in their perivascular toxicity when compared to the irreversible indolent tissue damage inflicted by drugs in the potent vesicant group.

Other anthracyclines, such as daunorubicin, epirubicin, and idarubicin, are potent vesicants (Doroshov 1996). Doxil (STEALTH liposome encapsulated doxorubicin hydrochloride) is an irritant. If Adriamycin is extravasated into perivascular tissue of your patient, the results may turn into one of your worst nightmares (Figure 6.2). In my opinion, there is no equal to the tissue necrosis that even small amounts of Adriamycin can cause to a limb. We always emphasize my favorite descriptive term, “vasosclerotic,” on our chemotherapy work order forms to warn our technical staff that localized tissue injury will result if there is a spill.

Most perivascular leaks are noticed right away as a “bleb” or swelling immediately adjacent to the venipuncture site. Or, the pet may experience overt immediate discomfort, crying out or struggling against the person restraining the animal for the injection. If a cancer patient fights restraint, recommend sedation for the safe administration of any caustic chemotherapy agent, especially Adriamycin. We insist on sedation to protect nervous and upset cancer patients from the nightmare of extravasation. I educate pet owners that “If we do not use sedation and your pet struggles, he may cause a mishap that could literally lead to the loss of his leg!” We rely on the attending staff to be vigilant in deciding which patients need sedation.



Figure 6.2. Extravasated Adriamycin site at 10 days showing early tissue necrosis. This lesion worsened over several months, exposing muscle, tendons, and bone.

It is recommended not to use acepromazine and phenothiazines (or any drug that causes arrhythmias or vasodilation) as a sedation drug when using Adriamycin. We prefer to use the low dose combination of DBA intravenously with Antisedan[®] reversal (Table 5.1) for healthy cancer patients. Some clinicians prefer Telazol[®] for immobilization of healthy fractious dogs. For patients with heart disease or advanced age, and for frail patients, we use a combination of fentanyl, a short-acting opioid, and midazolam, a short-acting benzodiazepine IV, or a combination of butorphanol and diazepam IM or IV. The preferred method for many clinicians is the use of sevoflurane inhalation anesthesia for masking or closed-chamber sedation/anesthesia, particularly for geriatric feline cancer patients. The objective is to make patients be still, for their own safety, during the administration of severe vasosclerotic chemotherapy drugs.

I came up with the theory that either the physical presence of the drug had to be altered or else we had to do much more to get the spilled drug out of the site. We rely on our nursing staff to point out loud and clear when even small, suspected extravasations occur.

The attending chemotherapy nurse and clinician must be on immediate alert. They must team up and act vigorously to literally remove every drop of the spilled drug from the perivascular site. Unfortunately, there is not much written on how to effectively do just that! Most textbooks say that whatever is done probably won't make a real difference anyway. So there is a sense of gloom and doom when Adriamycin is extravasated. That situation was unacceptable for me when looking at the risk-benefit ratio for my patients. It made me rethink the situation.

Occasionally, a spill may go undetected and untreated only to be noticed anywhere from 1 to 10 days after treatment. The caregiver calls the office with complaints that the pet has pain, is limping, has swelling or desquamation, or is licking the venipuncture site.

The extravasation site may not look threatening at first, even after the first 3–10 days or well into the second week. Vincristine sloughs are evident within the first 1–7 days. The damaged tissue forms necrotic crusts, causing the injured skin to stiffen like leather. The patient will lick the site and may exhibit pain by holding up the leg or limping. When the dead tissue sloughs off, it may leave a deeper ulcer, which eventually heals over a 6-week period.

Adriamycin sloughs may begin to show only after 7–10 days. The spill area appears inflamed for another 1–3 weeks. The lesion then slowly worsens as the weeks and months wear on. The ulceration and tissue necrosis from Adriamycin will gradually infiltrate and spread deeper and deeper, exposing muscle, tendons, and bone. The area of eschar (a slough produced by a thermal burn or corrosive agent or gangrene) enlarges and deepens, forming necrotic sequestration of tissue that may become infected and then this case turns into the worst nightmare that one can imagine.

Why the tissue damage spreads is poorly understood but be sure to understand that the eschar from an Adriamycin spill will continue to fungate for longer than 3–4 weeks (the time frame given in most textbooks). In actual fact, the effects of an Adriamycin extravasation will persist for months—more than 3 months, in my experience—and will involve an area much larger than that affected by the initial spill. Be sure to understand that tissue damage will continue to worsen over these months. The injured tissues will not heal or regenerate. There is tremendous and severe pain, swelling, and corruption of the tissues of the entire limb.

In most cases, amputation becomes the only option, due to the extensive and irreversible nature of the tissue necrosis. Do we continue the futile nursing care, despite the pain, because the pet's primary problem is cancer? There is no easy way out of this situation. Deciding whether or not to recommend amputation of a geriatric patient's leg when the patient may die from cancer in the near future is truly a nightmare. After your recommendation, the nightmare of making the decision is passed along to your client.

Inexperienced clinicians and nursing staff may not fully understand the consequences of an Adriamycin spill because it doesn't really look so bad at the beginning. It is easy to initially understate the ramifications to pet owners, especially when trying to comfort them. In my opinion, Adriamycin spills must be accurately and honestly described to clients from the start. The client must be carefully counseled and warned of the fact that the wound will most likely get worse with time despite the best bandage-changing and nursing care. To explain the gravity of the situation to a client, I say, "Unfortunately, we had an accident while administering chemotherapy today. Some of the drug leaked outside of the vein. This is called 'extravasation' or a 'spill,' and is, unfortunately, always a danger when using these drugs. Although this drug is very good at killing cancer cells, when it is in direct contact with tissue it behaves like an acid. The drug may continue to destroy tissue relentlessly, despite our best efforts to halt it. In the worst case scenario, we may, regrettably, have to recommend amputation to stop the pain."

Please explain extravasation to clients who want to know why you insist on suggesting sedation for each Adriamycin treatment.

Can We Prevent Extravasation?

Prevention of disaster is the very best control. First, set your staff up to prevent extravasation of any chemotherapy drug. The chemotherapy room should be quiet and free of distractions. The nurses should be focused and should not be given cross-orders or be pressured to hurry through the procedure. There must be a clean stick into the vein when placing the catheter. There must be constant visual and hands-on monitoring of the intravenous injection site to ensure that the needle is still in the vein during the entire administration of every drop of the drug.

Some oncologists propose the use of an indwelling catheter and dilution of the Adriamycin into a small bag of saline that is infused over a 30–45 minute period—this technique may yield the largest extravasations. Other oncologists prefer to run the Adriamycin IV through a well-placed indwelling catheter simultaneously with rapidly flowing saline over a period of 15–20 minutes. The oncologists and oncology nurses I've spoken to feel most comfortable with direct, close supervision of every drop of Adriamycin using very small gauge butterfly catheters (no larger than 23 gauge).

The total calculated dose of Adriamycin is diluted in a 12 cc syringe with sterile saline to 10 ml for the average cat. We dilute the dose for dogs to approximately 1 ml/lb with sterile saline or sterile water, for injection using a 35 ml syringe for small dogs and a 60 ml syringe for large dogs. The carefully placed butterfly catheter is flushed with saline. The Adriamycin solution is administered while frequently pulling the syringe back just enough to see blood in the hub of the syringe. This verifies that the catheter remains well positioned and not up against the wall of the vein. We administer Adriamycin to cats over a slow bolus over 5–7 minutes and to dogs at a slow, steady infusion rate over 15–20 minutes. In our experience, the intense, hands-on, direct visual supervision during the administration of diluted solutions of Adriamycin to well-behaved or sedated patients works best to avoid the nightmare of extravasation.

An excellent suggestion to prevent extravasation appeared in the "Tech Talk" section of the *Veterinary Cancer Society Newsletter* (Rose 2004). Rose recommends using a small gauge butterfly catheter with 12-inch tubing. She attaches a three-way stopcock to the catheter and places a 12 ml luer-lock syringe with 0.9% saline solution at one port and the chemotherapeutic drug at the other port. Flushing before and after drug administration is easily performed without switching from one syringe to another. The chemotherapy nurse monitors flow by continuous aspiration of small amounts of blood to verify placement of the catheter in the vein during the entire administration of the drug (Figure 6.3).



Figure 6.3. A small gauge butterfly catheter with 12-inch tubing attached to a three-way stopcock (a). This setup can be used for convenient flushing with a 12 ml luer-lock syringe filled with 0.9% saline solution. This technique facilitates flushing and delivery of chemotherapy without changing syringes (b).

Extravasation Site Treatment in the Literature

All references instruct the attending doctor to act immediately. They recommend not removing the catheter, but rather keeping it in place to cleanse it before withdrawing it. Use a syringe to remove as much drug as possible from the catheter, tubing, and tissue. Removal of 5–6 ml of blood in a cat and 10 ml in a dog should be adequate. Insert a 27-gauge needle into the spill bleb and aspirate as much of the drug as possible to minimize the amount of drug at the site. Some references then say to administer the “appropriate antidote” or flush saline through the catheter to dilute residual drug, then to use ice cold packs or cold compresses for Adriamycin, actinomycin-D, and mechlorethamine spills. The compresses are recommended for 6–10 hours.

All references agree that warm compresses should be placed on vinca alkaloid and etoposide spills for the first 3–4 hours. These procedures are recommended to minimize the vesicant’s toxicity. The objective is to spread the vinca alkaloid with warm compresses to disperse the drug into the circulatory system. The opposite idea is to use cold compresses to localize Adriamycin spills to reduce its toxicity. Are you thoroughly confused yet by this? The most disheartening thing to read in the literature is that all experts agree that nothing, including the recommended “antidotes” in the following section, seems to work when dealing with anthracyclines extravasations! I could not accept this hopelessness and still get to sleep at night.

Recommended “Antidotes” for Extravasations

Most references suggest using a compound called DHM3 or the timely use of dexrazoxane (Zinecard[®]) injected directly into the tissue area of the spill within 3 hours of the accident. Some oncologists use IV Zinecard at 10 times the Adriamycin dose within 3 hours and at 24 and 48 hours after a spill (Vail 2006b). These measures are anecdotally reported to help offset the damage from anthracycline spills.

This may indeed help if the compounds are readily available and used in time. Unfortunately, some spills are not detected until the patient has begun to exhibit a slough lesion. The price of Zinecard is \$250.00 and \$350.00 for the 250 mg and 500 mg vial, respectively. Zinecard is used in humans to reduce the cardiotoxic effects of anthracycline drugs. Some references say that using 1 ml of 1/6 molar isotonic sodium thiosulfate for each ml of extravasated cisplatin can inactivate it. This antidote is recommended only if a large amount of cisplatin is extravasated. Hyaluronidase at 150 units/ml is recommended at 1 ml for every ml of extravasated vinca alkaloid or etoposide. This is purported to enhance absorption and disperse the extravasated drug. Topical dimethyl sulfoxide (DMSO) or infiltration of the area with 1 mg/kg of hydrocortisone or using intralesional dexamethasone is considered controversial and most references say that using these anti-inflammatory agents is probably a waste of time. Since the consequences of extravasation add up to an iatrogenic event, I was still dissatisfied with this information.

Dr. Steven Swaim, professor emeritus at Auburn University, specializes in wound management. Dr. Swaim suggested to me that hydrophilic wound dressings be used over extravasation sites, because these dressings act to pull the body's homeostatic fluids up through the tissues to bathe the wound tissues from the inside out. This may help to reduce edema and bathe the wound with antibiotic-containing fluids if the patient is on systemic antibiotics. Theoretically, hydrophilic dressings should also help remove the caustic agent from the tissues and stimulate the healing process. Dr. Swaim prefers to use CaraSorb M-FDG[®], a product by Carrington Laboratories containing acemannan (derived from aloe vera). It stimulates macrophages to produce cytokines and growth factors needed for indolent wounds. Using this product may have potential benefit, but there are no clinical studies to assess its value in managing extravasations.

Overall, in my practice there was a feeling of dread, helplessness, and hopelessness surrounding the situation of extravasation. We felt that if we were going to work every day with these drugs for our entire careers, we needed to do something about this problem.

An Aggressive Approach to Extravasation: “The Villalobos Modified Snakebite Slit Technique”

The literature makes only fleeting mention about flushing extravasation sites with saline and mentions caution for this procedure, as it may indeed spread the drug to a deeper or wider area. I determined to find a better technique for flushing.

There is only one way for me to sleep without nightmares when dealing with Adriamycin extravasations. We treat every Adriamycin spill like the worst snakebite on earth and we treat it immediately. First of all, there is no blame or anxiety placed on the technician who observes and/or reports the spill. Rather than putting tension in the air, there should be only encouragement and gratitude for the informant. The attending doctor needs to know if there is even a suspicion of extravasation because the patient's well-being is clearly the first priority. Accidents happen and pride and feelings are hurt, but those issues need to be set aside to rescue the patient from the nightmare that extravasation can become.

After the initial aspiration from the catheter and the bleb are completed, we infiltrate saline into the site as described earlier. The team preps the leg for surgical incision and at this point, I take charge.

Using the bevel of a sterile 18-gauge needle, I make at least 10–30 vertical, deep skin incisions (slits). The slits extend into the perivascular SQ tissues in a “lettuce bag” pattern as staggered parallel incisions. The slits should extend beyond the entire extravasation site and 360 degrees around the entire limb (Figure 6.4). We then run copious amounts of saline or isolyte solution through the entire site and around the limb with the philosophy of flush, flush, and flush and then flush some more.



Figure 6.4. Cartoon showing the “lettuce bag” or the staggered parallel incision pattern used over the extravasation site in the “Villalobos Modified Snakebite Slit Technique.” Saline is run into the site and milked out through the incisions. This flushing process allows spilled adriamycin and other spilled vasoclerotic drugs to exit the perivascular tissue. Figure contributed by David Perrot.

We gently squeeze or “milk” the tissue bleb site during the entire time that we are flushing. I may poke the 18-gauge needle into deeper parts of the limb, into muscle and fat, to let solution infiltrate deeper and allow the vesicant drug to ooze out. Hopefully, every drop of the offending vesicant will percolate out through the skin slits in a diluted fashion. On one occasion, we were pleased to see the distinctive red color of Adriamycin as it exited the tissue. In a typical 60-pound dog, we may flush 1–2 liters through the extravasation site over a 30–45 minute period, depending on which drug was spilled.

I recommend using nothing short of this extreme measure to get every drop of vesicant drug out of the spill area, especially if the spill involves Adriamycin. We send the patient home with a light wrap and instructions for the family to apply cold compresses 20 minutes on, 20 off for the next 24 hours. The patient is rechecked weekly for 3 weeks to monitor for tissue damage, infection, and healing of the skin incisions.

As soon as we started using this technique at our clinics, we were able to completely avoid the nightmares that are so predictable with extravasations of any type, but especially with Adriamycin. We have shared this procedure with many colleagues (because it works), christening it the “Villalobos Modified Snakebite Slit Technique.” I feel confident that you will find similar success when dealing with extravasations using this practical technique. It has the potential to minimize unnecessary suffering for the patient, the pet owner, and the practitioner.

Judd's Case (Everybody Loses with Extravasations)

Judd Dow, a 13-year-old M/N Malamute, was receiving Adriamycin for anal sac adenocarcinoma with medial iliac and lumbar node metastases. Judd was a huge Malamute with pre-existing degenerative myelopathy and weakness in his hind limbs. Judd was doing well until a hind leg extravasation occurred. The spill involved the recurrent tarsal vein in Judd's hind limb. This spill was a nightmare case for the owner and for a young attending oncologist, who may never before have experienced the full extent of necrosis that a large Adriamycin spill can cause.

Judd's owner came to me for a second opinion. I did everything in my power to keep the client from targeting her anger at the well-meaning attending doctors and staff.

I encouraged her to continue seeing her original oncologist and staff for wound care. I told her to retain confidence in the practice because they are dedicated, have a very good reputation, and are highly respected in the veterinary community. I mentioned that they might be gracious enough to absorb some of the expense for the long-term wound care that Judd would most likely need.

As the ordeal of wound care wore on, the oncologist asked two board certified surgeons to look at the wound. They attempted to debride the necrotic tissue twice and helped set up the wound management program for daily bandage changes and inspections. At one time, Judd was hospitalized for 3 weeks on IV antibiotics and extra wound-care sessions to deal with sepsis. This effort dragged on over 3 months. Judd had the best wound-care management, but to no avail. The festering wound extended down through the muscle and to bone. The ligaments became detached after months of wound care, expense, and discomfort.

The surgical specialist ultimately recommended amputation rather than reconstruction. This was a great disappointment to the owner, after an earlier promise of reconstruction and after the extended and extensive hardship of treating the wound. Of course, chemotherapy was discontinued during the months of wound care, and the cancer progressed.

Judd's owner could not fathom an amputation along with the degenerative myelopathy and the fact that Judd had progressive metastatic cancer in his abdomen from primary anal sac adenocarcinoma. The family regretfully elected euthanasia.

Later on, the owner needed to vent. She was angry and inconsolable because Judd had been doing well in chemotherapy until the spill occurred. She felt that the doctor was not truthful with her about the situation from the start. I explained to her that the young doctor may have never seen an extravasation before and may have been unaware of what was ahead, because not much detail has been written about it. Ultimately, all parties concerned suffered. The client wanted to pursue litigation despite my discouragement and despite the valiant efforts of the practice where the extravasation occurred.

With over 35 years of experience in oncology, I have seen just about everything there is to see. Extravasation is an accident. If it is not spotted at the time and not treated aggressively, it spells disappointment, disaster, and nightmare. There is no winner here.

Extravasation Summary

Client PR is very touchy in this type of situation. The best you can do is to provide support and remain understanding of the pet owner's grief and resentment. Be sure to tell the owner that you feel terrible about it and that it is one of the risks that the field of oncology endures. Tell them that it takes courage to use chemotherapy drugs but that, like penicillin, it saves lives despite adverse reactions.

At each recheck, sympathize with the client's grief and dismay. Some clients will be able to resolve their anger and blame and others will not. It is important to remain in partnership with the client and commit to dealing with the immediate issues of pain control, extended care, or a decision to debride or amputate.

It is because of scenarios like Judd's that I am compelled to write so extensively about potent vesicants and extravasation. This is an extremely important issue and I hope that you will avoid extravasation in your practice. In the best interest of the patient, most oncologists recommend that general practices using Adriamycin should not allow technicians to perform the infusions. Chemotherapy nurses at specialty practices are highly trained and competent for this procedure, but the consequences of a spill are so dire that technicians in general practice should not be asked to take responsibility. It may be best for the attending doctor to administer all chemotherapy drugs in the general practice setting. Again, chemotherapy should be done with no other activity going on in the area. Some doctors prefer to give all vesicant chemotherapy to cats while they are under Isoflurane or Sevoflurane sedation/anesthesia.

Treatment for Chemotherapy Toxicity

The treatment of toxicity and adverse events from chemotherapy is usually based on common sense based on empirical medicine. Clients need to take action at the first sign of toxicity.

For mild gastrointestinal reactions such as inappetence, nausea, and vomiting, we generally use metoclopramide (Reglan). For refractory vomiting, use more potent antiemetics such as ondansetron (Zofran), Anzemet, and Kytril. As an alternative to stocking these costly drugs in your hospital, the client can purchase them at a pharmacy with a prescription. Consider using mirtazapine (Remeron®). This antiemetic has antidepressant, anxiolytic, and hyperphagic action at a fraction of the Zofran cost. Use $\frac{1}{8}$ – $\frac{1}{4}$ of a 15 mg tablet every 72 hours for cats and $\frac{1}{8}$ –1 tablet every 24 hours for dogs (Cahill 2006). See package inserts for empirical doses and precautions. To treat diarrhea and colitis, use sulfasalazine (Azulfidine®), sulfadimethoxine, metronidazole (Flagyl), and Tylosin®. We may instruct clients to use over-the-counter Pepto-Bismol®, Kaopectate®, and/or Immodium as needed. If a geriatric oncology patient exhibits any adverse event over grade 2 (moderate) with GI signs accompanied by listlessness, then hospitalization and supportive care are recommended.

Hypersensitivity reactions such as rash, pruritis, urticaria, hives, and wheals may occur during or following chemotherapy administration. Acute anaphylaxis or anaphylactoid reactions require immediate attention. These adverse reactions respond quite well to diphenhydramine (Benadryl®) at 2–4 mg/kg IM and dexamethasone at 0.5–1 mg/kg IV. We generally pretreat all of our canine cancer patients with IM benadryl at 1 mg per pound and both canine and feline patients with IM or IV dexamethasone at 4 mg/m². IV pretreatment precedes drug administration while IM or SQ pretreatment is given 5–20 minutes prior to administration of all predictably allergenic drugs such as L-asparaginase and Adriamycin. Taxol requires an astute pretreatment protocol to minimize GI, CNS, cardiovascular, and anaphylactoid reactions. Prepare patients the night before with oral prednisone at 2 mg/kg. Pretreat with benadryl at 4 mg/kg IM, cimetidine at 4 mg/kg IV, and dexamethasone SP at 2 mg/kg 30–60 minutes before Taxol, which must be administered IV slowly over a 3- to 4-hour infusion.

Sepsis and tumor breakdown syndrome are true oncologic emergencies. The treatment is empirical with IV fluid support, electrolyte balancing, antibiotics, symptomatic care for vomiting and diarrhea, and supportive care in the hospital. Anthracycline-related cardiomyopathy and heart failure is poorly responsive to therapy and has a poor prognosis. It is best to avoid cardiotoxicity by proper

patient selection. Use an EKG and monitor cardiac function with echocardiography before each administration of Adriamycin. Be aware that cardiotoxicity develops more often in breeds predisposed to dilated cardiomyopathy and in patients that approach the cumulative toxicity dose, which ranges from 180 mg/m² to 240 mg/m². Consider using dexrazoxane (Zinecard) as a cardioprotectant when Adriamycin is the best option or the only effective agent, or the pet relapses without it. Zinecard at a 10:1 dose ratio is given as a slow IV bolus starting 30 minutes prior to administration of Adriamycin (Vail 2006b).

Summary: Adverse Effects of Cancer Therapy in Geriatric Pets

Adverse effects are an unintended but not unexpected sequelae in the management of geriatric cancer patients. Surgery, radiation, and chemotherapy induce specific adverse effects that can be graded according to severity. The caregiver needs education regarding what to expect and when to expect adverse events. The care and management of adverse effects should be prompt to spare the geriatric oncology patient further stress. Be sure to avoid extravasations by having a strict protocol for administration of vasosclerotics, especially when using Adriamycin in nervous or fractious patients. Empathize with caregivers and be sure to apologize whenever an adverse event occurs.

The Role of Radiation Therapy in Cancer Management

Education is going from cocksure ignorance to thoughtful uncertainty.

Donald E. Thrall, DVM, PhD, DAVCR, N. Carolina State University, College of Veterinary Medicine

The specialty board of veterinary radiation oncology was established in 1994 and now offers residency programs in radiation oncology. Veterinary oncology became more sophisticated during the 1970s. Many veterinary radiologists and oncologists, myself included, incorporated RTx into their practices to control tumors with used equipment from the human side. Radiation therapy is involved in the management of 50% of all human cancers. Approximately 7,500 radiation therapy machines are in use for people worldwide.

The Hi-Art[®] TomoTherapy unit, developed by researchers in Wisconsin and considered to be the biggest innovation in RTx since the 1950s, combines a linac and a CT scanner. The linac is mounted in a large doughnut and rotates around the patient in a helical fashion, while the CT scanner provides on-the-spot imaging. Its radiation beam is computerized to avoid healthy organs while striking the tumor from a variety of angles. This fusion unit has a \$3.2 million price tag for installation at major hospitals.

Now, veterinary facilities are beginning to install used and new linacs. With the constant upgrading of diagnostic and treatment equipment in human hospitals, our profession is inheriting used linacs at reasonable prices. A growing number of veterinary teaching hospitals have linacs and North Carolina State University College of Veterinary Medicine recently purchased a used linear accelerator for \$100,000. As prices drop, and if maintenance contracts are reasonably priced, veterinary cancer patients will have more access to linear accelerators. There are approximately 50 RTx facilities devoted to the treatment of companion animal tumors in the United States and Europe and we can expect more in the future, as graduates from the residency programs enter practice.

The average age of household dogs and cats in the United States has gone from 4 to 6 years old. The aging of America's pets will produce a huge number of geriatric oncology patients. If we go by an estimate that there are 65 million dogs in the United States today, that half of them die of cancer and that hemangiosarcoma composes 7% of cancers in dogs, we can estimate that this cancer will affect up to 2.5 million of the dogs currently owned in the country. The percentage rises when we focus on breeds with predilection such as German Shepherds Dogs and Golden Retrievers (Lamerato-Kozicki et al. 2005).

We can also estimate the number of FVAs to be as many as 22,000 cats per year (Ford 2004). A rising percentage of pet caregivers will seek help from your clinic, asking for specialty care for their pets with cancer. Many of these cases will need RTx.

The lack of available facilities, risk to critical tissues, and the requirement for general anesthesia were limitations for electing RTx as an option. Cost and transportation logistics are additional factors for many pet owners. These reasons kept RTx in the background as a seldom-used modality in veterinary cancer medicine. Today, we use safer anesthetics or heavy sedation for geriatric cancer patients. The new generation of RTx machines is safer; linear accelerators cause less damage to tissues surrounding tumors than cobalt machines and are ideal for use in small dogs and cats. RTx is becoming more available at veterinary teaching facilities and at customized veterinary facilities in major cities.

New graduates are familiar with RTx because most contemporary veterinary schools have state-of-the-art equipment and offer radiation oncology services. New graduates are also familiar with the risk-to-benefit ratio of RTx for geriatric patients. In short, RTx is becoming a realistic and available option for pet owners who can access a facility and afford the cost.

When recommending RTx for a geriatric cancer patient, first establish if the elderly pet is a good candidate for RTx. Do a thorough evaluation of the patient for tolerance to multiple anesthetic procedures and a thorough evaluation of the malignancy, to rule out metastatic disease prior to RTx. Many geriatric oncology patients will be eliminated as candidates due to compromised organ function. Chief concerns would be renal, hepatic, cardiac disease, and body condition. If the tumor is staged as localized, if it is not highly metastatic and is potentially responsive to radiation, then RTx is a good option for treatment.

At the initial stages of the workup, the attending doctor needs to decide about imaging with CT or MRI. The radiation oncologist may prefer CT for initial imaging because it is also used for computer-assisted treatment planning and thus accomplishes two steps. Initial imaging with MRI may provide valuable information but it may not integrate with CT-based dosimetry treatment planning. Requiring CT as a second step is unnecessarily costly for clients and creates more stress for older patients. Cancer patients receiving RTx for oral or nasal cancer must have complete dental cleaning and extraction of all loose teeth to completely eliminate plaque and clear up infection, which becomes a third step.

Uses of Radiation Therapy

RTx is used principally for local tumor control and palliation (treatment with non-curative intent). RTx is most successful when used in truly localized radiation-responsive neoplasia. RTx is most often used post-operatively to sterilize residual disease in surgical fields. It may be used preoperatively to shrink large tumors, making them more amenable to surgical excision or as a single modality to save structures in cases where the cancer is staged as local and believed to have low metastatic

potential. RTx is used in combination with chemotherapy, hyperthermia, targeted therapy, and so forth, to enhance local control. Because RTx is strictly a localized treatment, other modalities are needed to address the metastatic potential of the particular cancer being treated.

If your client is considering RTx as an option, an early referral for consultation will save steps. CT scans are programmed to interface with and reconstruct images for 3D computerized treatment planning in place of MRI. The closer the CT scan is to the time of treatment, the more accuracy there is because tumors change shape and size over time. This has been a major problem in human RTx. It is now being addressed with new combination units such as the Hi-Art TomoTherapy unit, which combines CT with radiation therapy.

Radiation therapy as a curative measure

To sterilize clean, narrow, or dirty margins in a sarcoma or carcinoma field as post-surgical follow-up.

As primary treatment for nasal tumors and facial SCC.

As primary treatment for some brain tumors.

As local control of oral tumors (acanthomatous epulis, SCC, fibrosarcoma [FSA]).

As preoperative treatment of soft tissue sarcoma (STS) to decrease size and viability of the mass.

As intraoperative therapy (using a megadose) to sterilize an open tumor bed (intracavitary).

As part of the induction protocol for anterior mediastinal lymphoma and as half body RTx in some induction protocols for canine lymphoma.

Radiation therapy as a palliative measure

To reduce cancer pain and tumor growth with osteosarcoma.

To shrink bleeding facial and nasal SCC.

To shrink oral and pharyngeal masses (SCC, malignant melanoma, FSA, tonsillar SCC).

To treat inoperable brain tumors.

To shrink mediastinal masses and large lymph nodes in resistant lymphoma.

To reduce the size of large primary or metastatic lesions.

Very simply, radiation kills cells by crippling their ability to repopulate. The energy beam breaks chemical bonds in DNA directly by ionization or indirectly by ionizing cellular water (Figure 6.5). This results in the formation of charged free radicals and active oxygen species that transfer energy to and damage DNA. Tumor tissue is more sensitive to RTx than normal tissue but adjacent local tissue still suffers from the standby effect. Acute and late toxicity may develop.

The dose of radiation is measured in units of energy deposited per mass of tissue. The units were originally called rads and are now called the gray (Gy). One hundred rads = 1 Gy = 1 joule/kg. The dose-response curve for RTx has a sigmoidal shape with curves at the bottom and top like a stretched out S-curve. The curve rises rapidly in a steep incline between the dose for tumor control and the dose for patient tissue toxicity (Figure 6.6). If treatment stops at a threshold dose of 40 Gy for a particular tumor and does not finish the total prescribed dose of 50 to 55 Gy, the probability of tumor control remains at the low end of the sigmoidal curve and minimal toxicity is expected. Conversely, if this patient receives more than 60 Gy, the side effects at the top end of the curve will be more likely to occur in the form of tissue morbidity.

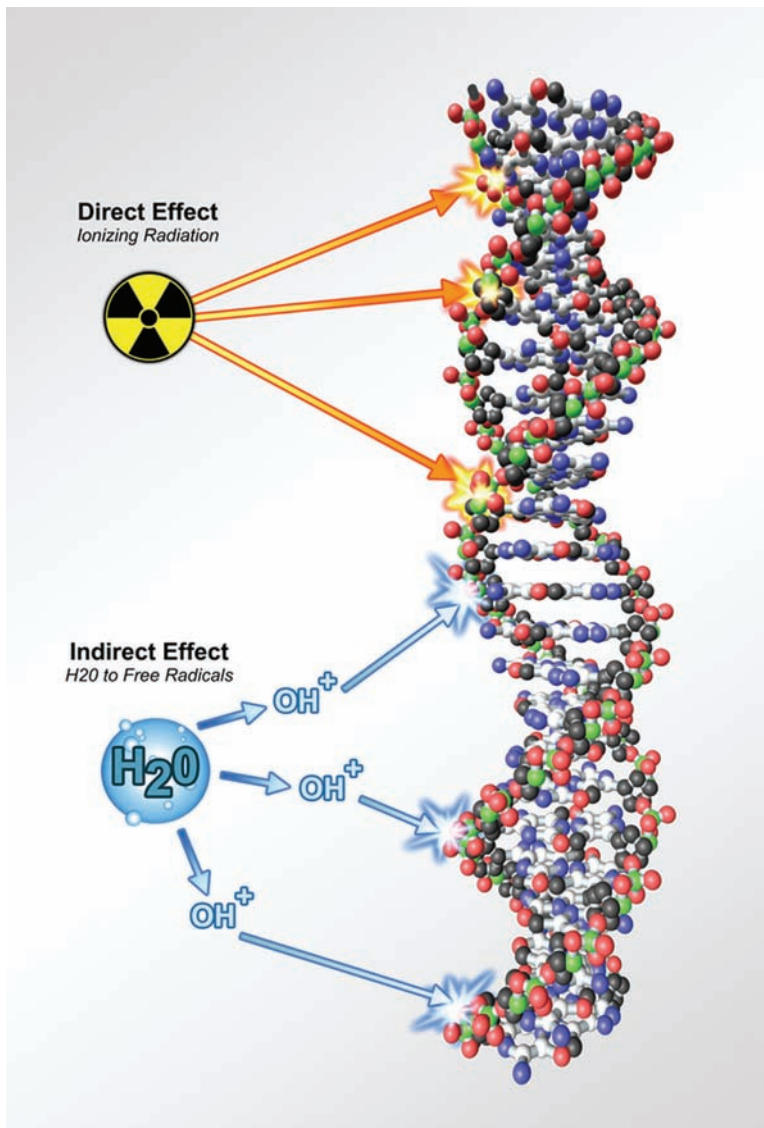


Figure 6.5. The radiation energy beam breaks chemical bonds in DNA directly by ionization or indirectly by ionizing cellular water, which results in the formation of charged free radicals and active oxygen species that transfer energy to and damage DNA. Figure contributed by Andrew Hoffman.

RTx doses generally range from 30 to 60 Gy, delivered in 4–30 treatment fractions over a period of 3–6 weeks depending on the intent of treatment (palliative or curative). The goal of the radiation therapist is to deliver the safest dose over the least amount of time so that the patient has the highest antitumor benefit and the lowest risk of immediate and delayed radiation side effects. RTx is delivered via external beam (teletherapy), via implantation of radioactive beads inside and around the mass (brachytherapy), or via radiochemicals that localize in specific sites (such as iodine 131 in hyperthyroid cats or samarium for osteosarcoma in dogs).

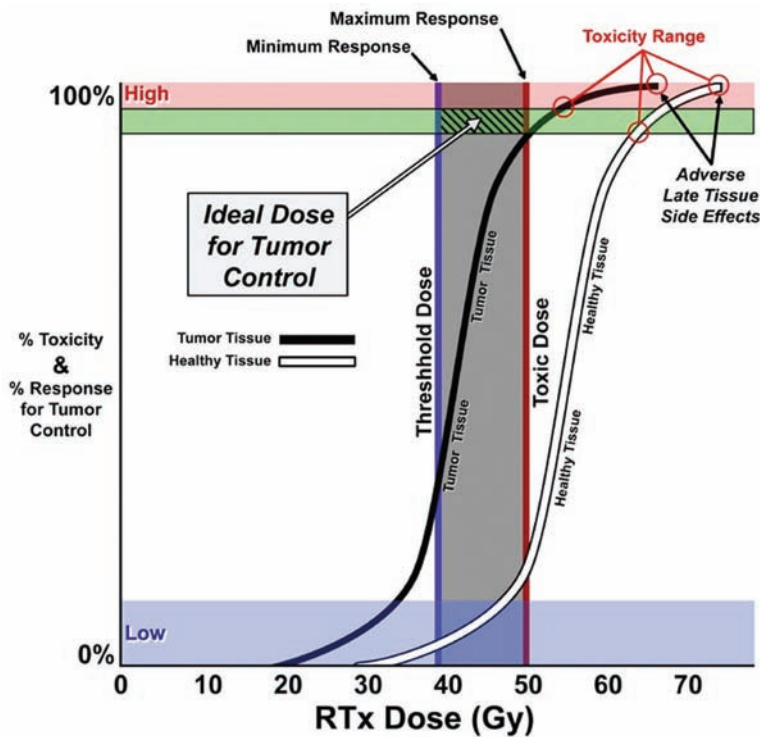


Figure 6.6. The dose-response curve for RTx has a sigmoidal shape with curves at the bottom and top like a stretched-out S-curve. The steep part of the curve rises rapidly between the dose for tumor control and the dose for patient tissue toxicity. Figure contributed by Andrew Hoffman.

Side Effects of Radiation Therapy

RTx is notorious for producing short-term and long-term side effects (Table 6.7). Most people know someone who has had radiation therapy. Clients often state their personal bias about RTx, based on their own experience with it through friends, family members, or self. Proper client education is the key to opening the door for the geriatric oncology patient to gain the benefits that RTx may offer.

Sensitivity of skin, mucous membranes of the oral cavity, eyelids, genitourinary, and the GI tract becomes the dose-limiting factor in external beam RTx. The hair coat in the RTx field generally falls out after 8–10 treatments. At this time, desquamation may appear and the area may remain alopecic for 1 or 2 months, following healing of the skin surface. Fur growth may be prolonged if the patient is having concurrent chemotherapy and it may grow back in a different color than the pet's normal coat. New hair growth in Siamese cats is black but generally grows back as white or gray hair in most other cats (Figure 6.7). Higher doses of RTx to the skin may completely damage hair follicles and in this case the fur never grows back.

When one or both eyes are included in the RTx field, conjunctivitis, kerato conjunctivitis sicca (KCS), and cataract formation are commonly encountered. This occurs most often when treating nasal, retro-orbital, and brain tumors. Radiation toxicity can be more objectively graded by using a scoring system ranging from grade 0 to 4, according to the Radiation Morbidity Scoring Schema

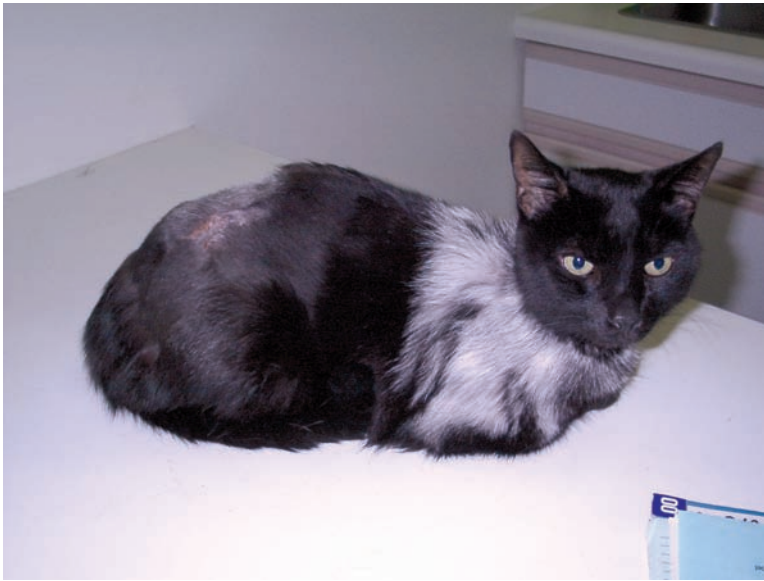


Figure 6.7. Notice the white patch over the radiation field in this patient, 3 years after treatment for FVAS. If higher doses of RTx are delivered to the skin, hair follicles may be completely damaged, causing desquamation and permanent alopecia. This cat was being treated for a new FVAS, which developed several months after a 3-year booster vaccination was administered in the left flank.

(Table 6.8). To find an in-depth Late Radiation Morbidity Scoring Schema, go to the Web site at www.rtog.org/members/toxicity/late.html.

Immediate or acute reactions occur in tissues that normally undergo mitosis, such as skin, gut, and bone marrow. Late reactions occur in tissues that have low regeneration rates, such as bone, nerves, brain, and the ocular lens. The skin undergoes desquamation both dry and moist and may exhibit pruritis, erythema, and rash similar to a burn. Mucositis with odoriferous salivation and secondary anorexia and weight loss often develop in those patients being irradiated for oral and nasal tumors. The symptoms begin when the patient is three-quarters of the way to completion of the RTx schedule.

At this stage, if pet owners were not prepared for the expression of side effects in their pet, they may wish to terminate treatment. Proper education and supportive care for each of their concerns is essential.

Support from the referring veterinarian is very important to help pets and their families endure the difficult times that RTx may impose. If the client stops treatments early, the rate of tumor response drops dramatically. We counsel pet owners during their times of frustration, especially when the patient has lost weight and is dealing with the adverse effects of mucositis. Some geriatric patients, especially those with concurrent disease, need more supportive care than others during the course of therapy. They may need daily SQ fluids, hand feeding, or tube feeding. We remind the client of the steep shoulder on the radiation response curve. This encourages the family to allow their pet to finish the prescribed treatment dose.

Pneumonitis and pericarditis with effusion may develop following radiation to the lung field. This is especially worrisome in cats treated with cobalt therapy units to control recurrence of FVAS. Cats develop cardiac and respiratory problems 4–6 months following the completion of RTx and may have to face pericardiectomy with fibrotic lungs. Colitis, tenesmus, and bleeding may result if the colon and rectum are included in the treatment field. Fibrosis and loss of elasticity of the bladder are

potential side effects of radiation to the sub-lumbar nodes. These side effects are inherent with the use of cobalt radiation therapy because the exit dose is the same as the entry dose. A bolus is used to offset this, but cats and small dogs are at risk for unwanted side effects from cobalt therapy units. Linear accelerators are able to mitigate the dose at a set depth. This is ideal for RTx treatment of mast cell tumors in dogs and vaccine sarcomas in cats.

Anemia and lymphocytopenia or general bone marrow suppression may occur when significant bone lies within the therapy field. Bones are subject to the delayed effect of necrotic sequestrum and this may occur years after treatment. Delayed effects such as xerostomia (no saliva) may appear after therapy of the oral cavity. Side effects from the treatment of brain tumors with RTx are rare in dogs and cats but may induce nausea, vomiting, pain, papilledema, and unresponsive neurologic problems related to late effect necrosis and myelomalacia of CNS tissue (nerve, spinal cord, brain).

Treatment of Radiation Side Effects

Patience and good nursing care are required to treat radiation-induced side effects. It is paramount to provide the best pain control possible for the patient. Without this, pet owners are likely to terminate treatment too early for their pet to receive any benefit. Counseling must be provided for frustrated pet owners, being sure to point out the steep shoulder on the dose-response curve. I tell pet owners that if they quit RTx before the protocol has been completed, they will have unwittingly put their pet through the first treatments for nothing.

The RTx site should be kept clean and treated with water-soluble aloe vera gel topical preparations used for burn patients. Oral mucositis is best treated by frequent oral lavage with saline and green tea. The patient must be fed a bland, soft-food diet. If anorexia prevails, the placement of a feeding tube to keep up the caloric intake becomes essential, especially in geriatric cats. Water-soluble ophthalmic steroid preparations may help manage conjunctivitis, provided there is no corneal ulceration. Artificial tears are indicated for dry eye (KCS). For radiation-induced colitis, use bland diet and the recommended low-residue diet; steroid enemas and stool softeners may also help. Steroids and antiemetics and steroid-containing otic solutions help to alleviate side effects from CNS radiation, but there is no effective treatment for late effects such as myelomalacia. Bone sequestra must be surgically removed.

Multimodality-Multidisciplinary Therapy

Geriatric oncology patients may require more than one modality of therapy to gain survival advantage (Table 6.6). The sequencing of surgery, radiation, and chemotherapy treatments is critical. Proper spacing of the various therapeutic modalities to attack the cancer at the onset is preferable to treating a recurrence. The choices made early in the treatment plan generally impact the geriatric oncology patient's overall quality of life and survival time.

Immunotherapy, Vaccine, and Gene Therapy

Cancer is particularly difficult to treat because the body does not recognize the diseased cells as foreign and does not create a significant immune response against the cancerous cells.

Phillip Bergman, DVM, MS, PhD

Immunotherapy

Immunotherapy in cancer medicine is the stimulation or arousal of the patient's own defense system to kill cancer cells. Immunotherapy requires the identification of tumor-specific antigen(s) that can become therapeutic targets. These targets may be growth factors or signaling proteins. The next step involves the cultivation, activation, and production of binding agents, or effector cells, to target the specific antigen(s). Another important component of immunotherapy is the reduction of endogenous and iatrogenic immune suppression.

Active and passive immunotherapy play a role in cancer management. There are numerous products on the market that claim to support the immune system in a general fashion. Most of these active immunotherapy agents are classified as non-specific immunostimulants such as bacterial agents, cytokines, NSAIDs, glycoproteins, supplements, and so forth (see the "Chemoprevention and Immunonutrition" section of this chapter). An example of an active specific immunotherapy agent would be a specific tumor cell vaccine. Unfortunately, tumor cells contain many antigens that are shared with the host. Tumor cells and their selected fragments have been used as vaccines with some success in malignant melanoma and renal carcinoma cases in humans. This type of vaccine technology, or molecular adaptations of it, may carry over into veterinary cancer medicine, particularly in the research and development of DNA tumor vaccines against malignant melanoma in dogs. Researchers at the University of Wisconsin and the AMC in New York City are working in this exciting area.

Vaccines for Cancer Therapy and Gene Therapy

Scientists have been able to create genetically altered tumor cells and effector cells that can be used to treat diseases including cancer. As gene mapping for humans and animals progresses, opportunities are emerging to harness gene therapy for veterinary cancer patients. Gene therapy, with its expanded applications, may become available to pets with cancer on a routine basis within a few years. At the 2001 annual meeting of the Veterinary Cancer Society, the keynote speaker and several presenters discussed potential uses of gene therapy for humans and animals with cancer.

Initially, the concept of gene therapy was developed to replace or repair defective or mutated genes. Genes are the biologic units of heredity situated at specific locations on chromosomes. Genes are self-reproducing segments of DNA arranged in coils of nucleotide protein molecules sequenced in double helix protein chains. Genes dictate the vast structure and function of cells.

Over the past decade, the field of gene therapy has expanded to include a number of new applications. Today, gene therapy is used to program cells to become susceptible, to become more resistant, and to produce large quantities of specific cell proteins (cytokines such as Amgen's Epogen[®]). Gene therapy is used to change immune responses, alter cellular functions, seek and destroy tumor cells, and promote other factors that favor survival of the recipient (Helfand 2003).

Genes are transferred to cells with vectors. Virus vectors are used to carry genes into proliferating cells (transfection). They convert their own ribonucleic acid (RNA) into DNA by transcription and then the DNA integrates into the cellular genome for replication of the desired gene. Selected retroviruses are engineered to enter proliferating cells and deliver therapeutic genes. Genes may also be delivered by other vectors, such as liposomes, or by direct injection into tumors, sometimes with the use of a jet gun.

Without using the complex jargon and terminology of genetics, proteonomics, and immunology, I will describe how gene therapy could be used for our patients to manipulate and alter populations of renegade cancer cells to behave as we want them to. Essentially, we want cancer cells to quit growing, quit invading, quit metastasizing. Ultimately, we want cancer cells to commit suicide.

Gene therapy is the special technology that can alter molecular function and signaling at the cell surface and affect downstream pathways. It is hoped that this technology will prove useful in combating certain tumors. Large molecules on the surface of cells (macromolecules) will serve as antigenic targets. One such macromolecule is a sialomucin known as CD34, existing on the surface of bone marrow cells. CD34 is used as a marker in assisting the selection of enriched cells for bone marrow transplants. Antibodies produced against CD34 bind to the population of enriched cells and isolate them from cells collected for bone marrow transplants. These isolated, enriched bone marrow cells can be used as the recipients of retroviral vector genes via transduction or transfection. The altered CD43 cells are then transplanted into the patient for treatment of various cancers and certain genetic diseases.

Gene therapy may also be used to manipulate the immune system cells of veterinary cancer patients, which would be programmed to internally recognize specific proteins and attack them, or bind to receptor sites that disable cancer cell proliferation. This would tip the immune balance back in favor of the patient's survival. Theoretically, molecular chemotherapy will allow us to "program" certain immune cells such as T-cells, B-cells, or natural killer (NK) cells to transform into stealth killer cells that will locate, recognize, attack, and kill the patient's cancer cells (Helfand 2003).

Suicide Genes

Another targeted gene therapy approach involves the delivery of suicide genes. Cells are recoded so that they will be programmed to die (apoptosis). Normal cells undergo a certain number of divisions before they die. Each time a cell divides, it snips off a timer protein (telomere) from the end of the chromosome. Cancer cells develop their own immortal phenotype by increased expression of the enzyme, telomerase. Telomerase reattaches telomeres back on to chromosomes. This type of aberrant repair liberates the cell from its natural time-clock, blocking senescence and death by apoptosis. Increased telomerase activity protects cancer cells from programmed cell death. I view telomerase as a mechanism somewhat analogous to the regrowth of a lizard's tail.

Because humans and animals share genetically similar telomerase, this research will benefit our patients as well. Telomerase is a promising target for gene therapy. Suicide genes that inhibit telomerase could potentially cause all types of cancer cells to die. Gene therapy can also confer susceptibility upon cancer cells to attract the influx of the patient's own immune cells, resulting in widespread host destruction of primary and metastatic tumor cells.

One of the most well-known normal tumor suppressor genes is the p53 gene, which plays an important role in the control of apoptosis. When p53 is deactivated or rendered nonfunctional, cells become immortal and neoplasia occurs. Correction of p53 deficits can be achieved by the transfection of functional p53 genes into tumors, directing the tumor cells to undergo apoptosis. According to this concept, suicide genes are delivered via genetic molecular therapy.

Another gene therapy approach is to kill bystander cells via "molecular chemotherapy." Transfected cells are engineered to activate certain cytotoxic agents within tumor cells. Transfected cells are delivered into tumors and genetically produce signals for tumor cells to leak toxins around neighboring cells, resulting in cell death. This is called the "bystander effect." An example of the

“bystander effect” is the engineered herpes simplex virus. It is used to transfect tumor cells and deliver genes that produce an enzyme that activates a prodrug into ganciclovir, which kills bystander cells.

Anti-Angiogenic Gene Therapy

Gene therapy may also target the ability of cancer cells to create new blood vessels (angiogenesis). The inhibition of angiogenesis (anti-angiogenesis) is big business for pharmaceutical companies that are developing several new drugs for the marketplace. One day we may be able to offer intravenous gene therapy capable of encoding anti-angiogenic genes to inhibit micro-vessel formation and thus shrink and kill tumors.

Humans and canines share an interesting gene called Canstatin, located in a small segment of the $\alpha 2$ gene chain that belongs to type IV collagen. Collagen appears to be similar across many species of animals, including man. Canstatin acts as an angiostasis agent because it inhibits the proliferation, migration, and micro-vessel tube formation of endothelial cells (cells that form the walls of blood vessels) and induces apoptosis of endothelial cells. Cloning the Canstatin gene yields a product called recombinant Canstatin, or rcCanstatin[®]. Delivering therapeutic amounts of rcCanstatin to cancer patients may be developed as another way to use genetically engineered products as part of overall gene therapy. Cloning and sequencing Canstatin and/or inducing its expression by using a vector that transfects carrier cells may prove useful in the development of new therapies against cancer. Intravenous Canine Endostatin[®] may become available for therapy for dogs at risk in the future.

Another method of gene therapy under study involves intratumoral injections delivering super antigens and certain cytokine (cell proteins that act as intercellular mediators) genes. Antigenic tumors such as malignant melanoma may be responsive to this type of gene therapy. In addition, combinations of gene therapy and immunotherapy agents such as interleukin-2 may be added to chemotherapy protocols in the future to increase efficacy against metastatic disease.

Clinical Trials in Gene Therapy

Some facilities are using gene therapy on a clinical trial basis. It is important to keep up to date on the subject, since your clients will certainly ask you about it. New names and terminology make up the complex world of gene therapy. Cell surface macromolecules and the milieu of proteins and molecules within cells create an intricate and vast “alphabet soup.” Explain to clients that gene therapy uses engineered bacteria, viruses, or liposomes as Trojan horses. These agents can penetrate into the target cells while secretly carrying weapons in the form of therapeutic genes.

Progress is on the horizon, but not without many setbacks and problems along the way. Ongoing and future clinical trials will attempt to evaluate efficacy and toxicity, using controlled double blind studies. Will veterinarians soon be using gene therapy in everyday practice? The answer is a robust “yes”! One such vaccine uses allogeneic tumor cells such as antigenically distinct melanoma cells from other patients of the same species. The canine melanoma cells are transfected with DNA encoded to produce human GM-CSF (an immunostimulatory cytokine similar to neupogen). This vaccine technology is being developed to fight canine malignant melanoma and is currently available from the research facilities at the University of Wisconsin (Kurzman et al. 2005; for information go to <http://www.news.wisc.edu/12063.html> or contact Kurzman at kurzman@svmvetmed.wisc.edu).

The New York City AMC is evaluating a xenogeneic (different species) DNA-based vaccine that codes for human tyrosinase, which is a glycoprotein essential in melanin synthesis. When the DNA vaccine places human tyrosinase into a canine or mouse melanoma patient, it is incorporated into the tumor but it is recognized as foreign by the patient's immune system. The xenogenic vaccine could break host tolerance against a self-tumor differentiation antigen. It may also induce antibody, T-cell, and antitumor responses. 245 dogs with confirmed malignant melanoma were treated with xenogeneic DNA vaccinations from April 2000 to February 2006 at the AMC. The vaccine was determined to be safe and potentially therapeutic for dogs that had local-regional control, including some dogs with advanced stage disease. This xenogeneic DNA-based vaccine may be released following USDA approval for immunotherapy against canine malignant melanoma (Bergman 2006). For information go to www.amcny.org/departments/ClinicalTrialsMelangreat50.htm. One day, gene therapy may be delivered to our hospitals, nicely packaged as preventative vaccines to spur the immune response against various tumor types for patients at risk for melanoma, hemangiosarcoma, mammary adenocarcinoma, or osteosarcoma.

Some types of gene therapy will offer genetic immunopotential (immuno-gene therapy). This technology may restore tumor suppressor (p53) function to improve and revive the sagging immunosurveillance system of aging geriatric patients. Imagine the benefits of its application as a prophylactic vaccine to protect our highest risk patients from developing neoplasia.

Despite its failures and side effects, gene therapy has ignited tremendous hope as a potential treatment for many poorly responsive and chronic degenerative diseases in addition to cancer. Side effects may include abnormal buildup of antibodies or antigens. During developmental stages, gene therapy may be found to have irreversible consequences. It may create chaos in the immune system or death. There are currently over five hundred gene therapy protocols being evaluated in human clinical trials that have the potential to treat everything from Alzheimer's to Parkinson's to immune and genetic disorders and cancer. Our geriatric cancer patients may benefit greatly from gene therapy in the near future. Stay in touch with developments in gene therapy to see how it may impact our veterinary cancer patients. Some feel that this technology can be used to protect high-risk breeds.

Monoclonal Antibodies

Another type of targeted therapy is immunotherapy, which employs reactive B-cells harvested from the spleens and lymph nodes of mice that have been injected with intact tumor cells or cell membranes. These stimulated B-cells are fused with an immortal cell line and cultivated as hybrid clones for their monoclonal antibody (MoAb) production. The antibody is given to the patient in the hope that lysis or phagocytosis or destruction of target cells will occur. The patient must have the proper antigen(s) present on his or her tumor cells for the MoAb to work. The technique is fraught with problems with host response against the MoAb or mouse antibodies, cross reactivity, tumor size, and heterogeneity, which hamper success. The most famous MoAb used in human medicine is the recombinant anti-HER2 monoclonal antibody, (trastuzumab) Herceptin®. Herceptin targets the oncogene Her-2-neu, which is over-expressed in some malignant breast cancers. If the patient is Her-2-neu positive, Herceptin is the mainstay for treatment (Love 2000).

Rituxan® is a genetically engineered MoAb that is directed against the CD20 antigen found on the surface of normal and malignant B lymphocytes. Rituxan is used in CD20 positive non-Hodgkins lymphoma patients and has been found to be helpful against other tumors as well. Infusion reactions and lymphopenia are common.

Veterinary MoAbs are on their way back into practice. Dr. Ann Jegulm pioneered the first commercially available MoAb for canine lymphoma. Clinical trials with canine MoAb 231 for lymphoma found that dogs had geographically variable results.

Summary: Immunotherapy, Vaccine, and Gene Therapy

There are currently over five hundred gene therapy protocols being evaluated in human clinical trials that have the potential to treat everything from Alzheimer's to Parkinson's to immune and genetic disorders and cancer. Our geriatric cancer patients may benefit greatly from gene therapy in the near future. Stay in touch with developments in immunotherapy and gene therapy to see how vaccines and delivery systems may impact our options for the treatment of veterinary cancer patients.

There is the potential opportunity that gene therapy will exert a preventative effect from cancer development in high-risk breeds. It would be ideal to have a panel of anticancer vaccines to protect our Boxers, Golden Retrievers, Bernese Mountain Dogs, and German Shepherd Dogs from their predilection for cancer. Imagine having a vaccine for all large-breed dogs that would protect them from osteosarcoma.

Chemoprevention and Immunonutrition

To cure sometimes, to relieve often, to comfort always—This is the first and great commandment.
Hippocrates

Chemoprevention and Immunonutrition for Cancer Patients

Chemoprevention is the concept of providing natural or synthetic compounds to reduce cancer risk in susceptible patients. Since cancer is a major cause of death in older pets, chemoprevention and immunonutrition are very appealing to pet caregivers. The mechanisms of these compounds vary and are not fully understood. They may reverse malignancy or intervene and suppress the multistep process of carcinogenesis. Some agents block or suppress mutagenesis, promotion, proliferation, angiogenesis, invasiveness, recurrence, or metastases. Other agents intervene with genetic mechanisms such as initiation, progression, and proliferation. Some agents induce differentiation of pre-malignant cells to prevent them from progressing toward malignancy (Bergman 1999).

Hundreds of natural compounds have been formulated as supplements or nutraceuticals with claims of anticancer effects. Some compounds have been shown to play a role in the cell cycle to reduce the risk of cancer. I like to call these natural compounds “foodaceuticals” as well as nutraceuticals to emphasize to clients that they are generally nontoxic and are found in nature.

Research shows that natural and synthetic substances augment the immune system, inhibit cancer, and yield positive clinical results in rodents and humans. Chemoprevention and immunonutrition are standard therapy at my clinics. They are an important arsenal in the way I conduct all levels of care in the battle against cancer for my geriatric oncology patients. Enhancing a patient's normal diet and adding special supplements is a useful modality that supports and improves the overall health of the geriatric cancer patient. Clients have repeatedly remarked that their geriatric pet was feeling younger,

looking better, and playing with toys again. We give credit for these pleasing reports to the supplements because experience tells us that chemotherapy does not provide this effect. Immunonutrition is very important in our oncology service. It plays a priority role in our palliative and Pawspace care programs.

Confusion and Controversy

It should be no surprise to find confusion and conflicting data in this field. Many agents have multiple effects. Some agents have potentially negative effects. Some agents under large-scale studies were stopped due to adverse effects. For example, beta carotene was stopped early for smokers in the CARET study. When given with retinol, the incidence of lung cancer increased. The NSAID Vioxx[®] was pulled off the market after a study found that it increased the risk for heart attacks in colon cancer patients. It seems that marketing, sales, and profits drive many drug companies, rather than the medical justifications and quality of their products. Perhaps this is not the forum for making this point, but many ethical issues are involved in the supplement and vitamin industry, including quality control. In the past, skeptics went so far as to say that nutritional supplements and megavitamin therapy for cancer was a profitable health-fraud industry (Curt 1990).

A paper presented at the 2004 Veterinary Cancer Society (VCS) meeting reported that dogs given NSAIDs were less likely to develop cancer and that the medication was well tolerated (Oberthaler et al. 2004). Hansen et al. reported on similar health benefits from a study of 575 dogs given NSAIDs in the 2004 American College of Veterinary Internal Medicine (ACVIM) Forum. This is no surprise, since oncologists have been using piroxicam for its anticancer effects for over a decade (Knapp et al. 1994). Despite renal, hepatic, and GI toxicity, it seems that the downside of using COX-2 selective NSAIDs in our veterinary patients may be minimal when compared to people. Exercise has also been shown to have a positive effect in longevity against cancer. A recent study found that women breast cancer patients who walk 3–5 hours a week are more likely to survive twice as long as similarly staged women with breast cancer who do not exercise. The same is true for geriatric dogs. We can presume that if geriatric oncology patients are entertained, exercised, and kept lean, they will actually live longer.

Pets at Risk

We know that Boxers, Golden Retrievers, Bernese Mountain Dogs, Flat-Coated Retrievers, and intact female dogs are at greater risk for developing cancer than other dogs. The risk for developing breast tumors in intact female dogs rises to 60% as they become geriatric. Dogs with osteosarcoma and hemangiosarcoma and cats with breast cancer that have had their malignant tumors removed are at very high risk for recurrence and pulmonary metastases. Cats operated on for vaccine-associated sarcoma and pets with solar-induced skin cancer are at high risk for recurrence in the vicinity of their tumors due to “field cancerization.”

Exposure to lawn chemicals (2,4-D) puts dogs at risk for lymphoma. Scottish Terriers exposed to lawns treated with both herbicides and pesticides are at seven times the risk for transitional cell carcinoma than unexposed dogs. Scotties are 20 times more susceptible to TCC than other dogs, according to a study by Dr. Lawrence Glickman et al. from Purdue (2004). Workers at Tufts found that cats exposed to cigarette smoke are at higher risk of lymphoma. Cats living with smokers or wearing flea collars have an increased risk for oral SCC.

Genetic mutations and environmental factors may cause damage, activation, and/or over-expression of certain mechanisms in the normal functions of repair genes, tumor suppressor genes, and suicide genes. Cancer is a multistep process involving initiation and promotion by these factors that tips the cascade of molecular and cell membrane signals and events that transition cells toward malignancy. A perplexing activation and proliferation of dendritic cells creates the confusing group of disorders classified as histiocytic diseases (Rassnick 2006). We know obesity, poor diet, and lack of exercise result in a shorter life span and increased risk of cancer in animals. It is well known that diet, lifestyle, and environmental exposure play a significant role in the incidence of cancer in humans.

Imagine the steps toward cancer as part of an intricate molecular choreography. Mutated DNA performs its immortal death dance. Renegade cells multiply and bypass surface signals for homeostasis. Cancer cells expand exponentially, creating chaos as they expand, twirling into neighboring cells and ultimately killing the host. In my opinion, immunonutrition and chemoprevention may re-choreograph and trip cancer at some of its intricate steps. Attention to diet, maintaining a lean body mass, and exercise along with the sensible use of immunonutrition and chemoprevention may add cancer-free years and longevity for our geriatric veterinary patients.

Highly metastatic cancers and most high-grade sarcomas prevail to kill their victims despite a timely and complete excision of the primary tumor. This aggressive biologic behavior results from the early dissemination of “scout” cells into the lymphatic and circulatory system before detection of the primary tumor. These abnormal aggressive scout cells acquire an immortal nature, evade and survive the body’s immunosurveillance, and are able to develop into new clones of cells that accumulate into metastatic tumors. The new metastatic clones are often more resistant to treatment than the primary tumor due to the hardness of their progenitor scout cells.

It would be ideal if there were a safe way to fortify high-risk breeds, exposed animals, and aging pets and post-op cancer patients against the ravages of cancer’s death dance. It seems obvious to me and to thousands of others in research and clinical medicine that people and animals can and do benefit from immunonutrition and/or chemoprevention. I started using anticancer supplements for my patients in earnest about 12 years ago, and the difference in my patients’ physical condition, quality of life, and survival times has been impressive.

The scientific community is taking a closer look at natural substances that modify the differentiation of cells. Other agents affect proliferation or mutation of cells as they leap from inflammation to premalignancy toward malignancy. The medical and scientific community has found it difficult to reach a consensus about nutraceuticals because the field and the claims are not regulated. Unfortunately, 38% of the compounds evaluated in the past for content in the marketplace were not trustworthy. One study found very few probiotic compounds to be reliable. Since it has been difficult to trust the available products, the supplement and nutraceutical field suffers.

The National Cancer Institute has a Chemoprevention Branch that funds studies to look at the efficacy of chemopreventive agents in populations of susceptible and high-risk patients. The results of these long-term studies will be published. No doubt there will be controversy over the data. For instance: Should you stop antioxidants during chemotherapy and radiation therapy or not? (Vajdovich et al. 2005). Is it better to drink a glass of wine three to four times a week for its resveratrol or should you get it from eating peanuts and raspberries instead? What effect do Vioxx[®], Celebrex[®], piroxicam, and other COX-2 inhibitors have on angiogenesis and apoptosis? Can NSAIDs be used to cytorreduce or palliate mammary tumors? (Dank 2006a). Can NSAIDs be used as prevention to lower the incidence or recurrence of various types of cancer? (Dank, Aung, and Yudelevitch 2005 and Dank 2006b).

It took 70 years for the scientific community to accept that vitamin C cured scurvy. It may take repetitious studies and more time before flavonoids, vitamin C, beta carotene, NSAIDs, selenium, vitamin A

(retinoids), inositol hexaphosphate, mannose, fucose (do not confuse this with fructose!), beta glucans, fatty acids, antioxidants, and so forth are credited for their roles in the battle against cancer.

A recent study led by Dr. Mark Levine from National Institutes of Health was reported on Medscape. Dr. Levine found that IV vitamin C has anticancer effects and selectively kills several different types of cancer cells while leaving normal cells unscathed. The cytotoxic effects of vitamin C did not depend on metal chelators but required hydrogen peroxide formation. Studies in the 1970s that first suggested the anticancer action of vitamin C were not duplicated properly in subsequent studies. The original work used a combination of oral and IV vitamin C at high levels and the subsequent studies only used oral vitamin C, which did not achieve adequate plasma levels. At this writing, a phase 1 trial is underway to establish the safety of IV ascorbate in patients with advanced cancer. Be sure to check www.Medscape.com to follow up on the results of Dr. Levine's trial.

Colleagues and members of our scientific community may dismiss, become indifferent, or discredit data about the efficacy and use of nutraceuticals and supplements. The training that many of our current physicians received was devoid of education in nutrition. It is not part of what they know. They can't believe or won't accept the available information. The scientific method is used to criticize and dismiss the Eastern concept that "food is medicine."

Many clinicians choose to uphold a double standard. They are against using supplements or immunonutrition, but they will accept the concept of chemoprevention. This same double standard is enacted every day in the field of oncology. This is because we, as healers, constantly use medications that we hope will win back a remission. Most of the second and third choice drugs that we use to treat resistant and metastatic cancer have little effect, but we give them with a "let's see if this helps" attitude. We are trying to make our patients better. The same holds true for any type of palliative therapy. If a treatment seems to be helping we are justified in continuing it.

The late Leslie R. Bennett, MD, and his colleagues Amos Norman, PhD, and Kai Iwamoto, PhD, inspired my epiphany regarding the impact that diet may have on cancer in 1989. Dr. Bennett was my research colleague during the decade that I was affiliated with the Animal Tumor Resource Facility at the University of California, Los Angeles, under the direction of Dr. Hal Snow. Dr. Bennett investigated the role of linoleic acid in protecting the small intestine in the mid-1950s. He wanted to revive and continue this early work with linoleic acid as his professor emeritus project. He asked me to help him investigate the role of linoleic acid and other fatty acids in tumor-bearing animals. We found some anticancer benefit in dogs with mycosis fungoides (Iwamoto et al. 1992) and brain tumors. Two dogs with mast cell tumors had adverse reactions with unintended histamine release, presumably due to degranulation syndrome.

Hundreds of distinguished researchers have published more than three hundred thousand articles and papers that have looked at the effect that antioxidants, fatty acids, glycoproteins, and hundreds of other natural compounds have on cancer. Journals such as *Nutrition and Cancer* and the *Journal of the American Nutraceutical Association* have presented evidence that shows that we can place our geriatric oncology patients on a better plane of health through immunonutrition.

Pet owners are constantly searching for the best supplements for their pets, especially when cancer strikes. It is not unusual to see pets that are being given 10–50 different supplements by the time they come in for consultations.

Mom Dog's Case (Help Clients Select Sensible Supplements)

Mom Dog Artsis, a 12-year-old F/S Shepherd cross, was given a poor prognosis following splenectomy and liver lobectomy for hemorrhaging metastatic hemangiosarcoma lesions. Her



Figure 6.8. Mom Dog Artsis was given 51 supplements by her family following emergency surgery for hemoabdomen due to hepatic hemangiosarcoma.

family members, a nurse and neurologist, purchased a variety of supplements that added up to 51 items (Figure 6.8). The family did their research and felt compelled to try to beat the odds against Mom Dog's survival. She only survived a few weeks post-op. I am sure that if Mom Dog's caregivers had known about suberoylanilide hydroxamic acid (SAHA), they would have searched for it as well. They would have used this histone deacetylase inhibitor based on Molly's case report in the December 2004 issue of *Veterinary and Comparative Oncology* by Leonard Cohen, MD (Cohen et al. 2004). SAHA failed to help one of my patients with hemangiosarcoma. A clinical trial is under way at the AMC to determine its efficacy.

Pet caregivers select available supplements based upon variable advice from the health food store-keepers, books, friends, the Internet, nutritional consultants, and animal communicators. It is time for contemporary veterinarians to look into the subject of immunonutrition and be able to recommend sensible supplements, which may benefit the geriatric cancer patient's health.

Immunonutrition Suggestions

There are hundreds of products and thousands of retail health food stores that market supplements. It is important to know and trust the quality of the product. We use the products mentioned in this section for our immunonutrition protocols because I know that the providers have proven in-house quality control. There are many other excellent providers that are not listed in this text. If you have confidence in the quality and consistency of their products they can be used in your protocols.

Educate clients that it takes time for the supplements and nutraceuticals to show their beneficial effect and change the pet's physiology. Cancer patients on immunonutrition seem to handle chemotherapy treatments with fewer adverse effects. We recommend continued use of the supplements long after the surgery, chemotherapy, or radiation therapy is completed with the goal of supporting the immune system and chemoprevention to increase the time to recurrence of the patient's cancer.

Inositol hexaphosphate (IP-6), or phytic acid, is a glycoprotein derived from rice. It is also derived from soybeans, sesame seeds, beans, legumes, and cereals. IP-6 is a polysaccharide found in fiber that has potent antioxidant and anti-carcinogenic action. It also enhances natural killer-cell activity and is beneficial for a wide range of metabolic conditions. For more information, visit www.phytopharmica.com and have your clients read the excellent book *IP-6: Nature's Revolutionary Cancer-Fighter* (Shamsuddin 1998).

Beta glucans are glycoproteins derived from the *Agaricus blazei* mushroom. Beta glucans stimulate macrophage activity; destroy viral, bacterial, and malignant cells; and increase the utilization of insulin. *Agaricus* products are used widely in Asia as a health supplement. Information on *Agaricus* is available at www.atlasworldusa.com.

Advanced Protection Formula (APF) Drops enhance the body's ability to handle the stress of cancer and its treatment. The formulation contains extracts from several types of Siberian ginseng. It increases the body's natural adaptogen activity during stress. Cancer patients show increased energy and increased appetite and maintain higher white blood cell counts while under the stress of chemotherapy. A modified formulation of APF Drops may also help increase insulin utilization in diabetic patients and may be used to help stabilize hyperglycemic cats. For more information contact Dr. Mike Van Noy at www.auburnlabs.com.

The multitasking function of the liver is essential for metabolism and the detoxification of most chemotherapy drugs. It is one of the primary targets for metastatic disease and may give rise to primary neoplasms. Many geriatric cancer patients have acquired nodular hyperplasia, chronic fibrosis, cholestasis, fatty liver, and buildup of pigments in hepatocytes. The liver also undergoes SAME deficiency and cellular damage with senescence. Evidence-based research has shown that SAME is helpful in restoring hepatocellular function and membrane integrity. I recommend SAME for its proven efficacy in restoring hepatic function and homeostasis. I also recommend milk thistle (silymarin) for its proven ability as a flavonoid to improve the solubility of bile and enhance the detoxification process. Milk thistle also prevents depletion of glutathione, raises glutathione levels up to 35%, and protects the liver from damage. It can be used for pets on chemotherapy to help the liver process and detoxify drugs. It is in several products designed for the liver such as Rx Vitamin's Hepato Support[®] and OncoSupport[®]. Rx Vitamins for Pets offers excellent high-quality supplements and support products formulated by Dr. Robert Silver. He asked me to assist in the formulation of OncoSupport for cancer patients. The compound contains Hepato Support and Nutrigest[®] with some reliable probiotic agents and cell wall lysate of *Lactobacillus rhamnosus*, arabinogalactan, and *Agaricus blazei*. This powdered formula reduces the number of supplements dispensed. For more information, visit www.naturaldvm.com.

I also place my geriatric cancer patients on Platinum Performance Plus[®] and RePress minerals as a comprehensive and beneficial vitamin supplement. This formulation contains over 40 nutrients and supplements. Some dogs get diarrhea due to the OM-3 fatty acids, so it should be introduced to the diet on a gradual basis. For information contact Dr. Doug Herthel at www.platinumperformance.com. Standard Process, a well-known whole food supplement company, offers the veterinary market quality products that are designed to provide nutritional support for various organs. For nutritional support for patients with anorexia or cachexia and for patients on feeding tubes, we use glutamine and

whey protein products and colostrum (GlutImmune[®] and ImmunoPro[®] and Organic Colostrum) from BioMolecular Sciences at www.GenomicWhey.com.

For oral detoxification, I prefer to use DeToxMax[®] from Bioimmune, Inc. I also provide selected patients with liquid Ultra Ascorbic C[®] and Immune Response Powder[®]. Bioimmune and Biomolecular Sciences provide excellent immunonutrition products and seminars with information. They recommend very demanding IV, PO, and hyperthermia protocols for people with advanced stage cancer. People with cardiac and endocrine disease also benefit due to the shared biologic mechanisms that are affected by using these products.

I found that it is very difficult to apply daily IV protocols for veterinary patients without the placement of vascular access ports. Therefore we generally use the oral preparations for our geriatric oncology patients. For more information visit www.bioimmune.com. The doses and special instructions that we use for most of the supplements discussed in this section are summarized for your convenience in Table 6.9.

Table 6.9. Doses for Immunonutrition and Chemoprevention Protocol Used by Author as Supplements for High-Risk Breeds, Senior, Geriatric, and Oncology Patients

Each geriatric cancer patient needs to be individualized. The one caution about nutraceuticals and holistic supplements is that many don't have specific doses. The maintenance dose is a reference but the providers may recommend more if the patient has cancer. Below are the doses and recommendations for use that we have experienced as helpful for our cancer patients. Do not use escalated doses of a product or compound that you are not familiar with.

- 1) Agaricus Bio[®] Capsules 600 mg: one twice daily per 15–30 pounds.
The capsule can be given directly by mouth or opened and placed in food or in gravy.
For cats, we use the Agaricus Extract Mate[®], which is a liquid.
The preparation is 300% more concentrated than the capsules.
We start cats with 3 drops once a day and may go up to 18 drops a day for cats with severe advanced stage cancer. There are 200 drops per vial so the client can figure out how long the supply will last.
It can also be used for advanced stage cancer in dogs as a loading dose.
The dose for advanced stage cancer in dogs goes up to ½ vial per day for large dogs. Available from Atlas World USA.
- 2) IP-6: One capsule per 10 pounds per day (divided BID). It is best utilized on an empty stomach.
Available from Phytopharmica/Integrative Therapeutics, Inc.
- 3) Platinum Performance Plus[®] for Canine:
This compound is a great vitamin supplement for geriatric dogs.
Place in moist food such as yogurt, gravy, or canned food.
It should be introduced into the diet gradually over 3–4 weeks.
The ideal dose is one tablespoon for 30 pounds per day, divided.
Some dogs have loose stools and some won't accept it. Keep refrigerated.
Platinum Performance Feline[®]: ¼ teaspoon in canned or wet food. Refrigerate.
- 4) Advance Protection Formula (APF) drops: 3 drops per 10 pounds once per day in food.
Available from Auburn Labs.
- 5) Onco Support: One to three scoops twice daily per 50 pounds. It also contains 600 mg of Agaricus per scoop. Rx Vitamins for Pets sends a taste enhancer if the patient refuses it.
- 6) Astragalus: Enhances the action of some chemotherapy agents such as carboplatin, according to a recent paper by the NCI.
- 7) Musculoskeletal Support: Helps to strengthen the patient and combat weakness. Other nutrients from Standard Process may be suggested to support organs that are compromised in the individual patient.

(continued)

Table 6.9. Doses for Immunonutrition and Chemoprevention Protocol Used by Author as Supplements for High-Risk Breeds, Senior, Geriatric, and Oncology Patients (*continued*)

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- 8) Idebanone: This is the water soluble form of CoQ10. It acts as an antioxidant and specifically protects myocardium. We use it to protect the heart from the cardiotoxic effects of Adriamycin.
- Note: Many clients become overwhelmed with the above suggestions. It is best to introduce additional supplements listed below on the second or third visit.
- For pets in Pawspice care, it is best to see the pet routinely (every 2–4 weeks if possible) for rechecks to monitor them.
- 9) DeTox Max: $\frac{1}{4}$ teaspoon per 10–15 pounds given orally every other night before bed. The patient must be given extra fluids with this product such as broth. If used in cats, SQ fluids may be needed. This product helps remove the heavy metal toxins from the body. DeTox Max is from www.Bioimmune.com.
- 10) Vitamin C: We use a liquid preparation, Ultra Ascorbic C[®]. It is a high-quality organically grown vitamin C from beets. Use $\frac{1}{2}$ teaspoon for 15–30 pounds twice daily. The Ultra Ascorbic C is from www.Bioimmune.com. They also supply a powder form.
- 11) Ambrotose: This supplement contains mannose from aloe vera.
- Use $\frac{1}{8}$ teaspoon once a day for cats and small dogs with cancer.
- Use $\frac{1}{8}$ teaspoon per 30 pounds daily for dogs with cancer. Available from Mannatech.
- 12) Fish oil is a source for OM-3 fatty acids. Use $\frac{1}{4}$ —one teaspoon per 15 pounds per day if the patient can handle it without developing diarrhea. Use a high-quality product such as Ultra EFA[®] from Rx Vitamins for Pets. It is not needed for pets on Hill's n/d[®].

Diet: Allow a gradual transition period of 2–4 weeks for the patient to adjust to the supplements. Encourage clients to feed their geriatric patients high-quality canned food or homemade diets only. Try to get all cats off dry food completely. They often do better on canned food. If the patient is being fed n/d, we do not use Platinum Performance or fish oil. This combination causes loose stools and/or diarrhea.

Note: The supplements for this protocol may be ordered and shipped from the author's home office if requested.

Nutritional Support for Older Cancer Patients

It is important to assess the body condition (1–9 scale), the nutritional status (malnourished vs. cachexia), and the appetite of the geriatric oncology patient as discussed in previous chapters. For patients not requiring hospitalization and parenteral nutrition, educating the caregiver determines that cancer patient's intake and well-being. The composition of a diet, its nutrients, and the level of food intake can have a surprising impact in the body at the molecular and genetic level (nutrigenomics). Food nutrients influence genes to prevent or enhance certain diseases. An improper ratio of nutrients in pet food may adversely affect organs. For instance, taurine deficiency causes retinal detachment and cardiomyopathy in cats. Overfeeding shortens the life span of dogs. Some pet foods are formulated to offer clinical improvement in chronic conditions such as renal disease, diabetes, arthritis, and cognitive syndrome by altering the action of proteins and enzymes in the body that contribute to the degenerative condition.

Our profession has grown up with a number of dichotomies. For instance, we all know that the feline is an obligatory carnivore. Yet, our companion animal community has been trained to feed cats a high-carbohydrate diet and has become accustomed to fat cats and diabetes as part of the norm. According to feline specialist Dr. Elizabeth Hodgkins, ACVIM, cats should not be fed dry food. They need high protein, moderate fat, and low carbohydrate diets from birth to death. This would be their natural diet in the wild state. According to Dr. Hodgkins, the short GI tract of the feline does not

appreciate cellulose as a dietary ingredient. Obese cats tend to have more satiety and lose weight on a strictly canned food diet. Diabetic cats fed high protein canned diets may decrease or drop their need for insulin and become normalized. For more information visit Dr. Hodgkin's Web site at www.all-about-cats.com. A number of my geriatric feline oncology patients with concurrent diabetes have normalized after they were taken off dry food and treated for their malignancies.

Diets for Geriatric Cancer Patients

When Dr. Gregory Ogilvie, ACVIM, was at CSU, he employed the well-known and well-documented theory that cancer cells utilize sugars and carbohydrates more readily than proteins and oils. Hill's Pet Nutrition, Inc., formulated a diet with increased levels of protein, fat, om-3 fatty acids, and arginine with reduced carbohydrate. The special diet intended to "Feed the patient and starve the cancer." Fifty lymphoma dogs were given the same chemotherapy protocol and divided into two groups. The group on the special diet had longer survival. The diet is currently available as Hill's Prescription Diet Canine n/d® (neoplasia diet). Many oncologists recommend n/d for dogs with lymphoma and for dogs receiving radiation therapy. To avoid diarrhea, we advise pet owners to gradually blend n/d into the patient's regular food until the majority of the intake becomes n/d. Seal remaining food in an airtight plastic bag to avoid oxidation. For more information visit www.hillspetnutrition.com.

Clients frequently ask for recommendations about nutrition for their geriatric cancer pet. Many caregivers want to customize their pet's diet to fight the cancer. They view nutrition as part of the therapy. Since dry pet food has, by its very nature, low protein and high processed carbohydrate content, I recommend a high-quality canned food for cats and dogs or a homemade special diet. For clients who are willing to prepare a homemade diet for their dog, I enthusiastically recommend the recipes in *Help Your Dog Fight Cancer: An Overview of Home Care Options*, by Laurie Kaplan. We keep an office copy of this book for clients to explore. The book is available at www.helpyourdogfightcancer.com.

I generally avoid condoning homemade strict vegetarian and raw meat diets for my geriatric cancer patients due to the potential for nutritional imbalances, safe handling issues, and increased bacterial content. Bacterial contamination could be problematic for geriatric cancer patients struggling with cancer-induced and treatment-induced immunosuppression. Some commercial vegetarian and raw diets are carefully balanced and may meet the requirement for dogs and cats. The safest raw diets are prepared with USDA-inspected meat for human consumption in high-quality kitchens and immediately fresh frozen. If the packages are kept frozen properly and thawed just before feeding, the contamination issue may be less of a problem for cancer patients. It is up to the doctor and the caregiver to verify that the chosen diet is nutritionally complete.

Summary: Chemoprevention and Immunonutrition

Chemoprevention and immunonutrition have become strong allies in the overall treatment of the geriatric oncology patient. During consultations, introduce nutrition on general terms, then specifically for the geriatric oncology patient. It is general knowledge that Americans are suffering an epidemic of obesity and diabetes because of fast food, a high-carbohydrate diet, and minimal exercise. Feeding exclusively dry food to cats would be synonymous to giving them a total diet of "kitty fast food." Clients readily accept the theory of "starving the cancer cells and feeding the patient." This is

an opportunity to switch the geriatric oncology patient's diet to a more calorie-dense higher protein diet such as n/d, a specially prepared diet, or a homemade diet. If the patient has a poor appetite or goes off food for 3 days, nutritional intervention and supportive care to maintain proper caloric intake is beneficial. The overall quality of life for cancer patients diagnosed at early and at advanced stage cancer may benefit from thoughtful immunonutrition and chemoprevention management.

Integrative and Alternative Medicine

Tis better to light one candle than curse the darkness.

Eleanor Roosevelt

When a geriatric cancer patient's caregiver is told that there is nothing more that can be done, the caregiver often seeks alternative, unconventional, and/or complementary therapies in hope that the pet may benefit. It is admirable that so many of our highly bonded clients leave no stone unturned when it comes to caring for their older pets with cancer. We owe these questing clients courtesy and respect for their determination and efforts.

PP Roederick, an 18-year-old F/S Siamese cat with two previous craniotomies for meningioma, presented with recurrence of blindness, circling, anxiety, and weakness progressive over 2 months. The family declined further Sx and RTx. PP responded very well to our Pawspice care program using an integrative protocol for 6 months. Her medical management consisted of oral prednisone at 5 mg BID, lomustine at 5 mg on days 1 and 5 every 30–44 days depending on her CBC, oil of evening primrose capsules at 1–2 (538 mg) BID (for linolenic acid), and Agaricus Extract Mate® (for beta glucan).

A survey of 356 human cancer patients who adopted complementary approaches for their treatment found them to be educated, intelligent, and unlikely to be persuaded that the therapy they employed is useless just because it has not been published in peer-reviewed journals (Cassileth et al. 1984).

Many practitioners don't agree with or know anything about the potentially adverse or beneficial effects of a particular complementary or alternative therapy or product chosen by clients to help their pet fight cancer (Lana 2006). We must avoid invalidating the client's search for non-conventional modalities to help a pet. The client may have invested great faith in a particular alternative therapy, and believing in a treatment is the preferred attitude for success. Crushing a person's hope is counterproductive and may turn them away from you. Therefore, it is best to incorporate the client's efforts into your treatment plan when possible and encourage the person to proceed with the benefit of your medical guidance.

Clients often tell me that they would do anything to save their pet. Many pet owners have embraced some aspect of holistic medicine for themselves or their pets. When the attending doctor makes jests, rolls back the eyes, dismisses, or disapproves of a client's choice to seek alternative therapy, the doctor alienates that client. If the pet shows a response to the dismissed therapy, the client is further alienated.

Cabo's Case: How and When Should One Stop Trying?

Cabo Greuel, a 12-year-old F/S Black Labrador Retriever, was diagnosed with end stage renal cell carcinoma (RCC) following signs of hematuria and "hobbling a bit." Elaine Greuel was determined to do everything possible for Cabo. Diagnostic imaging revealed that Cabo's left kidney was three times normal size and that she had five pulmonary metastases. Her BUN

was 35 and her creatinine was 2.4. Cabo had a “great” response with deracoxib. Elaine searched the Internet, consulted with several oncologists, and brought in a stack of downloaded information. After our consultation, Elaine elected to enter Cabo into Pawspice with palliative chemotherapy. We used carboplatin, pain management, and our immunonutrition protocol including Oncosupport and Renal Support[®] in an integrative approach.

Cabo experienced adverse events with grade 3 lethargy, vomiting, and diarrhea after her first CTx treatment, despite precautionary dose modification and using oral Reglan and Azulfidine from her cancer care package. To avoid repeat toxicity, we opted to split her total dose over an 8-day period. Cabo’s tumor growth stabilized with no progression for 3 months until the carboplatin failed to help. Her tumors enlarged as we tried other drugs to no avail. Elaine wanted to pursue further options despite my counsel to discontinue CTx and accept the sad fact that Cabo’s days were numbered.

Elaine could not give up because Cabo remained in good spirits. I informed Elaine about small molecule research and that some agents had helped humans with RCC. Elaine wrote, “I tried to contact all of the pharmaceutical companies but no luck.” She purchased three or four more alternative anticancer products during this time. She wrote, “Dr. Cheryl London called me back from Davis and felt very badly about Cabo, but said there is nothing out there and that she would take Cabo as one of her patients if there was. . . . We decided to try the interferon therapy with Dr. Greg Ogilvie being we didn’t have too many options left so we wanted to give this a try. Cabo has been given five doses now and tolerates it very well with no side effects other than lethargy.”

Elaine explained that she felt compelled to keep trying as long as Cabo was fighting the cancer. Her BUN was 39 and her creatinine was 2.9 when she was off piroxicam and on tramadol for the discomfort. She wrote, “At this point, there is not much to lose and maybe a little hope to gain, but we know that’s slim.”

Six days later, Elaine wrote, “Cabo was having trouble breathing all day yesterday and I noticed her gums were no longer pink and she was wobbly. As I was running her to Dr. Saunders, her primary veterinarian, she passed out in my arms. Dr. Saunders revived her. She fought like anything and even waited for Dave and Nikki to get home . . . We even went back to bring Blaze to see her one last time and . . . say goodbye . . . I am so sad. Dave’s heart is ripped out like mine . . . We just wanted you to know how much we appreciate everything you have done for her and all your love and caring helped us tremendously. Please keep in touch with us.”

When alternative therapies are used in combination with conventional therapies, they are considered to be complementary. Doctors that condone or use complementary therapies in concert with conventional treatment are involved with or practicing integrative therapy.

Accept Clients as Valuable Partners

The most important issue to clarify with your clients is that they should not forgo a known treatment for an unknown or, worse yet, an unsound therapy that lacks credibility (Miller 2005). Clients often feel that the alternative treatment is nurturing their pet. Go back to the old principle, “Do no harm.” If the cancer patient is handling treatments with no innocuous or adverse side effects from alternatives, then be willing to work with the combination that the client has put together for the pet.

The most commonly used alternative therapies that have appealed to my clients to use for their pets are nutraceuticals, diet therapy, metabolic therapy (including megavitamin therapy, orthomolecular or high dose vitamin C therapy, enzyme therapy, cellular therapy, detoxification therapy, and more), acupuncture/acupressure, massage therapy, chiropractic adjustment, herbal medicine, homeopathy (using very dilute solutions such as rescue remedy), energy field, and magnetic therapy. There are many other types of alternative therapies, including immuno-augmentive therapy, oxygen, light, shock wave therapy, crystal, and aromatherapy. Most of these treatments are innocuous. Some may be beneficial and some are probably ineffective.

The exception is with herbal medicine. Herbs have the potential to cause problems or create drug interactions, especially in geriatric patients on polypharmacy for concurrent conditions. The clinician must review herbal products and supplements to discover any herb-drug interactions they may cause when given with the patient's conventional medications.

Herb-Drug Interactions

Combining herbal products with conventional drugs and anticancer therapy may result in beneficial effects, no effect, or antagonistic interactions for the patient (Robinson 2006). There are two basic types of interactions between herbs and conventional drugs. A pharmacokinetic interaction affects the absorption, distribution, metabolism, or elimination of the herb(s) or drug(s), causing either an increase or a decrease in the amount of drug available to the patient. A pharmacodynamic interaction alters the way in which a drug or herb affects a tissue or organ system, causing either a synergistic or antagonistic herb-drug interaction (Carson 2002). Pharmacokinetic and pharmacodynamic herb-drug interactions may affect the activity of antibiotics, cardiac glycosides, insulin, steroids, chemotherapy, and so forth, while exerting a protective and/or antioxidant effect for the liver, gut, kidney, heart, and immune system.

Antioxidants may be the most commonly used alternatives by owners of pets with cancer. Some oncologists prefer that herbs and antioxidants are not given to their cancer patients while they are receiving conventional chemotherapy and radiation therapy. The rationale for this precaution is based on the theory that part of the efficacy of the therapy is based on the generation of free radicals, especially true with Adriamycin. This recommendation is controversial and has been shown to be equivocal. My preference has always been to provide antioxidants to geriatric cancer patients so the patient receives their benefits during all types of conventional cancer treatments, including immunotherapy and gene therapy. For detailed information about the pros and cons regarding antioxidant therapy, please consult the suggested reading list for herb-drug interactions at the end of this chapter.

The introductory list of commonly used products and their potential drug interactions (Table 6.10) will acquaint you with how some commonly used herbs can interact, both positively and negatively, with some of the drugs that we employ in veterinary medicine (please note that the list is not complete). Clients will appreciate your acceptance of their contributions to their pet's care when you review the herbal products and supplements that they have chosen to give their pets. Keep in mind and inform clients that their aging pet may be more susceptible to herb-drug interactions due to decreased ability to absorb, metabolize, and excrete a polypharmacy of conventional drugs and herbal preparations.

For in-depth information, refer to *The Complete German Commission E. Monographs* and other suggested readings listed following the references at the end of this chapter. We as veterinary practitioners need to educate ourselves on this subject and apply pressure to increase the number of useful scientific studies performed in the growing field of integrative medicine.

Table 6.10. Drug-Herbal Interactions

Herb	May:
Agaricus blazei	Counteract negative immunosuppression of steroids Increase insulin utilization, affecting insulin dosage
Aloe vera	Increase potential toxicity with cardiac glycosides and antiarrhythmic agents
Astragalus	Impair immunosuppressive effects of cyclosporine, azathioprine, and methotrexate Increase immune stimulating effects of interleukin-2 and acyclovir Enhances the effect of carboplatin
Bromelain	Enhance some antibiotics Improve efficacy of some chemotherapeutic agents (vincristine and 5-fluorouracil)
Burdock	Necessitate adjustment of insulin dosage due to hypoglycemic effects
Cayenne	Protect stomach from adverse effects of aspirin Enhance absorption of theophylline
Echinacea	Decrease effects of immunosuppressive drugs Enhance phagocytic immune function
Garlic	Behave similar to burdock with antiplatelet activity similar to ginkgo
Ginger	Help decrease nausea associated with chemotherapy
Ginkgo biloba	Increase antiplatelet effect of aspirin
Ginseng (APF®)	Regulate adaptogenic responses to stress, CTx, and RTx Potentiate corticosteroids Increase insulin utilization affecting insulin dosage
Goldenseal	Increase or decrease cardiac effect with cardiac glycosides Increase or decrease blood pressure effects of antihypertensive agents
Hawthorn	Behave similar to goldenseal for cardiac glycosides
Kava Kava	Potentiate substances acting on CNS
Licorice	Increase potassium loss with steroids and diuretics Increase sensitivity and potentiate toxicity with cardiac glycosides Reduce ulcer formation from aspirin Potentiate corticosteroids
Ma Huang (ephedra)	Cause excessive nervous stimulation and weight loss with theophylline Cause dangerous hypertension with selegiline Increase clearance of dexamethasone
Marshmallow	Delay absorption of drugs taken simultaneously
Milk Thistle	Prevent liver damage Promote liver support with hepatotoxic medications like acetaminophen and anticonvulsants Prevent nephrotoxicity from cisplatin
Nettles	Enhance anti-inflammatory effect of drugs
Rehmania	Antagonize suppressant effects of steroids
St. John's wort	Decrease digoxin, theophylline, and cyclosporine levels
Valerian	Potentiate effects of barbiturates
Not Herbs	
CoQ10 (Idebanone)	Protect heart from Adriamycin toxicity with antioxidant effect
IP-6	Regulate cell surface signaling to inhibit cancer

Source: Adapted from Carson, K.M. 2002. *Veterinary Practice News* 16 (6):36, with permission.

Summary: Integrative and Alternative Medicine

Advanced stage cancer and recurrence may preclude curative conventional therapy. Whether you agree or disagree about the efficacy of a particular alternative therapy chosen by clients to help their pet fight cancer, we must respect their quest. We must avoid invalidating the clients' sincere efforts to help their geriatric oncology pet feel better. Believing in the alternative treatment is part of its prescription for success. It is not fair or courteous to crush a person's hope, but we must help clients realize what to expect from the patient's particular tumor type and stage of disease. Therefore, it is best to incorporate clients' efforts into your treatment plan when possible and encourage them to proceed with the benefit of your medical guidance. Many of our deeply bonded clients would do anything to save their pet. If the pet shows a response, the client may feel less inclined to follow your advice in the future. Be sure to have a working knowledge of the basic products that are used in herbal medication and their potential adverse effects. In this way, you can integrate the complementary care into your treatment plan and oversee the patient's medical treatments to ensure that the patient avoids adverse herbal-drug interactions.

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Chapter 7

Pain Control for the Geriatric Cancer Patient

The question is not, can they reason, nor can they talk, but can they suffer?

Jeremy Bentham

Your geriatric cancer patients experience pain on a regular basis. In the geriatric patient, cancer pain is often compounded on top of pre-existing concurrent chronic pain.

In 1972, in order to better help my own veterinary cancer patients, I visited human cancer patients and asked them to describe the sensations they were feeling. They discussed their pain and I then extrapolated this information to apply to my cancer patients. At that time there was no information about cancer pain and pain management for pets. Ignorance about animal consciousness blocked intuitive realizations about the ability of animals to perceive and experience physical pain and emotional maltreatment (Dawkins 2005). Fears of creating addiction blanketed the professions against ministering to painful people and animals (Rollin 2005). Ideologically pure science did not accept that animals had consciousness and so it was acceptable to ignore a pet owner's plea to alleviate his or her pet's pain. Attending doctors simply passed over claims about pain with a counterclaim (Dawkins 2005).

That old thinking has changed radically. But there is still a paucity of papers about cancer pain in geriatric dogs and cats. Therefore, this chapter is written mostly from personal experience, paralleling the experience of esteemed colleagues and honoring the memory of thousands of my cancer patients.

It is up to you, the contemporary veterinarian and healer, to be attentive when clients feel or assume their geriatric companion animal is in pain. We can't fully understand the dimensions of pain experienced by another person or being unless we have the misfortune of experiencing that same pain ourselves. Veterinarians need to trust and believe their clients' hunches about pain in their geriatric pets. Clients often sense their old pet's distress or notice behavior changes and need us to minister to the reality of the pain.

When a geriatric cancer patient does not display overtly painful behavior in the exam room, don't conclude that the pet is not in pain. Cancer pain may be more obvious in the home setting when the pet is quiet and not on guard. Cancer pain attacks people randomly and especially at night. Many pet caregivers experience their pet's whimpers and agitation from cancer pain during the night. A caregiver knows their pet intimately better than the veterinarian does and their observations should not be invalidated.

The most painful cancers involve expanding lesions of the head and neck, bone, liver, GI, CNS, and urogenital tract. Invasive sarcomas, ulcerated skin tumors, inflammatory carcinoma, and any

advanced stage visceral cancer, such as malignant histiocytosis, are also very painful (De Lorimier and Fan 2005). Anticipate, therefore, that almost all cancer patients have pain. Be proactive to alleviate it. Your job is not merely to treat the cancer but also to treat the pain.

Geriatric cancer patients often present in a double calamity with the unrelenting stress of pre-existing chronic pain. Age-related chronic pain causes stress and adversely affects the immune system, emotions, and overall health status of the patient.

Treating Pain Is Good Medicine

Inherent survival instincts dictate animal behavior to mask pain and keep moving with the pack. This survival instinct remains in domestic animals and is present even in our domesticated household pets. The stoic nature of animals persists well into their geriatric years. Dogs with chronic steady pain will still follow their family members from room to room. Dogs still want to go out for their walks and some will even run with their master or mistress despite chronic debilitating pain. They may be diagnosed with severe osteoarthritis or osteosarcoma or an abdominal mass within days of a sporting activity.

Geriatric dogs may simply slow down or not be able to go the normal walking distance, due to pain, without exhibiting overt signs of pain. Dogs and cats with primary or secondary orbital and brain tumors most likely experience moderate to severe headache pain but they can't communicate this to us. It is often a shock for families to learn that their pet endured the pain and discomfort of bone cancer or a huge abdominal mass or a chest mass while keeping up nearly normal appearances.

Dogs, especially the working breeds, often have their caretakers completely fooled about their pain to the point where they may think that nothing is wrong. One minute we must trust the caretaker's intuition; he or she knows better than we do about whether the pet has pain. Yet, it is here that we are faced with the art of medicine in that many times the caregiver is clueless about the pet's pain. This is not contradictory. It is simply that both situations are true. It may be due to breed and species variation, communication level, and intimacy of the bond shared between the pet (sending) and caregiver (receiving) pain signals.

I have consulted with many pet owners who sincerely felt that their osteosarcoma dog was not in pain despite the fact that their dog would not put weight on the cancerous leg. When we point out to them that not bearing weight on a leg is a screaming pain signal, they began to understand that they were not receiving the only communication that their pet could give them about bone cancer pain.

Most pet owners do not recognize the pain, discomfort, and disability of respiratory compromise. Many cats with anterior mediastinal lymphoma and dogs with pulmonary effusions must go into respiratory distress and crisis before their condition is realized. When I interviewed people with cancer, they listed respiratory distress at the top of their most stressful and painful experiences.

Geriatric dogs and cats are often presented with cancer pain, yet pain medication ranks low (if at all) on the attending doctor's priority list during the automatic workup for diagnosis. Develop a knee-jerk response to provide pain relief medication from the very start for conditions that you can reasonably assume are painful. It is appropriate to give pain medication to a patient in pain even before subjecting the patient to the rigors of a workup. I call this attentive, responsive, caring medicine.

Treating cancer pain is often the only option that we can offer for compromised geriatric patients, especially those with advanced stages of cancer. Do not miss the opportunity to treat pain. Clients have come to me for a second opinion after their veterinarian explicitly told them that their geriatric pet was in pain and should be euthanatized. In one case in particular, this patient somehow left the

doctor's office with absolutely no pain control medication. Pain was the prevailing diagnosis providing the rationale for the pet's death, and yet the doctor offered no options that would allay the pet's pain. The clients felt that their veterinarian had no concern or compassion for their pet and did not understand or respect the special relationship and The Bond that they shared with their pet. This cry for help has spanned my entire career.

Drs. James Gaynor, Peter Hellyer, Robin Downing, and others helped to organize the International Veterinary Academy for Pain Management. They teach that pain management is good medicine (Hellyer and Gaynor 1998). When you recognize, acknowledge, and treat pain aggressively in your geriatric patients, you will create a higher quality of life for those patients and you will also create very grateful and loyal clients. Dr. Gaynor says, "Recognizing the close bond between pets and owners is crucial to understanding the importance of pain management. People suffer and become depressed when their pets suffer. Alleviating their pet's pain makes the owner feel better, too" (Gaynor 2004).

The veterinarian has two simple but obligatory tasks to perform regarding pain in a geriatric patient: The first is to recognize pain and eliminate it, and the second is to anticipate when pain will occur and prevent it. Ask owners if they sense that their pet is in pain. Achieving proper pain control may initially require a combination of drugs. In the comprehensive treatment of geriatric cancer patients, the attending doctor addresses pain directly with a well-thought-out treatment plan that has been explained to the medical staff as well as the caregiver.

We can refer to well-thought-out management plans in specialized texts and articles for specific procedures and conditions (Tranquilli, Grimm, and Lamont 2004; Greene 2002). The pain management ladder (Figure 7.1) serves as an excellent guide to assist decision making. A strategic plan against unnecessary pain in your clinic should include recognizing and treating acute pain, chronic pain, and cancer pain while treating induced iatrogenic pain on a pre-emptive basis.

Pre-emptive pain control is the use of anti-pain drugs before a painful event, such as a biopsy or surgery or radiation therapy, with medications that allow the patient to avoid pain all together. If the patient is to receive chemotherapy, surgery, or radiation therapy, the attending surgeon works to control anticipated pain that results directly from the procedure or its side effects.

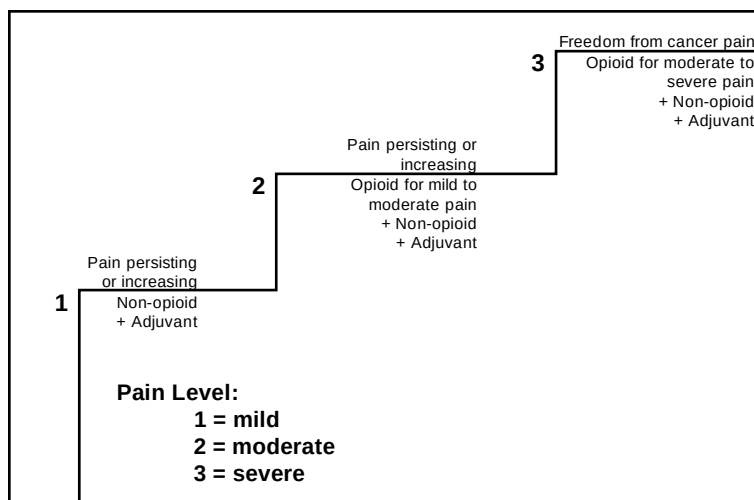


Figure 7.1. World Health Organization Analgesia Ladder, with permission from WHO.

Topical anesthetics are used for all catheter placements. A “cancer care package,” including antiemetics and colitis therapy, can be provided for all chemotherapy cases. Always provide pre-emptive and post-operative pain control for surgery cases.

For the patient receiving radiation therapy, provide topical anesthetics and soothing creams. Instruct the client to apply the preparations on the radiation therapy field before the burn and desquamation lesion become visible. It is very important to provide pain control for the pruritis, pain, discomfort, and anxiety caused by radiation therapy burns. I have consulted many clients who abandoned therapy for their pets due to inadequate pain control for chemotherapy reactions, extravasations, biopsy procedures, surgery, or radiation therapy. In short, if any one of these painful issues is not recognized and treated pre-emptively or directly after onset, the client may discontinue therapy in order to rescue the pet from suffering and, as a result, the patient’s cancer may recur.

Pain Pathways

Be able to recognize all forms of pain and understand its mechanisms. This is important for the care and management of the geriatric oncology patient. The terms used to describe pain classify pain by its duration, intensity, and origin. Pain can be intermittent, chronic, or acute. It can be mild, moderate, or severe. It can originate from somatic, visceral, or nerve tissues and it can be generated from both central and peripheral sensitization. Because so many geriatric cancer patients have concurrent chronic pain from osteoarthritis and dental disease, they probably experience and endure all aspects of pain simultaneously while we are trying to guess about it. Feline pain is less recognized than canine pain due to the inherent silent and solitary nature of the feline personality.

The anatomic and physiologic functions that relay pain to the brain begin with a mechanical, thermal, or chemical stimulus. Tiny afferent nerve endings in the skin, muscles, joints, periosteum, viscera, and subcutaneous tissues transmit pain signals to myelinated A delta nerve fibers and unmyelinated C nerve fibers. These nerve fibers pass through the dorsal root ganglia and enter the dorsal horn of the spinal cord into the gray matter, where they synapse with second order neurons and excitatory and inhibitory interneurons. The signal is transmitted to the brain along the spinothalamic tracts.

The tiny nerve endings that transmit and conduct pain are called “nociceptors.” “Nociception” is the term used to describe how the body is alerted to and perceives pain. Myelinated A beta fibers transmit sensations such as touch, pressure, movement, vibration, and proprioception. In addition, a non-painful stimulus, such as touch, that is transmitted by the A beta fibers can become altered or sensitized in the dorsal horn neurons and thus be perceived by the patient as pain. This painful condition is allodynia and it is very resistant to pain control medications. A dog may yelp and a cat may hiss in pain when touched or picked up. Other factors may influence pain perception, causing increased sensitivity to touch (hyperaesthesia) or an exaggerated response (hyperalgesia) to a light pinch (Lascelles 2003).

Pain often has deeper roots in our senior and geriatric cancer patients because of the phenomenon of sensitization. This is the prolongation and exaggeration of pain. Sensitization occurs most often in untreated or undertreated painful patients. This hypersensitivity occurs peripherally along the spinal cord, and centrally in the brain. Modulating cytokines such as the prostaglandins, histamine, serotonin, tumor necrosis factor (TNF), and bradykinin become unregulated as part of the inflammatory process and may contribute to the phenomenon of peripheral sensitization.

Spinal cord sensitization results when N-methyl-D-aspartate (NMDA) receptors on dorsal horn neurons are activated. NMDA receptors are located on the C fibers and, when stimulated, cause an additive spinal pain called “wind up.” Sensitization also occurs in the brain by agents such as substance

P and glutamate. Some dogs occasionally exhibit phantom pain after amputation of a leg. Because of these phenomena, the veterinarian must treat pain aggressively from the start with a combination of analgesics, tapering the dose later (De Lorimier and Fan 2005).

In a 1999 paper in *JAVMA*, Dr. Frank McMillan pointed out that opioid peptides activate receptors on lymphocytes and macrophages. Opioid receptors are also found in the GI tract, all through the body, and on certain cancer cells. The CNS has receptors for all sorts of immunopeptides and cytokines produced by lymphocytes and macrophages. This bi-directional communication between the immune system and the nervous system serves as a functional link among the body's cellular defense and repair mechanisms, endocrine glands, brain, behavior, mood, and emotions.

Pain causes anxiety, fear, and helplessness in animals. Stress and negative emotional states lower the body's immune resistance to cancer and enhance tumor cell growth and metastases. From the information available about pain, we can conclude that pain adversely affects the animal's quality of life, overall health, and survival. In short, pain is carcinogenic in our geriatric veterinary patients.

Cancer-Induced Pain

Cancer causes pain directly and indirectly, acutely and chronically, in many ways and at any location in the body. Tumors cause pain directly as they expand due to pressure, tissue destruction, invasion of surrounding structures, and obstructing the normal flow of stool, urine, and bile. Cancer causes pain indirectly via inducing stress and inflammation (Figure 7.2). This type of pain is most dramatic with inflammatory mammary adenocarcinoma (Figure 7.2) and mast cell tumors (Figure 7.3). Paraneoplastic syndromes cause pain indirectly by manifesting abnormal signs unrelated to the primary tumor, as with hypertrophic osteopathy, hypercalcemia, and peripheral neuropathies. Secondary metastatic nodules and lytic lesions may cause pain by invasion of bone, brain, lung, viscera, serosal capsules, digits, orbits, and so forth.



Figure 7.2. Inflammatory adenocarcinoma.



Figure 7.3. Interdigital dermoid cyst.

Bone Pain

Bone tumors create primary and secondary lytic and proliferative lesions that can be very painful. Osteosarcoma (OSA) generally creates solitary lytic and blastic lesions that erode, expand, and stretch the periosteum of the appendicular skeleton. Lesions appear in the ribs, skull, and axial skeleton less commonly. OSA patients most likely experience chronic throbbing bone pain with episodes of acute aching that worsens on weight bearing and movement. Animals exhibit their appendicular bone pain by limping. However, because the forbearance of dogs is to remain cheerful, eat, and wag their tails despite pain, many pet owners don't understand the magnitude of their dog's malignant bone pain. Some stoic dogs are diagnosed with OSA only after a pathologic fracture. Malignant melanoma and squamous cell carcinoma that arises from the digits causes erosion of the digits and mimics painful osteomyelitis. Animal suffering has been and is still being underestimated because animals don't communicate their pain in the way that humans would expect them to.

Multiple myeloma causes multifocal painful, lytic lesions in the spine and long bones. Lesions may also cause painful compression of the spinal cord resulting in paresis or paralysis. Synovial cell carcinoma and other tumors that involve joints cause pain by stretching the joint capsule, invasion of bone, disrupting ligaments and adjacent structures. Carcinomas and sarcomas that metastasize to bone, as a secondary target, cause pain most commonly in the lumbar spine, long bones, and digits. Intravenous bisphosphonates may help alleviate lytic malignant bone pain in geriatric dogs and cats (De Lorimier and Fan 2005).

Head and Neck Pain

Cancer mimics oral osteomyelitis when malignant melanoma and squamous cell carcinoma (SCC) efface the bone of the dental arcades. Oral cancer causes severe mandibular/maxillary pain as the tumor expands and as teeth become loosened (Figure 7.4). The patient may have halitosis, salivation,



Figure 7.4. Fleshy oral tumors are often traumatized by teeth and infected with gingivitis organisms as they enlarge. The lesion originally looks like infected teeth. It forms an ulcer in the location where teeth were extracted previously (a). Then over 60–90 days, it may develop into an invasive mass involving the maxilla and nasal cavity, such as the fleshy lesion shown here (b).

and dysphagia. The condition may go unnoticed or be tolerated by the family during the early stages. Fleshy oral tumors are often traumatized by teeth and infected with gingivitis organisms as they enlarge (Figure 7.4b).

Nasal passage tumors cause discomfort due to nasal discharge, infection, and obstructive stridor (Figure 7.5). They cause pain due to turbinate and sinus destruction and facial deformity (Figure 7.6). Neoplastic tissue from primary nasal cancer may invade the orbit and brain. This causes exophthalmia, retrobulbar swelling, pain upon opening the mouth, localized meningitis and severe headaches, CNS signs, and seizures. Chondroma Rhodens originating at the ramus of the mandible, orbital tumors, middle ear tumors, and oral tumors that involve the temporomandibular joint may cause pain



Figure 7.5. Fifi Vines, a 12-year-old, 20-pound cat, has nasal respiratory adenocarcinoma. Infected nasal tumors cause discomfort due to nasal discharge, and obstructive stridor and pain due to turbinate destruction and facial deformity.



Figure 7.6. Frontal sinus tumors cause pain due to accumulation of mucus, bone destruction, and sinus headache.



Figure 7.7. Cabo Palmer, an 8-year-old Rottweiler with osteosarcoma, had pain when opening his mouth.

when opening the mouth (Figure 7.7). Tonsillar SCC, pharyngeal, laryngeal, and thyroid tumors cause respiratory discomfort and pain as they expand, causing esophageal and airway obstruction.

Abdominal Pain

Abdominal malignancies cause visceral pain directly due to tissue destruction, invasion, expansion of organ capsules, and distention of the peritoneum. Cancer causes abdominal pain indirectly by obstructing flow or pushing other organs aside, causing pain and discomfort.

Carcinomatosis is the condition of multiple metastases of a carcinoma or sarcoma throughout the entire abdominal or pleural cavity. Carcinomatosis lesions injure the serosal lining, causing abdominal effusions and distension. These patients are in discomfort and have moderate to severe visceral pain (Figure 7.8).

Abdominal neoplasia may invade and obstruct organs, vasculature, and lumens such as the intestines, the bile duct, ureters, or urethra. Abdominal cancer pain results from disrupted digestion, elimination, and urine outflow. The patient experiences visceral discomfort, nausea, vomiting, constipation or diarrhea, cramping, ataxia, and lethargy and may cry or grunt when lifted, when lying down, or when palpated. All of these visceral feelings need to be considered painful despite the stoic appearance of the geriatric pet.

CNS, Spinal Cord, and Nerve Pain

We need to presume that most of our brain tumor patients have headache pain prior to and in addition to exhibiting neurologic signs, behavior changes, ataxia, and seizures (Figure 7.9). We as caregivers can only guess at the magnitude of our patient's headache pain. Nerve sheath, spinal cord, and brachial plexus tumors are often very painful due to their tissue of origin causing neurogenic and neuropathic pain. Any tumor that compresses the spinal cord, such as multiple myeloma, lymphoma, and malignant melanoma, may induce severe agonizing pain.

Inflammation and Pain

Cancer pain is aggravated by inflammation and/or infection at the tumor site. Old animals often have chronic inflammation with dental disease and arthritis so their pain is compounded. We see this compounding effect commonly in oral, nasal, ear, canal, nail bed tumors, prostate carcinoma, transitional cell carcinoma, and most dramatically in inflammatory mammary adenocarcinoma (Figure 7.2). Malignant pain from inflammation and pruritis arises with ulcerated dermal tumors, especially degranulated mast cell tumors, squamous cell carcinomas, transmissible venereal tumors, inflammatory



Figure 7.8. Mitzie Karsch, a 13-year-old Beagle, with abdominal distension from end stage hepatocellular carcinoma.



Figure 7.9. Bear Clinton, a 12-year-old Labrador Retriever, exhibiting head tilt and facial paralysis due to choroid plexus carcinoma of the brain stem. He responded to steroids and supportive Pawspice care program with Roger for 1 year.

carcinomas, sweat gland and apocrine gland carcinomas, cutaneous hemangiosarcomas, epitheliotrophic lymphomas, cutaneous histiocytosis, and some soft tissue sarcomas.

Nervousness Plus Anxiety Equals Emotional Pain

Many geriatric cancer patients exhibit nervousness and anxiety at night due to their cancer. Others are very anxious during the car ride to each visit. Some cats are miserable during the entire visit and may defecate or vomit in their containers. These behaviors are indicators of emotional pain. A pet's anxious behavior may lead clients to stop visiting your hospital for treatments. I suggest prescription sedative medications be given to relax these nervous and upset patients. The client can administer the medication at home, an hour before the hospital visit. Oral medications such as diphenhydramine (Benadryl®), butorphanol, and/or diazepam are effective. The owner can also give the pet Rescue Remedy® to see if it helps calm the patient. For patients that put up a fight against being given oral medications, we suggest that the client give the pet an injectable relaxing agent instead. For willing clients, we provide instruction until they are comfortable with the procedure.

The client and pet may become demoralized if they have to constantly struggle with oral chemotherapy medications. Hard-to-medicate patients and fractious cats, or any cat with an oral tumor, feel less stressed and experience less pain when they are given injectable medications at home (antibiotics, steroids, analgesics, etc.).

We send injections home in prepared syringes at the proper dose for the client to administer as needed. Each syringe is capped and gets a fresh needle just before administration to avoid blockage. When a nervous pet must be hospitalized or have a procedure, we comfort the owner with the assurance that we will use an injection to relax the pet. On occasion, we may give diazepam and/or butorphanol

IV to gain an immediate effect. We may give a follow-up dose in SQ fluids to extend the relaxation effect over a long car ride home.

My last choice for fractious or aggressive geriatric pets is acepromazine. Phenothiazine drugs are alpha-1 antagonists. They block vasoconstriction, cause vasodilation of arterioles, and lower blood pressure. They are not safe to use for aggressive or fractious patients or for patients receiving Adriamycin. However, since acepromazine has a prolonged tranquilizing effect, it may be the best choice for stressed, hypertensive, nervous patients that need to stay in the hospital all day. We occasionally dispense it, when necessary, for tranquilization as long as it is safe for that particular patient.

Short-Acting Immobilization for Chemotherapy

Our oncology staff strives to relax or immobilize nervous or rebellious cancer patients during the administration of all vasosclerotic chemotherapy agents. This allows us to avoid the issues of the patient struggling, the use of restraints, and the dangers of extravasations. When we administer Adriamycin chemotherapy, there are no exceptions to this rule. For healthy cancer patients under 8 years of age, we coadminister low dose Domacetin®-butorphanol-atropine (DBA) IV for relaxation. This combination is smooth, safe, and easily reversed with Antisedan® (Table 5.1).

Occasionally, a patient has dysphoria (restlessness or malaise) or residual sedation effects following DBA. We suspect the dysphoria is due to butorphanol, so it is not used for these patients in subsequent visits.

For geriatric patients, and for any patient with suspected cardiac or renal problems, avoid the alpha-2 agonists medetomidine (Domitor®) and xylazine, because they cause reduced cardiac output by as much as 30–40%. This may adversely affect renal perfusion in geriatric patients with concurrent heart disease and/or CRF that cannot compensate for decreased cardiac output.

The current preference for sedation of geriatric patients is to use an opioid such as fentanyl at 20 to 40 ug/kg IV, IM, or SQ with a short-acting benzodiazepine, such as midazolam at 0.05 mg/kg or 0.1 mg/lb IV, IM, or SQ for relaxation and analgesia. The effect of fentanyl is gone in 30–45 minutes. Atropine would still be used with this combination as a premedication to prevent bradycardia.

Fractious cats and aggressive miniature toy breed dogs need to be handled very gently. Take every precaution to avoid putting geriatric oncology patients into a state of catecholamine overload. If the IV, SQ, or IM route of sedation is too stressful for them, we gently place the patient into an inhalation chamber for induction with isoflurane or sevoflurane. Then transfer the patient to the procedure table and place a butterfly catheter while keeping the patient under light anesthesia with a face mask (Jaffe et al. 2003).

If the patient requires a procedure or prolonged chemotherapy infusion lasting over 10–15 minutes, or if administering a highly vasosclerotic drug, consider intubation. If the procedure takes only a short time, a mask and pulse oximeter monitoring are standard procedure. Patients return to full consciousness quickly and safely. Return nervous cats to their carrying cases as they start to awaken so that they feel secure. Additionally, consider administering SQ fluids and vitamins as supportive care for geriatric cancer patients during procedures that require sedation, anesthesia, and/or chemotherapy.

Confronting the Brutality of Pain

The veterinary profession has a huge historical deficit for not confronting pain in animals. Our lack of intuitive knowledge about recognizing and treating pain was brutal and almost unforgivable.

Our profession is made up of clinicians who never intended to be brutal. However, most veterinarians who graduated more than 10 years ago confess ignorance of the reality and the amount of pain that their patients experience.

Ten years ago, there was no formal training to recognize pain, evaluate its severity, and control it immediately or pre-emptively. Even today, during consultations, many oncology clients feel that their pet's cancer pain was passed over by their attending doctor. Unfortunately, in many instances, cancer pain is still not properly addressed by clinicians. We must admit to a profession-wide historical and ongoing failure in this area. The universities now actively educate students about the prevention and treatment of pain in all species of veterinary patients.

Contemporary veterinarians must understand the science of pain and make every effort to recognize and confront pain in their geriatric patients. Patients recovering from surgery experience pain. Chronic diseases in geriatric pets, such as arthritis and dental disease, cause pain.

We must anticipate cancer pain that attacks our geriatric oncology patients quietly, right under our noses. For these reasons, we must set up protocols to recognize and offset pain, especially cancer pain and post-operative pain, as a hospital service policy.

Pain Scales and Scoring Charts

Various pain scales are proposed to measure factors such as heart rate, vocalization, restlessness, cramping, crying, hunching, thrashing, and agitation. Temperature, heart rate, respiratory rate, and pupil size are not reliable signs for assessing cancer pain or perioperative pain (Lascelles 2003). We are clearly at a disadvantage in recognizing the pain of oncology patients recovering from surgery.

Introduce your nursing staff to one of the proposed pain scales. Post a pain scale that they can use as a guide for on-the-spot decision making and to alert the doctor in charge for instructions to administer additional pain medication for the patient as needed. Studies have shown that no pain scale is reliable to assess pain accurately because the assessments are subjective. Proper assessment of pain requires focus, intuition, common sense, and interaction with the patient.

The pain scoring chart used at Colorado State University has a 0–24 point span (Table 7.1). Patients that rate over 14 points are considered painful enough to qualify for medication. When there is doubt, patients should always be given the benefit of pain medication. The patient's response to the analgesics can be used as a tool to evaluate the presence or absence of pain. Pre-emptive pain medication should always be given if you expect that a procedure or condition should be causing pain.

Agonist Opioids

The most effective agonist opioids work by blocking the conduction of pain signals. Opioids attach to mu receptors located in the superficial dorsal horn of the spinal tract. Two other types of opioid receptors, delta and kappa, play a lesser role in pain management. Receptors are also found in the spinal cord, brain, and joints. Morphine is a pure mu receptor agonist. Opioids such as morphine, oxymorphone, hydromorphone, fentanyl, buprenorphine (a partial agonist), butorphanol and nalbuphine (agonist-antagonists), and tramadol (an opioid-like drug) are commonly used to alleviate cancer pain for veterinary patients.

Table 7.1. Pain Scoring System at Colorado State University

Observation	Score	Criteria
Comfort	0	Patient asleep or calm
	1	Awake, interested in surroundings
	2	Mild agitation, or depressed and uninterested in surroundings
	3	Moderate agitation, restless and uncomfortable
	4	Extremely agitated, thrashing
Movement	0	Normal amount of movement
	1	Frequent position changes or reluctant to move
	2	Thrashing
Appearance	0	Normal
	1	Mild changes (eyelids partially closed, ears flattened or carried abnormally)
	2	Moderate changes (eyes sunken or glazed, unthrifty appearance)
	3	Severe changes (eyes pale, enlarged pupils, "grimacing" or other abnormal facial expressions, guarding, hunched-up position, legs in abnormal position, grunting before expiration, grinding of teeth)
Behavior (unprovoked)	0	Normal
	1	Minor changes
	2	Moderately abnormal: less mobile and less alert than normal, unaware of surroundings, very restless
	3	Markedly abnormal: very restless, vocalization, self mutilation, grunting, facing back of cage
Interactive Behaviors	0	Normal
	1	Pulls away when surgical site touched, looking at wound, mobile
	2	Vocalizing when wound is touched, somewhat restless, or reluctant to move but will if coaxed
	3	Violent reactions to stimuli, vocalizes without touching the wound, snapping, growling, or hissing when approached; extremely restless or will not move when coaxed
Vocalization	0	Quiet
	1	Crying, responds to calm voice and stroking
	2	Intermittent crying or whimpering, no response to calm voice and stroking
	3	Continuous noise that is unusual for the animal
Heart Rate	0	0%–15% above preop/normal value
	1	16%–29% above preop/normal value
	2	30%–45% above preop/normal value
	3	>45% above preop/normal value
Respiratory Rate	1	16%–29% above preop/normal value
	2	30%–45% above preop/normal value
	3	>45% above preop/normal value

Source: www.colostate.edu/depts/lar/Pain_Assesment.doc.

Side effects encountered are constipation, sedation, dysphoria, and respiratory depression. Opioid effects are difficult to monitor, especially in post-operative patients.

Opioids lower the heart rate for a longer period of time than their analgesic effect. After the opioid is no longer controlling pain, the heart rate may continue to be low. Therefore, a low heart rate should not be interpreted as a sign that the medication is still active. Instruct your staff to monitor

respiration rate rather than heart rate for patients on opioids to determine if the patient is experiencing pain.

Morphine

Morphine syrup at 0.5 mg/kg every 4–6 hours PO may help relieve pain for dogs and cats. Codeine can be used at 0.5–2 mg/kg. It can be prepared as a 5 mg/ml transdermal lecithin gel or cream. Cats may benefit with 0.1 ml of the gel rubbed in the pinna every 6–12 hours as needed.

Fentanyl

The transdermal fentanyl pain patch (Duragesic[®]) is my favorite choice for control of severe pain from surgical procedures and for cancer-bearing geriatric dogs and cats. Limb amputation, mandibulectomy, and nosectomy all cause great initial discomfort in cats and dogs. I prefer not to release these patients until they are at least 48 hours post-op. For nosectomy and most intense surgical oncology cases, we recommend the placement of a follow-up pain patch about 72 hours following the placement of the initial patch.

Fentanyl patches become effective 6–12 hours after application in cats and may last up to 5 days. Use a dose rate of 1–2 ug per pound/hour or 2–5 ug/kg per hour for dogs and cats. For cats under 7 pounds and small dogs, expose half of the membrane of a 25 ug/h patch for the first 3 days and then expose the other half of the membrane for the second 3 days.

Leave the pain patch on until suture removal and then remove the patch painlessly and dispose of it properly. Early removal of the patch may pull skin and hurt, causing localized ulcers at the site. Sedation, bradycardia, nausea, ileus, or respiratory depression are possible adverse effects. These signs are more likely to appear in smaller geriatric patients with a fentanyl pain patch.

Oxymorphone or Hydromorphone

Oxymorphone or hydromorphone injections are helpful at 0.05–0.2 mg/kg to control moderate to severe pain but the effect only lasts for 2–4 hours. Buprenorphine is helpful in that it can be given at 0.02 mg/kg sublingual every 6 hours for cats. Dogs can be given codeine at 1–2 mg/kg PO every 8–24 hours for mild to moderate pain. Codeine has a shorter duration in cats.

Butorphanol

Butorphanol (Torbugesic[®]) is a mixed agonist-antagonist opioid. It helps to settle patients down but does not alleviate moderate to severe pain. This effect lasts only about 40 minutes. It may be adequate following minor procedures and superficial surgery but is unreliable when used in this manner. Butorphanol is definitely not an adequate analgesic at low doses. I find it inadequate and too short acting for moderate and severe pain even when given at frequent and higher doses. Its sedation effect outlasts analgesic effect by 2–4 hours. Therefore, many patients are suffering while still sedated. The patient may vocalize, but all too often the pain is not recognized or acknowledged due to the sedative effect. All too often, vocalizing, painful patients are chalked off as screamers because of dysphoria or an adverse excitement effect from butorphanol.

I no longer use or trust butorphanol as a primary analgesic. In the past, we relied on it for its antiemetic and sedation properties for dogs receiving cisplatin. We may dispense it to reduce stress in nervous patients that have carsickness, utilizing its antiemetic and sedative effects. Butorphanol can be used in dogs at 0.5–2.0 mg/kg every 8 hours and in cats at 0.2–1.0 mg/kg every 6 hours.

Butorphanol is helpful at night for its sedation and antitussive effects. It can be helpful in combination with other more effective analgesics to relax painful or restless geriatric cancer patients

experiencing discomfort associated with metastatic pulmonary disease. Butorphanol helps to diminish cancer-induced coughing and stridor as well as some forms of chemotherapy-induced nausea and vomiting.

Butorphanol should not be used in combination with a fentanyl pain patch because it is a mu receptor antagonist. In injectable form, it can be used as a constant rate infusion during anesthesia and recovery for surgery patients where respiratory depression is a concern. It works synergistically with local analgesics and NSAIDs.

DBA

In our practice, we routinely use butorphanol in combination with domitor and atropine (DBA) as an IV cocktail for minor procedures in healthy patients (Table 6.3). DBA is our chemical restraint of choice for healthy fractious patients needing chemotherapy. Patients are reversed with antisedan and able to leave the office within minutes with minimal residual sedation effects. DBA is not recommended for use in geriatric oncology patients. The action of medetomidine, an alpha-2 agonist, causes reduced cardiac output and potential perfusion problems for older dehydrated patients and for those with renal or cardiac disease.

Tramadol

Tramadol (Ultram[®]) is a very effective central acting opioid that can be used in dogs and cats. It works quickly within 15–20 minutes and has a peak effect at 2–3 hours. It has a wide dose range for efficacy. If the initial dose is not effective, it is worth a try to double and triple the baseline dose of 1–4 mg/kg BID or TID. Oral tramadol at 3 mg/kg was unable to help one of my patients, a geriatric Golden Retriever suffering with anxiety from a skull tumor that applied pressure on the meninges and brain.

Tramadol should not be used in epileptics or in patients that develop cancer-related seizures. It is available in 50 mg scored tablets. Within the dose range, a 10-pound cat would need an eighth of a pill up to a third of a pill. Tramadol can be formulated by a compounding pharmacy as a 5 mg/ml liquid for use in small, frail geriatric cats.

Buprenorphine

Buprenorphine injectable may be given IV, IM, or SQ to dogs at 5–20 ug/kg and at 5–10 ug/kg to cats every 6–8 hours. It may be more effective than other opioids for analgesia in cats (Smith 2005). The oral preparation of buprenorphine is well absorbed and makes a good choice for home administration by caregivers.

NSAIDs for Cancer Pain

There is good reason to use NSAIDs to alleviate cancer pain because of their added anticancer and chemoprevention advantage against many carcinomas, osteosarcoma, and melanoma (Boria et al. 2005). However, we must exercise thoughtful caution using NSAIDs in geriatric cancer patients, especially in the face of polypharmacy. Dogs metabolize NSAIDs readily, while cats metabolize them more slowly. This produces variable toxicity issues for cats. Many geriatric dogs presenting for cancer treatment have a history of long-term NSAID use for chronic osteoarthritis pain. There is no doubt that dogs with arthritis enjoy a better quality of life on NSAIDs.

While the more selective cyclooxygenase enzyme (COX-2) inhibitors such as meloxicam, firocoxib, deracoxib, carprofen, ketoprofen, and etodolac may be less toxic than aspirin, they are similar in their analgesic effects and they all have some COX-1 inhibitory effects. Therefore, any NSAID can cause GI and renal problems and more so in older, more frail geriatric cancer patients.

NSAIDs are contraindicated in patients with congestive heart failure due to their antidiuretic effects. NSAIDs are contraindicated in frail patients with poor hydration status and pets with impaired renal function. NSAIDs are more likely to induce GI, renal toxicity, hepatotoxicity, and drug interactions in compromised geriatric cancer patients.

The newer NSAIDs show less inhibition of COX-1 (the essential or constitutive prostaglandins needed for GI mucosal integrity) but they are *not* more protective of renal function. The kidneys uniquely express both COX-1 and COX-2 constitutively and can be injured by any type of NSAID. If the source of the patient's cancer pain is induced by inflammatory prostaglandins, then selective COX-2 NSAIDs are the best choice because they strike at the inflammatory mediators. If the cancer patient has visceral cancer pain from organomegaly, an opioid is a better choice to alleviate this type of pain. Inherently nephrotoxic NSAIDs are contraindicated for geriatric oncology patients with cancer-related blood dyscrasias, clotting abnormalities, von Willebrand's disease, poor perfusion, and concurrent steroid therapy.

Acetaminophen (Tylenol[®]) provides analgesia at 10–15 mg/kg every 8 hours for 5 days and then 10 mg/kg every 12 hours as needed for long-term therapy (for dogs only, *NEVER* cats). It is fatally toxic in cats at small doses, causing methemoglobinemia. COX-3 enzyme has been identified and found to be a site of action for acetaminophen (Lascelles 2003). Researchers may find that this COX-3 site plays a role in pain pathways or may play a role in explaining the feline's unique toxic reaction to this particular NSAID. Tylenol can be used alone or in combination with codeine. It has no renal toxicity and it is easy on the GI tract and may be a good choice for canine geriatric cancer patients. Some use it in combination with other COX-2 inhibitors but caution is advised.

Baby or buffered aspirin at 10 mg/kg twice daily for dogs and at 48–72 hour intervals for cats is a helpful recommendation for cost-conscious clients. It is important to strongly recommend GI protectants for geriatric oncology patients receiving aspirin and other first generation non-selective NSAIDs to minimize the effect of gastric ulceration. I routinely recommend GI protectants such as famotidine (Pepcid[®]) for patients on chemotherapy, especially if they are also on any type of NSAID or steroid.

Meloxicam

Meloxicam alleviates pain very effectively in cats and dogs. For cats, the dose is variable depending on the experience of the attending clinicians. Cats can be given meloxicam daily for a short period of time not to exceed 4 days post-op at 0.1 mg/kg of lean body weight every 2–3 days. For chronic cancer pain in cats, it must be given only two to three times per week if using this higher dose. Others use meloxicam liquid post-operatively for 2 weeks to control pain in cats on a tapering oral dose. They start with 0.2 mg/kg on day 1, then split it to 0.1 mg/kg for the following 4 days, then split again to 0.05 mg/kg for 10 days. The dose can be split again down to 0.025 mg/kg for a daily maintenance dose for chronic pain if needed.

Meloxicam is a new generation NSAID approved for a one-time injection for pain control in cats. It is ideal in the post-operative setting and as a supplement for the fentanyl pain patch. Be sure to inform cat owners that only certain NSAIDs can be tolerated and must be used with specific instructions for proper dose and frequency. You must take every opportunity to inform and caution all cat owners never to use tylenol (acetaminophen) due to fatal met-hemoglobinemia. Cats do not have the hepatic glucuronidation enzyme systems to metabolize acetaminophen in a timely fashion. Some

NSAIDs such as baby aspirin, piroxicam, carprofen, meloxicam, and firocoxib have been safely used in cats when spaced at alternate-day intervals; however, this usage is off-label.

Piroxicam

Piroxicam (Feldene[®]) is the first choice of many oncologists for general cancer pain control when renal function is normal. This non-selective COX inhibitor serves a dual role as a pain control drug that has anticancer effects. According to previous studies, piroxicam was an effective single agent in transitional cell carcinoma (Knapp et al. 1994). In combination protocols for bladder cancer, piroxicam helped remission rates increase from 20% to 70% when used with cisplatin and from 10% to 40% in combination with carboplatin (Boria et al. 2005). However, toxicity was objectionable and the authors do not recommend this protocol for therapy.

Piroxicam has also been helpful against osteosarcoma, squamous cell carcinoma, and some sarcomas. Thalidomide, the notorious NSAID that caused birth defects in humans, has anti-neoplastic properties but is costly and not widely available.

The role that NSAIDs play against cancer is not completely understood. Inhibition of COX-2 seems to be the foremost anticancer mechanism attributed to NSAIDs. COX-2 is over-expressed in tissues exposed to carcinogens such as cigarette smoke and certain chemicals.

The role that NSAIDs play in reducing COX-2 expression in tumors may justify their use as adjunct therapeutic and chemoprevention agents in the battle against cancer. The manufacturers of NSAIDs are very interested in establishing a database to define the actual benefits of using NSAIDs as chemoprevention agents and as therapeutic agents for the treatment of cancer. The Vioxx[®] fiasco and related lawsuits have discouraged further large-scale studies in the chemoprevention arena.

Veterinarians must stay abreast of new data and stay up to date about chemoprevention for cancer management.

Bisphosphonates for Bone Pain

Intravenous bisphosphonates (pamidronate, Aredia[®], and Zometa[®]) are more potent than oral Fosamax[®]. Pamidronate at 1.4 mg/kg IV may alleviate lytic bone pain in geriatric dogs and cats when administered IV on a monthly basis or as needed (De Lorimier and Fan 2005). It can be administered on the same day as chemotherapy. Clients need to be on high alert to use pre-emptive antiemetics at the first sign of nausea or vomiting. Be sure to check the Internet for current information, dose, and price if you plan to use bisphosphonates. These products are costly. Oral use has not been fully investigated but esophagitis and gastritis may present serious consequences.

Contraindications for NSAIDs with Concurrent Conditions

If you use NSAIDs in geriatric cancer patients with concurrent conditions, you may put them at risk for side effects. NSAIDs are contraindicated with conditions such as CRF, dehydration, hypotension, liver disease, GI ulceration, IBD, coagulopathy, non-compressible bleeding (hemangiosarcoma), asthma, pulmonary disease, and shock. NSAIDs should not be used as preoperative analgesics; however, they can be safely used post-operatively. NSAIDs are contraindicated with other drugs such as steroids, diuretics for congestive heart failure (CHF), ace-inhibitors, and cyclosporine. There may be more drugs to add to this list after this writing, so be sure to check.

Using NSAIDs during surgery is dangerous for geriatric cancer patients due to adverse effects with renal compromise, CRF, CHF, hypovolemia, hypotension, and coagulation problems. Opioids are the best choice for geriatric cancer patients undergoing surgery. Opioids are more versatile, more effective against severe pain, and safer than NSAIDs.

GI Protectants

Famotidine, cimetidine, sucralfate, Prilosec, sucralfate, and other GI protectants are very helpful to minimize the side effects of gastrointestinal ulceration associated with the use of NSAIDs, especially for aspirin and piroxicam. The pain relief of all NSAIDs parallels the baseline relief provided by aspirin. We all have clients who feel that one product works miracles over another. Therefore, it is reasonable to recommend another NSAID to see if the patient has a better response.

Steroids

Never let a patient die or suffer without the silver bullet. Over the years, I have found steroids to be a great friend to cancer patients. Prednisone or dexamethasone alleviates mild to moderate inflammatory pain and can abate severe neuropathic pain. Injectable steroids can help alleviate swelling and inflammation for cats with oral neoplasia and also serve as appetite stimulators. Cancer patients with dysorexia due to oral, esophageal, or visceral neoplasia must experience severe hunger pangs and pain. It is our duty to do all that we can to compassionately alleviate the pain and discomfort of chronic anorexia in our cancer patients.

Oral, intravenous, and intratumoural injections of steroids for residual and inoperable mast cell tumors have been helpful to reduce pain, inflammation, and cytoreduction. Steroids have played an important role in the medical management of pain for most of my brain tumor patients.

Steroids such as megestrol acetate (Depo-Provera®) and Nandrolone® injections may stimulate the appetite and create a sense of well-being. Some use Winstrol-V® for this purpose; however, in my experience, it does not increase appetite. These steroids may reverse catabolism and help many failing, anorectic geriatric cancer patients.

Bear's Case (Steroids Can Help Brain Tumor Patients)

Bear Clinton, a 12-year-old M Labrador Retriever mix, was diagnosed with an inoperable choroid plexus tumor. The MRI indicated that the tumor was very large. It was not amenable to radiation therapy. Bear was circling to the left and ataxic with left-sided facial paralysis. Bear was given a very poor prognosis by our radiologist, who felt that euthanasia would be appropriate at any time.

Roger, the caretaker, entered Bear into our end of life Pawspice program. Bear received palliative medical management with an initial injection of 8 mg of dexamethasone IV followed by oral prednisone at 30 mg/m² and oral lomustine at 80 mg/m² in divided doses over 4 days. To our amazement, Roger returned with a normal-acting dog on the next recheck. Bear responded to injections of dexamethasone on an as needed basis. Injections varied from once a month for the first 6–8 months and increased in frequency as we approached his 1-year anniversary with brain cancer (Figure 7.9).

Multimodal Therapy for Cancer Pain

It often takes more than one class of pain medication to control cancer pain. Never hesitate to enlist adjunctive help and acupuncture to fully control your geriatric cancer patient's pain. When adequate analgesia is not given at the start of a painful event, the omission of control may allow the pain to

progress and become chronic pain. Since animals are stoic about their initial pain, we can presume that a great deal of chronic pain in geriatric cancer patients goes untreated.

Using amitriptyline (or other tricyclic antidepressants), gabapentin (or other anticonvulsants), bisphosphonates, and/or amantadine (or other NMDA receptor antagonists) may enhance your efforts to alleviate cancer pain. Pain has the physiological effect of creating intense anxiety and stress. Using anxiolytics can be very helpful to ease the tension for overtly anxious patients.

Alternative Therapy

Using acupuncture to help alleviate pain can be very rewarding. Acupuncture and complementary medicine may help alleviate tension and create a sense of well-being that offsets pain. Acupuncture sessions can also be very nurturing for the cancer patient and may comfort and empower the caregiver as well.

Other modalities of alternative and supportive care, such as chiropractic, cold packs, hot packs, electrical stimulation, low-level laser therapy (Shearer 2004), massage therapy, prolotherapy, and magnetic therapy, may complement pain control efforts and further alleviate cancer pain (Robinson 2005). If and when clients seek complementary care to alleviate their pet's pain, encourage the caregiver to give it a try. Anecdotally, the geriatric oncology patient may benefit.

At our practice, we have witnessed a relaxation response in many anxious patients and equally anxious clients who were simultaneously given the solution called Rescue Remedy®.

Combinations

The combination of NSAIDs and opioids is very helpful for controlling moderate to severe pain. The fentanyl pain patch combines well with NSAIDs such as meloxicam for a post-operative nosectomy in a cat. Deracoxib or carprofen may be prescribed for a dog following amputation to supplement a fentanyl pain patch. The pain patch also combines well with oxymorphone and hydromorphone.

Naloxone reverses the pain patch's negative opioid side effects, such as respiratory depression, bradycardia, dysphoria, noise sensitivity, hypothermia, vomiting, and diarrhea. The analgesic effect of the pain patch remains intact while the opioid reaction is reversed.

Various NSAIDs complement the fentanyl patch and are routinely given to older dogs for severe post-operative pain and for chronic cancer pain control. Tramadol may also be coadministered with NSAIDs for improved control of cancer pain. The fentanyl pain patch or oral tramadol can be combined with steroids to achieve excellent pain control for moderate to severe pain in both cats and dogs. Amitriptyline or clomipramine may be helpful in reducing anxiety, stress, and pain when used in combination with NSAIDs, opioids, or steroids. Tricyclic antidepressants would be a good option for a patient like Bear Clinton, the dog just discussed. Bear was treated successfully with steroids for a large choroid plexus tumor. The steroids alleviated Bear's circling, head tilt, and facial paralysis.

Cats and NSAIDs

Meloxicam is one of the few approved NSAIDs for cats, although carprofen, ketoprofen, and aspirin are commonly used. Meloxicam is ideal in combination with the fentanyl patch to alleviate chronic

oral cancer pain for cats. It is approved for one-time injection in cats. Administer meloxicam as the patient is recovering from anesthesia as a supplement to a freshly placed pain patch. It provides immediate pain relief for cancer patients undergoing painful surgical procedures such as mandibulectomy or thoracotomy. The effects of a meloxicam injection wear off over 24 hours while the fentanyl patch takes effect. This combination provides even, sustained pain control for feline patients that have normal hydration and renal function. Precautions should be taken as with all NSAIDs.

Meloxicam liquid can be used post-operatively for 2 weeks to control pain in cats on a tapering oral dose, starting with 0.2 mg/kg on day 1. Half of this dose (0.1 mg/kg) is given on each of the following 4 days and then it is halved again to 0.05 mg/kg for 10 days. For further use, the dose is halved again to 0.025 mg/kg once daily.

The long-term use of NSAIDs in cats has not been specifically studied for hazards and drug interactions. However, experience with piroxicam in feline oral SCC cases has given myself and others confidence. The extra-label and judicious usage of NSAIDs can benefit the quality of life and the survival of geriatric feline oncology patients if the patient's hydration and renal function are maintained within normal limits.

Surgery and Painful Procedures

Anticipate that any surgical procedure, including any type of biopsy, will create pain for the patient. If the cancer patient presents in pain, take measures to provide pain medication immediately. Alertness and attention to every level of pain is always greatly appreciated by the pet's family. Provide pain medication as a premedication treatment prior to placement of indwelling catheters and before beginning preparation for diagnostic and surgical procedures as described earlier.

The alpha-2 agonist medetomidine (Domitor[®]) can be given IM to provide mild relaxation and sedation during the preparation process for healthy patients. Pretreatment or mixing it with atropine helps prevent bradycardia and emesis but it does not increase cardiac output, which is the reason to avoid using it in geriatric patients. Medetomidine has an opioid-sparing effect.

All alpha-2 agonists, especially xylazine, cause emesis in cats and bradycardia and hypertension in both dogs and cats and are contraindicated for geriatric patients with myocardial or renal disease. We use the low dose DBA combination IV in healthy patients for its immediate sedation, analgesia, and immobilization effect. This combination is excellent for minor procedures in healthy cancer patients such as Tru-cut, punch and bone marrow biopsy, or wound debridement and cryotherapy. We use high dose DBA if more analgesia is needed. It is best to avoid alpha-2 agonists for older geriatric patients and for any age patient with renal or cardiac problems.

My favorite systemic pre-emptive pain control for surgical oncology procedures in geriatric patients is the Duragesic pain patch. It releases fentanyl from a transdermal membrane into the circulatory system over a 3-day period in dogs and a 3–5 day period in cats. It is safe and effective for moderate to severe levels of pain. The big problem with pain patches is the variation of time to effect from animal to animal and dog vs. cat. It may take up to 24 hours for full analgesic effect in some dogs, whereas 70% of cats experience full effect within 6–8 hours.

We don't want 30% of our surgery patients to suffer perioperatively because their blood levels of analgesic are too low. That is why, when possible, we place the pain patch the night before surgery for dogs and the morning of the surgery for cats. Because of the variable delay in onset of analgesia, it is important to administer fentanyl by SQ injection at 20–40 ug/kg hourly before and after surgery, until the fentanyl pain patch has reached its full effect.

Midazolam at 0.1 mg/lb SQ, IM, or IV causes muscle relaxation and prolongs the relaxation effect of fentanyl injection. Benzodiazepine tranquilizers are the best choice to coadminister with fentanyl and other opioids, to relax geriatric or debilitated patients. This combination is safe for pre-sedation and pre-anesthetic protocols in critical patients. Avoid using acepromazine in geriatric oncology patients.

The best choice for induction and anesthesia of geriatric cancer patients at this writing would be IV propofol, intubation, and sevoflurane or isoflurane inhalant anesthesia. The induction, anesthesia, post-operative pain control, and aftercare protocols for emergency, routine, and aggressive surgical oncology procedures described in chapters 18 through 20 of W.B. Morrison's book *Cancer in Cats and Dogs* are excellent references (2002).

An injectable NSAID such as meloxicam or carprofen helps alleviate pain in the immediate post-operative period. A continuous rate infusion of microdose ketamine, which is an antagonist for NMDA receptors, can be very helpful during surgery and in the immediate post-operative period to complement the fentanyl patch as well as other opioids.

A contemporary multimodality approach for pre-emptive pain management has always been direly needed for aggressive surgical oncology procedures. Now we can successfully perform amputation, mandibulectomy, maxillectomy, thoracotomy, and so forth without hurting our patients. There is no longer any excuse for hurting our patients with definitive surgery that many tumors require for curative intent.

Using Local Analgesics

We use topical lidocaine gel, refrigerant anesthetic spray, or local infusions of lidocaine directly on areas that we intend for venipuncture and for painful procedures. We use topical lidocaine gel at IV and FNA sites. We administer injectable lidocaine at biopsy sites and around superficial cutaneous tumors in addition to lidocaine gel before applying cryotherapy. The typical cryotherapy patient may be a white cat with facial SCC. Two percent lidocaine at 3–5 mg/kg must be used with caution in cats due to its narrow margin of safety. It is safest to draw up the total dose ahead of time for small patients and dilute it if a larger volume is needed for infiltration of the surgical site. We perform cryotherapy most often in Whippets, Italian Greyhounds, and Pit Bull breeds with solar-induced superficial cutaneous hemangiosarcomas and SCC. Occasionally, we treat small superficial mast cell tumors with cryotherapy. Dogs with cutaneous solar-induced SCC and hemangiosarcoma have field cancerization, which means that they return periodically with new lesions needing cryotherapy.

We administer IV or IM sedation to relax most of our cryotherapy patients in addition to using topical and local anesthesia. Geriatric cancer patients need special attention paid to assuage their pain and anxiety, especially for repetitious procedures that have caused them pain in the past. We must anticipate their emotional state and pain levels and treat them resourcefully before they become agitated or fearful.

Epidurals and Local Pain Control

Local, regional, and epidural anesthesia can offset suffering from severely painful procedures that create tissue damage. This technique is underutilized in our profession. Researchers at Johns Hopkins found that opioid receptors are upregulated in inflamed tissues. Receptors will respond for up to 48 hours if the tissue is given intraoperative morphine at low doses. Butorphanol acts synergistically

with local anesthetics. Use a nerve block with bupivacaine at 1.5–2 mg/kg 10–15 minutes prior to digit and limb amputations. Epidural blocks, local nerve blocks, and regional blocks eliminate pain. Bupivacaine, or any other long-acting local anesthetic, infused along nerves and onto surgically traumatized tissue, blocks post-surgical suffering for 6–8 hours.

Perioperative Pain Control

From the time of hospitalization for surgery to the time of discharge, we owe the geriatric oncology patient as much comfort and protection from pain and emotional distress as possible. Aside from the humane benefits of perioperative analgesia, geriatric oncology patients undergoing surgical procedures have reduced requirements for anesthesia, smoother recovery, and shorter hospitalization periods as a plus. Improved anesthetics are safer than ever for geriatric patients and very helpful *BUT* their downside is rapid return to awareness and perception of pain (McMillan 2005). Inhalation anesthetics that are eliminated rapidly leave the patient conscious and starkly devoid of analgesia. The patient recovers consciousness, is alert within moments, and is fully able to feel pain resulting from the surgical procedure. Therefore, pain control is needed during recovery and throughout the first night post-op, on a set schedule. We must anticipate that all surgical patients will feel pain upon regaining consciousness. If a pain patch is placed just before the surgical procedure and has not yet reached a therapeutic blood level, it is important to provide preoperative and post-operative pain relief with the use of fentanyl or morphine or oxymorphone injections.

The goal is to make sure that the recovering patient is sleeping comfortably and is pain-free until the pain patch is fully effective. The attending doctor should leave written instructions to the nursing staff and prepare them to administer effective pain control medication on a set schedule or by constant-rate infusion. The goal is to allow the patient to sleep comfortably for 12–24 hours after intense surgical oncology procedures such as mastectomy, liver or lung lobectomy, splenectomy, large sarcoma excision, amputation, thoracotomy, rib resection, mandibulectomy, maxillectomy, enucleation, nosectomy, rhinotomy, and so forth.

Good post-op pain control is essential. Monitor your geriatric cancer patients overnight with observant and caring nurses trained to assess pain. Train your staff to use the CSU pain chart as a standard reference (Table 7.1). Train your nursing staff to look for increased panting and heart rate, crying, and restlessness in dogs. Cats exhibit pain with behaviors such as crouching, hiding, hunching, aggression, and holding the head in a down position. Since opioids slow the heart rate, this is not a valid parameter for patients on opioids. A veterinary staff properly trained to look for perioperative pain is invaluable to the clinician toward ensuring that no patient suffers needlessly.

Constant monitoring of the patient is the key to successful post-operative pain management. When the local infusion of bupivacaine wears off, the patient may become very painful. The nursing staff should be told when to expect the bupivacaine to wear off and should be on alert to determine exactly when the patient needs additional pain control.

Discharge all post-op cancer patients with some form of oral pain control medication. Contemporary clients expect to exit the hospital with the acknowledgement that their pet's procedure was painful. Pain relief medications should be dispensed to them so that they can sustain analgesia at home at least for the following several days. I recommend sending a second pain relief drug as a backup for the pet caregiver to use in the event of breakthrough pain. This will limit patient suffering and client anxiety as well as phone calls of concern in the late hours of the night.

It is very important to provide enduring post-operative pain control medications effective enough to truly relieve pain and suffering for an appropriate period of time. All too often, clients have told me that they stayed up all night with a painful pet. Omitting control of some types of pain is inexcusable, such as a pet that is whimpering or crying after an amputation. Do not fail to provide your surgical oncology patients multimodality pain control to avoid the following scenario.

Sam's Case (Don't Fail to Provide Enough Analgesia)

Sam, a M/N 11-year-old Labrador Retriever, developed a large hemangiosarcoma originating in his left quadriceps muscle. His family reported that Sam cried and whimpered for hours after being sent home 1 day following his hind leg amputation. His surgeon was unavailable at night, so they took Sam to an emergency room at 2:00 A.M. for a pain injection. Sam got only 1–2 hours of relief from that injection and started crying again at 4:00 A.M. The clients were frustrated with the attending surgeon and the emergency room doctor because they did not provide more potent and longer-acting pain management. Somehow the amount of pain control dispensed did not acknowledge or address the severity of Sam's pain.

Compounding Pharmacies

Compounding pharmacies prepare palatable formulations that are easy and safe for the pet owner to use at home. Pain control medications are formulated so that a measurable aliquot can be identified and given for small dogs and cats. When engaging a compounding pharmacist, state clearly the desired dose and frequency of medication that the patient is to receive. For instance, the piroxicam dose for both dogs and cats is 0.3 mg/kg. We use a 10 mg capsule every 24–48 hours for a 60-pound dog and 1 mg every 48 hours for a cat. To order compounded piroxicam for a cat, I specify: "Piroxicam, 1 mg PO every 48 hours." This dose would be one-tenth of a 10 mg capsule or tablet. Because cats generally enjoy the taste, liquid meloxicam packaged with a clearly marked dosing syringe is a very convenient NSAID for pet owners to use.

Pain Control for Pawspice Care

Terminal geriatric cancer patients often live stoically with moderate to severe pain, even with hypertrophic osteopathy from pulmonary tumors. We counsel and encourage pet caregivers to enter our palliative end of life hospice care program, or "Pawspice." The Pawspice program places pain control as a top priority. We generally offer the pet owner the option of placing a fentanyl pain patch every 3 days. We shave both back legs of the patient and demonstrate the proper application and wrapping of the pain patches. The pet caregivers are asked to return their pet's used fentanyl patches at recheck for proper disposal. For cats and small dogs weighing less than 20 pounds, we instruct the caregiver to uncover half of the patch to provide adequate pain control for 72 hours, then to uncover the other half, which should provide analgesia.

Nalbuphine

The generic form of nalbuphine is a convenient and inexpensive home care injectable pain medication. We use nalbuphine for cancer patients that fight oral medications, are intolerant of pain patches,

or have resistant pain. It is a great option for dealing with resistant pain and/or for pet owners on a budget. Nalbuphine is a narcotic agonist-antagonist that provides pain relief for moderate to severe pain and calms the patient without a heavy sedative effect. Be sure to specify that you want the generic injectable nalbuphine when you order it to save money. Patients experiencing pain generally require subcutaneous nalbuphine injections every 6–8 hours.

Nalbuphine is a good choice for cats with oral tumor pain, especially lingual squamous cell carcinoma. The dose ranges from 0.2 to 0.5 mg/kg given SQ as needed two or three times daily for dogs and 0.1–0.3 mg/kg three to four times daily for cats. Nalbuphine may be sent home for SQ use without the typical narcotics precautions. Nalbuphine has fewer sedation effects than other similar analgesic compounds.

Alaska's Case (Nalbuphine Helps Caretakers and Pets Say Goodbye)

I used nalbuphine occasionally to help Alaska, my own beloved 12 ½-year-old Great Pyrenees, with arthritis and degenerative myelopathy. Nalbuphine helped Alaska to sleep comfortably, yet she was able to get up and move to another resting spot when she wanted to. After 18 months of slow decline in Pawspice care, we helped Alaska cross the rainbow bridge.

When I knew that Alaska was nearing the end of her journey with us, it was very important to me that her final moments were free of pain or anxiety. I gave Alaska a 10-times dose of nalbuphine IM. She became very relaxed yet could still lift her head and look at us. She remained aware of our love and attention. The nalbuphine made Alaska's final moments painless and peaceful and allowed me to insert a butterfly catheter easily to prepare for our final farewell.

Adverse Drug Reactions and Interactions in Pain Control

The cadre of drugs used for pain control will continue to grow and become an everyday routine consideration for geriatric oncology patients. It is essential for the contemporary clinician to be familiar with the potential for adverse reactions related to analgesics and adjunctive drugs used for comfort care in the geriatric oncology patient. We must distinguish the adverse effects of analgesics or their drug interactions with chemotherapy drugs from symptoms of progressive disease. Another problem with pain control drugs is that most strong analgesics also have sleep-inducing effects with uneven durations of activity. A geriatric oncology patient may be under sedation while being left without adequate analgesia.

Opioid Side Effects

All opioids have the potential to cause constipation, ileus, urinary retention, and sedation. These physiologic effects may be more pronounced with polypharmacy. When giving a tranquilizer to a geriatric cancer patient on opioids, the initial dose should be reduced by 30–50% to avoid sedation. All opioids have a sparing effect for induction and anesthetic agents and caution is required to use these drugs to effect when coadministered with pre-med opioids. Atropine is routinely used in sedation and anesthetic protocols to prevent bradycardia. It also reduces GI motility and can act synergistically with opioids to induce ileus.

Several of my geriatric oncology patients have exhibited adverse signs of opioid excess with fentanyl pain patches at the recommended dose. Using a full 25 ug pain patch for old cats less than

10 pounds is excessive. We expose one-half of the pain patch for all older patients under 12 pounds. The remaining half is exposed after 72 hours. Several of my older cancer patients also experienced bradycardia and dysphoria with pain patches. We instruct clients to remove the patch if the patient exhibits adverse side effects. It may take up to 24 hours for the fentanyl level to drop and the patient to normalize.

Carmen's Case (Fentanyl Patches May Cause Side Effects)

Carmen Ashlock, a 37-pound 11-year-old Springer Spaniel, needed pain control for hypertrophic pulmonary osteopathy (HO). One of her legs was very swollen and painful due to concurrent infection. HO was due to a large pulmonary metastasis from her 5-year battle with mammary adenocarcinoma (Figure 7.10). Carmen initially responded very well to pain alleviation, but on day 2 she became anorectic, then started whimpering the next morning. An emergency clinic diagnosed her with life-threatening ileus and urinary retention. These adverse signs started 50–60 hours after placement of a 50 ug pain patch in a very sick geriatric oncology patient.

Steroids Plus NSAIDs Equals Trouble

Take every precaution to avoid the simultaneous use of steroids with NSAIDs. This combination invites severe, hemorrhagic GI ulceration and potential perforation. Although it would be ideal to be able to use both steroids and NSAIDs for pets with brain tumors, we must not use these two drugs simultaneously. On rare occasions, I may use this combination as a one-time-only initial dose along with injectable and oral famotidine and then discontinue the NSAID.

The advantage of using steroids to reduce brain tumor swelling is clinically more valuable to the patient than the NSAID effects. Steroids may also relieve pain, create a sense of well-being, and increase appetite for cancer patients. For these reasons, I prefer to use steroids rather than NSAIDs



Figure 7.10. Hypertrophic osteopathy due to pulmonary metastasis from a 5-year course with mammary adenocarcinoma. Carmen Ashlock, an 11-year-old Springer Spaniel, needed pain control for her condition, which was complicated with concurrent infection of the left foreleg. There is a fentanyl patch on her left hind leg.

for brain tumor patients. PUPD, restlessness, panting, weight gain, hepatopathy, and arousal caused by steroids may preclude their use in the geriatric oncology patient. NSAIDs inhibit platelet function and gastric acid inhibition, which erodes the prostaglandin-driven protective mucous layer of the stomach. This leads to GI ulceration and hemorrhage, which is poorly tolerated by most geriatric oncology patients with chronic anemia. NSAIDs may also interact with the clearance of chemotherapy drugs, especially hepatotoxic or nephrotoxic drugs such as cisplatin. For unresponsive pain add tramadol at 4–6 mg/kg every 6–12 hours.

Gabapentin (Neurontin[®]) is an anticonvulsant that may alleviate chronic neuropathic pain in combination with NSAIDs or steroids at 10 mg/kg every 6–12 hours. It may also relieve chronic headache pain. Evaluation of this effect would need to be a subjective observation made by the pet's caregiver. The dose may be increased to effect. There are no studies for reference.

Summary

Pain management was not taught in veterinary schools until the 1990s, following the passing of the 1985 federal animal welfare law. This law recognized pain and distress in laboratory animals (Rollin 2005). Dr. Charles Short and Dr. Alan Van Posnak edited *Animal Pain*, one of the first veterinary books to influence how we address animal suffering (1992). The ravages of cancer pain destroy the animal's immediate quality of life. If cancer pain is not properly addressed, the bond that holds our profession together will literally suffer a dead end. Pain has the power to short-circuit the human-animal bond because our historical answer to an animal in pain has been euthanasia. If the painful cancer patient is prematurely extinguished without the benefit of pain control, we have not served our patient's or our client's best interest.

Contemporary pain management in geriatric cancer patients enables cancer patients and their distraught families to have peace of mind. Veterinarians and staff now have the tools to recognize and understand the complexity of chronic pain syndromes and their relation to cancer pain in geriatric patients. We can understand the biology of pain and the pharmacology available to alleviate it. We can adopt management plans for specific procedures and conditions using the pain management ladder (Figure 7.1).

We have the obligation to create a more comfortable quality of life for our geriatric cancer patients while they live with cancer. When cancer pain is unresponsive to our best contemporary efforts, then we can justifiably help our geriatric patients to find peace by way of euthanasia. If our clients feel satisfied with the quality of life that their companion animal experienced through our pain management program during the battle against cancer, then our job is well done.

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Chapter 8

Decision Making with Advanced and Recurrent Cancer in the Geriatric Patient

No one should have to choose (in the either/or model of medical care) between fighting their cancer or receiving palliative or hospice care—care that offers comfort through prevention and relief of physical, psychological, social and spiritual distress. Patients nearing the end of life can, and should, receive both at once (in the new simultaneous care model).

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Epidemiologic trends in our society show that both human and pet populations are aging. This means that veterinarians will encounter more cancer in older pets than ever before and they will be caring for them. Therefore, recurrence and relapse in geriatric oncology patients will become a more common clinical problem. Unfortunately, there is a paucity of literature, training, and experience to assist practitioners in the decision-making process for intervention against advanced and recurrent cancer for geriatric oncology patients.

Attitudes about aging pets are also changing. Caregivers are proud of their older pets and they want them to live as long as possible. People need and seek more services for their geriatric pets as they undergo normative aging. Aging is associated with reduced immune competence, thymic involution, T-cell deficiency, accumulated exposure to carcinogens, inflammation, and genetic damage (decreased DNA repair, defects in tumor suppressor genes, etc.), which are major factors increasing susceptibility to infection and cancer in the elderly (Kennedy 2004).

The contemporary pet owner is willing to deal with the pet's age-related medical conditions, such as arthritis, dental disease, renal disease, heart failure, endocrine disorders, neurologic problems, and so forth. These coexisting problems turn into threatening comorbidities when the geriatric patient is burdened with neoplasia. These comorbidities may worsen and become a more ominous hobble when dealing with advanced stage cancer, recurrence, or relapse in geriatric oncology patients. The geriatric oncology patient's coexisting problems are competing for treatment. The attending doctor must balance the patient's multiple pathologies against the risk-benefit ratio of the pending treatment. If the expected outcome is roughly comparable between two types of treatment, clinical judgment would elect the least stressful treatment for the geriatric oncology patient.

There are no controlled clinical trials addressing advanced stage or recurrent cancer in geriatric pets. Therefore, the attending clinician must glean applicable information from available relevant data, blend this with common sense and patient-specific, client-oriented decision making. If we can improve the outcomes and/or quality of life for older cancer patients challenged with advanced stage cancer or recurrence, we may satisfy our client's wishes for honoring their human-animal bond and gain a richly rewarding experience.

Emotional issues surface when a geriatric cancer patient develops advanced stage cancer, recurrence, or relapse. The dread of recurrence beats upon the emotional heartstrings of the geriatric cancer patient's

family. Issues with frustration, attachment, anticipatory grief, guilt, depression, and resignation as well as hope and determination strum upon the core fibers of the pet owner's character. These concerns and the decision-making process are very difficult to deal with. There is no perfect choice. This chapter offers guidance in decision making and weighing probabilities when the odds are contradictory.

During consultations, as the attending doctor you must admit and remove your own personal age and cancer treatment biases. Many pet owners have told me that they felt that their doctor was insensitive to their hope and grief or was fatalistic, impatient, or rushed. Sometimes there is too much control followed by too few options offered for management of advanced stage cancer or recurrence for the geriatric oncology patient. The client feels let down. He or she feels that the doctor gave up on the old pet just when the pet needed help the most.

The Need for Family Practice Skills

People of all personality types and means bring their personal pets to veterinarians for help. Pet owners openly define their pets, to themselves and others, as members of their family. The pet as part of the family has evolved into a social consensus ethic (Rollin 2005).

Most veterinary students in the United States are currently taught to parallel the pediatrician's model for small animal practice, whereby the pet is considered a member of the family. Graduates leave the university with excellent textbook and disciplinary knowledge. However, there is a big gap between knowing how to act and what to do in situations of complexity and high client need and actually doing it.

People bring their four-legged family members to veterinarians, counting on their professionalism. Because people entrust us with their companion animals, veterinarians have the increased obligation to understand attachment and acquire good communication skills. Contemporary practitioners must keep apace and assume a multidimensional role as family practice veterinarians (Timmons 2005). Use as a checklist the proficiency skills proposed for the formation of the Society for Family Practice Veterinarians (Table 8.1).

Many graduates leave veterinary school with few skills in communication and practical wisdom. If only we could strip down the communication barriers between doctors and pet owners. Often, clients experience profound insensitivity on the telephone or at the front desk, when speaking to hospital personnel. A busy hospital receptionist may place a client phone call on terminal hold. Staff workers often fumble with medical record keeping, bungle record transfers, or overbook appointments. The brisk attitude of a receptionist or an officious office manager can extinguish a client's loyalty to his or her veterinarian's animal hospital. Rushed 10-minute office visits limit oral narratives and leave caregivers deprived of valuable practical wisdom and advice that they so desperately need. Oftentimes, the client feels abandoned with no positive support to deal with the geriatric pet's advanced stage cancer or recurrence problem.

Ethics, Economics, and Empathy Issues

Bernard E. Rollin, PhD, is a University Distinguished Professor and Professor of Philosophy and Animal and Biomedical Sciences at Colorado State University. He is a well-known bioethics speaker who airs many basic ethics issues. In his papers "Oncology and Ethics" (2004c) and "Euthanasia and

Table 8.1. Veterinary Family Practice Skills and Knowledge

Animal abuse	Maintaining a culture of self-renewal (knowledge and skills)
Animal welfare	Managing referrals
Behavior	Media interactions
Clinical genetics	Mentoring
Communication	Nutrition
Community issues	Pain management
Community outreach	Physical therapy
Complementary medicine	Preventative medicine
Conflict management	Principles of education
Disaster medicine	Risk assessment for companion animals
End of life issues	Service and performance animals special needs
Financial issues	Shelter medicine
Information management	Understanding attachment
Jurisprudence	Zoonoses
Leadership and teamwork skills	
Lifespan approach to health care systems	

The Program for Veterinary Family Practice recognizes that the relationship between companion animals and humans has evolved dramatically during the past few years. Pets are likely to be treated like a member of the human family, and that family is demanding more sophisticated medical and surgical care for the pet. The Program for Veterinary Family Practice is a resource for teaching veterinary students, veterinary practitioners, and veterinary staff the knowledge and skills necessary to nurture the bond between pet and owner and to enhance the well-being of both, in the process of providing excellent health care for the non-human family member. This new program is being taught at University of California, Davis, School of Veterinary Medicine under the direction of Dr. Richard Timmins.

Quality of Life” (2006), Rollin exposes and ponders the following insightful questions: “What are the animals’ best interests? Given the nature of animal consciousness and mentation limits, it is above all else not suffering, We need to realistically assess what the animal is experiencing and not prolong life at all costs. The oncologist must be careful not to put the client’s interest in prolonging life above terminating the animal’s suffering. In addition, currently trendy talk in veterinary circles may seduce the veterinarian away from that ideal; to wit, the claim that veterinarians serve the human-animal bond. This, in my view, is wrong and dangerous, for it treats an abstraction as a reified (enforced) entity. Veterinarians serve the animal and must work through the client. They do not serve, in the end, ‘the bond.’ ”

Rollin asks every veterinarian to decide his or her answer to what he calls the “Fundamental Question of Veterinary Ethics”: “To whom does the veterinarian owe primary allegiance; owner or animal?” (2004c). We can layer more issues from the rapidly growing field of geriatric oncology into Rollin’s basic ethical questions about practice, such as: Has the demand for geriatric companion animal care been raised higher than seasoned practitioners are prepared or willing to offer? Can we properly educate caregivers to make informed decisions for treating recurrent cancer in their geriatric pets? Can we trust caregivers to know or want what is best for their aging pet? Should the veterinarian bear the burden of animal advocate? Should the veterinarian become the shoulder and the counselor for distraught pet caregivers who would do anything to save their aging pet from cancer? What can we do for pet owners who are caught in “analysis paralysis” or religious or cultural factors and cannot make a decision? What do we do about deeply bonded clients who want to continue treatment despite the veterinarian’s recommendation to stop?

In 2003, I had the pleasure of presenting case reports in lectures titled “Ethics, Empathy, and Economics” alongside Dr. Rollin at Midwest and AVMA conferences. He believes that veterinarians owe primary allegiance to the animal. We bantered back and forth in our presentations. In contrast to his statements, I expressed my beliefs that veterinarians who are in private companion animal practices all around the world do, in fact, serve the human-animal bond; that veterinarians owe their primary allegiance to the human-animal bond (“The Bond” is often the real reason we entered our profession to begin with), and that The Bond is what confers a tremendous societal and personal value on a particular pet patient.

The Bond does not diminish with a pet’s age or medical history. On the contrary, clients have told me that The Bond with their pet grew stronger as they nurtured the aging pet during an illness and especially during treatment for cancer. Honoring the human-animal bond inherently includes reverence and respect for quality of life as a personal ethic and as an appreciated and highly valued social aesthetic.

It is exactly that unique entity (the human-animal bond) and the fear of losing The Bond that motivates people to seek care for their pets. The Bond drives pet caregivers into our hospitals. The Bond is the force that created the demand that elevated our medicine to today’s high-tech level. Our personal and professional ethics should always serve the patient’s needs while honoring the human-animal bond of the unique family attached to that animal. We must balance these needs when dealing with recurrence, relapse, or metastasis in our geriatric oncology patients.

An Inherent Conflict of Interest

Rollin and various esteemed colleagues asked haunting questions in a series of lively panel discussions at major professional meetings across the nation. Rollin insists that we ask ourselves these revealing questions about conflict of interest.

Has the high-tech megapractice ascended into a new realm of economics and ethics? Do doctors in superpractices that have the megafacilities and rotating schedules make decisions that favor the pet or the pet owner? Or do they make decisions that favor their practice’s financial interests and their own personal percentage of gross income as per payroll arrangements? Are we redrawing the line of pet advocacy in the emergency room? When do veterinarians need to exert their professional authority and become the advocate for their patients to avoid unnecessary suffering, prolongation of life, and expense?

Veterinarians must constantly juggle ethical, economic, and empathy issues in daily practice. Conflict of interest is inherent in running a business and practicing medicine. This conflict of interest is unavoidable in the decision-making process for geriatric oncology patients needing treatment or Pawspice care.

All veterinarians in private practice have an inherent conflict of interest. We are caught up in the financial web of a “pay for services rendered” profession. Every hospital displays a sign saying “Payments are due when services are rendered.” Essentially, we tell our clients “Pay as you go.”

Veterinarians may have school loans, living expenses, personal ethics, evidence-based medicine, scientific references, and the limitations of an in-house pharmacy that can all influence decision making. In practice, associates are often asked to “hurry up” in exam rooms and accept a double booking appointment schedule. The associate’s performance and average client transaction (ACT) is tracked on the practice computer for percentage income and contract negotiations. These factors easily create a conflict of interests that affects patient care.

Conflict of interest emerges between you as the healer and you as the wage earner, entrepreneur, and/or researcher. If you are running late or feel fatigued, these issues drift in and out of focus. These deep personal conflicts of interest and biases exist and they must, consciously or subconsciously, heckle every practitioner at one time or another. Your biases, personal baggage, and pressures impact every decision you make and have the potential of steering your decision-making process onto the wrong course.

As the attending doctor, you will have to wade through these issues concerning personal ethics, practice philosophy, multilevel economics, and empathy. If the atmosphere in your clinic is rushed, the result will be a lot of dissatisfaction on both sides of the exam table.

Yet another conflict of interest issue that places a layer of professional disconnect between associates and their clients: Some associates feel resentment against their private or corporate employers who care only about “the bottom line.” Many associates have trouble integrating their ideal personal ethics into the established practice philosophy. Practice owners and associates, feeling overbooked and overworked, often reprioritize their time in ways that diminish client relations and patient care.

How do these conflicts of interest affect patient care when associates and seasoned veterinarians encounter an emotionally and ethically charged consultation? It takes time to help relieve client confusion and emotions in the area of decision making. “In the 1980s, Dr. Marvin Samuelson showed that ethics decision-making occupies the single largest portion of a practitioner’s time, yet education in ethics is scarce in veterinary schools” (Rollin 2004b).

Schedule enough time to carefully discuss all of the available options. For patients with recurrence, give your original level of care and concern. For patients with advanced stage cancer, offer a wide range of options and referral for consultation with the appropriate specialists. Consider the needs, the physiologic condition, and the personality of the pet along with the wishes and financial ability of the owner. If you fail to consider all of these issues, you diminish the special doctor-client relationship that has the potential to work wonders.

How Far Is Too Far?

Many generalists, including veterinarians from other countries and specialists from other fields, feel that American veterinary oncologists in particular may go too far in the management of cancer (Rollin 2005). This would hold true in cases of recurrent cancer in geriatric pets. They may have entrenched feelings that it is wrong or inappropriate to treat cancer in animals, particularly if the animal is geriatric or if the cancer is advanced or disseminated. Others feel that older pets are too fragile or do not have the life expectancy to justify cancer treatment as worthwhile. These doctors may also eschew radical surgical oncology procedures such as amputation, nosectomy, or mandibulectomy for healthy cancer patients. They may feel that these procedures are disfiguring or unfair to the pet, especially if the cancer patient is older.

Nosey’s Case (Old Pets Are Treasured as the Road Gets Bumpy)

Nosey Summers, a 13½-year-old English Cocker Spaniel, was referred for consultation for management of chondrosarcoma, which caused a large painful swelling of her right distal radius. Her comorbidities were chronic bilateral purulent otitis, chronic ocular discharge, cardiomegaly with bradycardia (HR = 60 bpm), and hepatomegaly with mild elevations of liver enzymes and mild anemia with 1+ spherocytosis. Chest radiographs were negative for metastatic

disease. Despite the guarded prognosis, the family elected disarticulation and no follow-up chemotherapy. Supportive therapy was provided pre- and perioperatively and Nosey recovered uneventfully. Later that year, Nosey was attacked by a coyote and rushed to an emergency clinic, which saved her life. Nosey lived happily until age 15½ when she reportedly had a “stroke,” which left her back legs paralyzed; however, it might have been due to unverified recurrence.

Some veterinarians openly express negativity about recommending chemotherapy and/or radiation therapy for their cancer patients. A high percentage of these same doctors are also less likely to promote home care support. They might not offer SQ fluids, feeding tubes, immunonutrition, mobility carts, or Pawspice care for geriatric cancer patients and their families who want to support them despite the cancer.

Patriarchal Practitioners

It is crucial that practitioners refrain from insisting, pushing, converting, or controlling their clients with only two choices, either aggressive care or euthanasia. This patriarchal approach is dictatorial and sends the message, “I am practicing ‘My way or the highway’ medicine.” It is not surprising that pet owners flee from this style of practice.

Patriarchal veterinarians unwittingly impose their biases on their clientele, claiming that their approach to medicine is down to earth and practical. They tell the pet owner what to think and what to do rather than helping clients make their own decisions. They often use expressions such as, “You should let nature take its course” or “You need to put him out of his misery.”

More progressive doctors have termed this approach as “minimalist medicine.” A minimalist doctor may be surprised when a client goes to the Internet or to some other animal hospital for a second opinion, palliative care, or Pawspice care services. Increasingly, pet owners want to keep their terminal pets comfortable at home. They want sophisticated supportive care until their pet passes away naturally or via at-home euthanasia.

It is understandable but not excusable that doctors may have difficulty scheduling enough time to weigh the issues and discuss all the options with their clients. A very narrow scope of options is provided for treatment of advanced stage cancer or recurrence in the geriatric pet when the doctor is indifferent, overwhelmed, rushed, patriarchal, or has a negative personal bias against treating cancer. People are aware that they must be their pet’s advocates. It is no wonder that many pet owners seek second and third opinions; consult the Internet and the alternative medicine field for a more inclusive set of options.

Framework for Decision Making

For a helpful framework for ethical decision making, refer to the modified steps outlined in Table 8.2. Use these considerations as a guide to help associates and clients make decisions. Always ensure that all parties, including you as the attending doctor, the hospital staff, and the family, must have consensus and comfort with the final decision. If there is disagreement, work to provide the family with more options, such as palliation or Pawspice care. There is no perfect choice, but the course taken should feel reasonably acceptable by those involved under the circumstances (McDonald 2003).

Table 8.2. Framework for Ethical Decision Making

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1.1	Be alert and sensitive to emotionally charged situations.
1.2	Identify what you know and don't know.
1.3	Summarize and discuss the decisions that need to be made.
1.4	Consider the context and clinical issues of the case.
1.5	Consider the patient's medical history/diagnosis/prognosis.
1.6	Consider if the problem is acute, chronic, critical, reversible.
1.7	Consider the goals of treatment and probabilities of success.
1.8	Consider the patient's quality of life with or without treatment.
1.9	Consider the merit for comfort and palliative care.
2.1	Consider the religious and cultural beliefs of the pet owner.
2.2	Consider the owner's financial situation.
2.3	Consider consequences of various decisions as they affect the pet.
3.1	Use the basic principles of ethics to guide decision making.
3.2	Ask if you are being loyal to a business concern or clinical study.
3.3	Ask if you are respecting the patient and family's wishes.
3.4	Ask if you are treating the client paternalistically or otherwise.
3.5	Ask co-workers and colleagues for their opinion and advice.
3.6	Always respect client confidentiality.
4.1	Propose and test possible resolutions.
4.2	Find the best alternative for the patient, all things considered.
4.3	Consider the impact on others involved in the case.
4.4	Maintain trust with the client.
4.5	Determine if you and others are comfortable with the choice.
5.1	Make your choice and accept responsibility for it.
5.2	Learn from the process knowing there is no perfect choice.
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Source: From an article by Michael McDonald adapted for the *Society of Veterinary Medical Ethics* (SVME) *Newsletter*, October 2003. The author, to make it more relevant for geriatric oncology patient decision making, has modified and made further amendments to the table.

Recurrence Bodes an Upset Lifestyle

Caregivers want to protect and defend their pets in the battle against cancer and its related health issues. They want their veterinary care team to go on the offensive and help them declare war against the advanced cancer or go into round #2 against a relapse or recurrence.

If the pet is a service animal for a blind, disabled, or wheelchair-dependent person or epileptic, the caretaker's quality of life is threatened. Apart from the emotional loss that many people with service dogs suffer, loss of the dog equals a loss of the person's independence, freedom, and security. It often takes months to years for a disabled person to receive and establish a working relationship with a new service dog.

Pets that participate in showing or agility or are involved in community service activities, such as Pet Partners or other animal-assisted therapy, share intense social connections with their caretakers. Many of these companion animals have a large fan club of school children and nursing home and hospital patients and their staff. Naturally, no deeply bonded family wants to see their geriatric pet die from cancer.

When recurrence appears, caregivers conjure up great fear that they will lose their special treasured relationship and their connection to the shared activities that represent and encompass their

bond. These same feelings occurred with the initial diagnosis and treatment but they recur with tremendous disappointment due to the more ominous threat of recurrence or relapse.

Deeply bonded caregivers often lapse into anticipatory grief. This intense type of grief is the fear of loss. Often the caregiver feels unsettled but doesn't realize why. Some clients hide their grief or feel disenfranchised because their friends do not understand the importance of the bond they share with their geriatric pet (Meyers 2000; Corbin 2004).

Elements of anticipatory grief underlie the commitment and are the driving force that creates the demand for and recent proliferation of high-tech veterinary facilities. Commitment is the motivating reason that the pet-owning community has created an increasing demand for more specialized and sophisticated medical and supportive services for their pets. This increasing demand includes improved primary cancer care and earlier diagnosis of cancer and its recurrence. It certainly includes thinking that veterinarians would have an open mind to treating advanced stage cancer and recurrent cancer in geriatric patients.

Anticipatory grief also drives an increasing demand for improved monitoring for treated geriatric cancer patients so that the recurrence may be found at its earliest stage. It drives the growing interest in chemoprevention and immunonutrition for at-risk patients. This segment (fear of separation) of the human-animal bond drives the senior and geriatric health care and wellness programs that are becoming so well promoted in contemporary practices. It also drives the demand for improved palliative care and end of life care services. Very simply, people do not want their geriatric pets to die. It is up to the veterinarian to identify which of their clients want nothing less than state-of-the-art services for their geriatric pet in the face of advanced stage cancer or recurrence. It is equally incumbent upon clients to make the attending doctor aware of the intensity and depth of their bond and their commitment to monitor for and treat advanced cancer in their geriatric cancer pet.

A short life expectancy is not a good reason for the clinician to turn the caretaker away and evaporate ongoing veterinary services. The veterinarian needs to find out whether or not that client wants to pursue sophisticated services to treat the recurrent cancer. The attending veterinarian made this assessment when the geriatric oncology patient was first diagnosed and must re-establish the intent for further therapy or palliative care. This information must be discovered dispassionately, in a non-judgmental fashion, with no attempt to impose the attending veterinarian's preferences on the client.

When treating geriatric oncology patients of deeply bonded families, the attending clinician must determine the level of service that will satisfy the owner yet still provide comfort and alleviation of cancer pain for the pet. These ethical issues have to be handled very delicately.

Veterinarians encounter dramatic highs and lows of human emotions on a daily basis. The doctor who jumps in and out of exam rooms like a rabbit is not dealing with his or her client's emotions. Most veterinarians practicing today received no training in this area in veterinary school, and so they avoid or deflect clients' emotions.

Many graduates and specialists are highly focused on the disease and its statistics and forget to notice, acknowledge, or serve the patient-client entity. They may be super technicians but lack interactive skills in communication, collaboration, interrelationships, and the needs of society. They may lack the perspective to learn about and understand the whole patient's *attaché* of family and environmental issues. Good communication skills are needed for these intimate consultations.

The aging pet population parallels the aging of the human baby boomer population. People expect their pets to have a longer and healthier life. The public is asking for our help and expertise and they are willing to pay for it even when cancer recurs.

Aesculapian Authority

As a profession, we must be wary of unscrupulous veterinarians. Our crooks are few and far between, but every profession has a sociopath here and there. They prey on the human-animal bond at the expense of the pet's quality of life and the pet caregiver's pocket book.

We must always remain true to the Veterinarian's Oath and remain ethical when helping the geriatric oncology patient's family make decisions. Personal ethics tell us not to lie, not to steal, not to take advantage of people, to be charitable, and to "do the right thing" for aging pets and their people.

Society has conferred trust upon veterinarians and other professionals, including priests and psychiatrists, via the Aesculapian authority. Aesculapius was the god of healing in Roman mythology. Aesculapius's staff, with its entwining snake, is the caduceus used as a symbol for the healing arts. The Aesculapian (Asclepiad) authority allows doctors to examine and make decisions for their patients. Society views violations of the Aesculapian authority as a heinous and serious crime of betrayal (Rollin 2000).

Since veterinarians are only human, a personal bias may show up in the way one steers a consultation. When advising a client, always ask yourself, "Might another clinician advise differently?" and "Would a second opinion disagree with the approach that I recommended?" If so, how? And why? And might they be right?

Perhaps we neglect to provide a referral for a second opinion out of fear that a referral would enter our client and their geriatric oncology pet into the mindless machinery of high-tech medicine, spending more money than we think they can afford. But the family veterinarian should not feel obligated to be an advocate of the client's pocket book. Are we being the pet's advocates or are we just trying to keep the client's business at our own hospital? Ask yourself these questions. Always examine and evaluate the methods you use. Look at the real reasons why you persuade clients to make decisions for or against caring for an aging pet's malignancies.

Rethinking Advanced Stage Cancer, Recurrence, and Age

I am in awe of The Bond that ties a family to this particular dog or that special cat. This awe drives my philosophy in caring for geriatric cancer patients and dealing compassionately when they are challenged with advanced stage cancer or recurrence. As pets get older, The Bond grows stronger. Pet lovers have a sincere longing to preserve their pet's life even in the face of recurrence, if the patient's quality of life can be maintained.

Geriatric patients are often denied conventional cancer care because of their perceived age rather than their physiologic age. Geriatric patients are underrepresented in clinical trials. They are routinely excluded from studies due to comorbidities and short life expectancy. There is no doubt that our profession has discriminated against aging pets and withheld cancer care simply because they are old.

Treating geriatric oncology patients for a primary cancer is complex and more challenging than in non-geriatric patients because of the common coexistence of other chronic conditions. At recurrence, each concurrent problem needs to be re-evaluated and compared to the patient's previous history. Any significant change deserves the full attention of the attending doctor. There may be residual consequences from the previous cancer treatment. A reasonable treatment goal would be to provide at least a 50% alleviation of each unmanaged concurrent problem if definitive therapy is elected. Pay

attention to all the conditions acquired over the lifetime of the geriatric patient with recurrent cancer to help that patient maintain a good quality of life.

We expect that recurrence, metastasis, concurrent disease, and/or organ failure will be progressive. Nevertheless, it is time to rethink how veterinarians can step up and partner with their deeply bonded clients to help them face these gripping issues and make their own choices. Are we going to help geriatric pets fight against advanced stage and recurrent cancer or will we abdicate without offering supportive care?

Many clients simply want support, basic advice, and training in end of life nursing care. Some of my clients have expressed that when they chose not to take the “high road” course of action recommended, their doctor became frustrated with them and lost interest in their pet. Many caregivers are told that conventional medicine cannot help their pet’s situation. When told that nothing can be done, caregivers often seek out other options, such as palliation or alternative care.

The Veterinarian’s Role in Decision Making

Take the time to properly research and think about a geriatric oncology case and all of the unique features that may positively or negatively influence the patient’s survival. Take the time to educate the client about the issues and the options in early, middle, and late stage recurrent cancer. Sadly, veterinary students are ill prepared to face these consultations and ethical issues when confronted by them in practice. Training is seldom provided, and when provided, it is often by unqualified personnel and delivered on the fly as an afterthought, in hallways or between exam room visits.

The issues of ethics, grief, and attachment education are generally not given formal curriculum time in veterinary colleges. Drills designed to teach students how to assist clients in decision making would prepare students to address clients properly, look them in the eye, answer their questions thoughtfully, communicate clearly, and get their point across in layman’s language (Milani 2001).

Some pet owners have confided that they felt completely misunderstood by their attending veterinarian or specialist. They felt their doctors had an indifferent, “take it or leave it” attitude. One couple reported that their veterinarian proposed a difficult radiation therapy protocol for their dog and then rattled off statistics and percentages, but never listened to them or answered their questions and concerns about their aging pet’s colitis and nervous personality.

Tiara’s Case (Treat Clients as Decision-Making Partners)

Tiara, an 8-year-old, 100 pound, F/S German Shepherd Dog, had bilateral tonsillar squamous cell carcinoma and early degenerative myelopathy. The family knew the prognosis was poor from a previous oncology consultation. Tiara was very aggressive in the exam room, lunging and barking at us.

After our consultation, the client thanked me for discussing ways to deal with Tiara’s obstreperous personality and for offering potential treatment options. She also thanked me for treating her as an intelligent person capable of making her own decision.

Then she told me that she had had breast cancer and that she was insulted when her own Los Angeles-based oncologist “talked over” her. After an evaluation, he spoke directly to her husband about her options without addressing her! She immediately changed oncologists and flew up to Stanford every 3 weeks for her treatments.

Because we showed no fear or dislike of Tiara for her aggressiveness, the family wanted us to treat her despite the poor prognosis. She was more than happy to sign an informed consent statement. Her signature verified the family's full awareness of the poor prognosis for Tiara, and their desire to provide treatment regardless.

Tiara received radiation therapy to both tonsils with concurrent mitoxantrone chemotherapy. This combination has a synergistic effect with radiation therapy against squamous cell carcinoma (SCC). We won excellent local control for more than 8 months. The SCC recurred in Tiara's trachea as a 2×2.5 cm mass located 7 cm caudal to her larynx. We suspected a poorly defined retropharyngeal mass as well. The family deliberated and decided that they felt very satisfied with the extra high-quality time that they had already gained. During her remission, Tiara's concurrent degenerative myelopathy became a mobility and incontinence problem. The family elected to provide Pawspice care for Tiara until her time came.

Veterinarians are expected to maintain the geriatric oncology patient's well-being, especially in the face of advanced stage cancer or recurrence. We are obligated to guard against unrecognized and unnecessary suffering in all of our cancer patients. We also have a social responsibility to ease the emotional pain of the pet's family members.

Clients are very needy during these difficult days of decision making. At the same time, they still have to go to work, perform their family obligations, and care for their ailing geriatric companion animal. We must ensure that the geriatric oncology patient's needs are met. Pain control and comfort must be the client's primary focus. To determine a pet's quality of life, caregivers may find it helpful to use the proposed HHHHMM Quality of Life Scale. The acronym stands for no Hurt, no Hunger, no Hydration problems, good Hygiene and Happiness, Mobility, and More good days than bad days (Table 10.1).

The companion animal community needs its veterinarians to be aware of and deal effectively with the internal torment of decision making. Pet owners may experience a heart-wrenching ordeal and go into grief right in the doctor's office. They feel an acute emotional wound when they get the bad news that their geriatric oncology pet has "mets" in the chest. The client projects the ravages of cancer as a threat to their pet and The Bond. They are projecting nothing but heartbreak ahead.

The veterinarian needs to be aware that the client may not be rational during the appointment. The client may disconnect from reality and be in a daze. This complicates the tasks of educating the client and assisting with decision making. It stresses the relationship between the veterinarian and client.

Stress and confusion between veterinarian and client have a negative effect on the geriatric patient. The cancer progresses and the pet's health may decline during the time required for the client to seek other opinions. The best decision is to help the pet owner enter the pet into some level of defined care, whether that care is to repeat another cycle of chemotherapy or another surgery or palliative radiation therapy or to enter an end of life Pawspice care program.

Expect Recurrence and Look for It

A good strategy for dealing with recurrence is to have an active surveillance program for all cancer patients at risk. Upon achieving remission, I tell clients that we want to do everything we can to offset recurrence. We also tell them approximately when the literature warns to expect recurrence or metastatic disease. For example, when a cat or dog with hemangiosarcoma or osteosarcoma survives 4 months without signs of recurrence, we congratulate the client and celebrate the winning of extra

quality time for their pet in the battle against cancer. At every recheck that yields clean radiographs and ultrasounds, I remind the clients that they have scored another run in the ninth inning and we are going into overtime. We congratulate the family for their success and celebrate the value and meaning of each “clean met check” (no metastasis). These are the joyful moments in oncology.

Ideally, when dealing with recurrence or relapse in a geriatric cancer patient, we would employ the basic principles of diagnosis and staging as outlined in chapter 5. It is imperative to assess the patient’s previous and recently acquired concurrent conditions. Define how these conditions will influence the patient’s tolerance to rescue or salvage therapy. Take a fresh look at the geriatric oncology patient’s current laboratory work, radiographs, and stage of disease and compare these data to the previous database.

Advanced stage cancer or recurrence may acutely impact the geriatric pet’s function and create an emergency situation. The pet is often rushed to an emergency facility for stabilization and workup. Many geriatric oncology patients are euthanized in emergency rooms due to acute manifestations of advanced stage cancer or recurrent cancer. Others are stabilized overnight so that the family can consult the pet’s primary care veterinarian or oncologist about further evaluation and decision making. All of this causes the caretakers great distress and panic. They will look to you for help and wisdom in the decision-making process.

Make a complete set of radiographs to look for metastases in three views of the chest and two views of the abdomen. Evaluate organ function tests and urine analysis. Assess the patient’s body condition (Figure 8.1). Document the geriatric cancer patient’s basic performance level assessment. Further imaging with abdominal and/or thoracic ultrasound may be helpful to detect metastases. FNA cytology or Tru-cut tissue samples may confirm the diagnosis without more invasive techniques. Attempt to restage the geriatric oncology patient using the TNM scale discussed in chapter 5 (Table 5.2).

Many geriatric patients with advanced or recurrent disease require further imaging under anesthesia for complete evaluation and staging. Before recommending any diagnostic test, determine the risk-to-benefit ratio of the test. How useful will the results be? How well do you expect the geriatric patient to tolerate the anesthesia required for additional diagnostic tests, such as CT, MRI, interventional radiography, or direct visualization with fiber optic scopes? If the test results will be useful for decision making, then the risk of general anesthesia for diagnostic procedures may be justified.

Physical Performance Assessment

Most veterinarians do not use scales such as the Karnofsky Performance Scale to evaluate their geriatric patients. It is time consuming, requires special equipment, and would have to be repeated periodically to gain value as a clinical tool for monitoring treatment success. The Modified Karnofsky Performance Scale measures patient activity from 0–4. In this scale, 0 is normal activity; 1 is acceptable function; 2 is compromised but able to eat, sleep, and eliminate properly (Activities of Daily Living [ADL]); 3 is disabled, anorectic, incontinent, or unable to get up to eliminate in acceptable areas; and 4 is moribund or deceased (Morrison 2002a).

We seldom conduct formal performance tests on geriatric cancer patients. However, we should discuss the patient’s physical ability with the family and use their comments to document a basic performance assessment. Using terms such as slightly, moderately, or severely compromised with low, medium, or good levels of performance are adequate for performance assessments. We can also use a 0–10 scale for mobility assessment using the proposed Quality of Life Scale (Table 10.1).

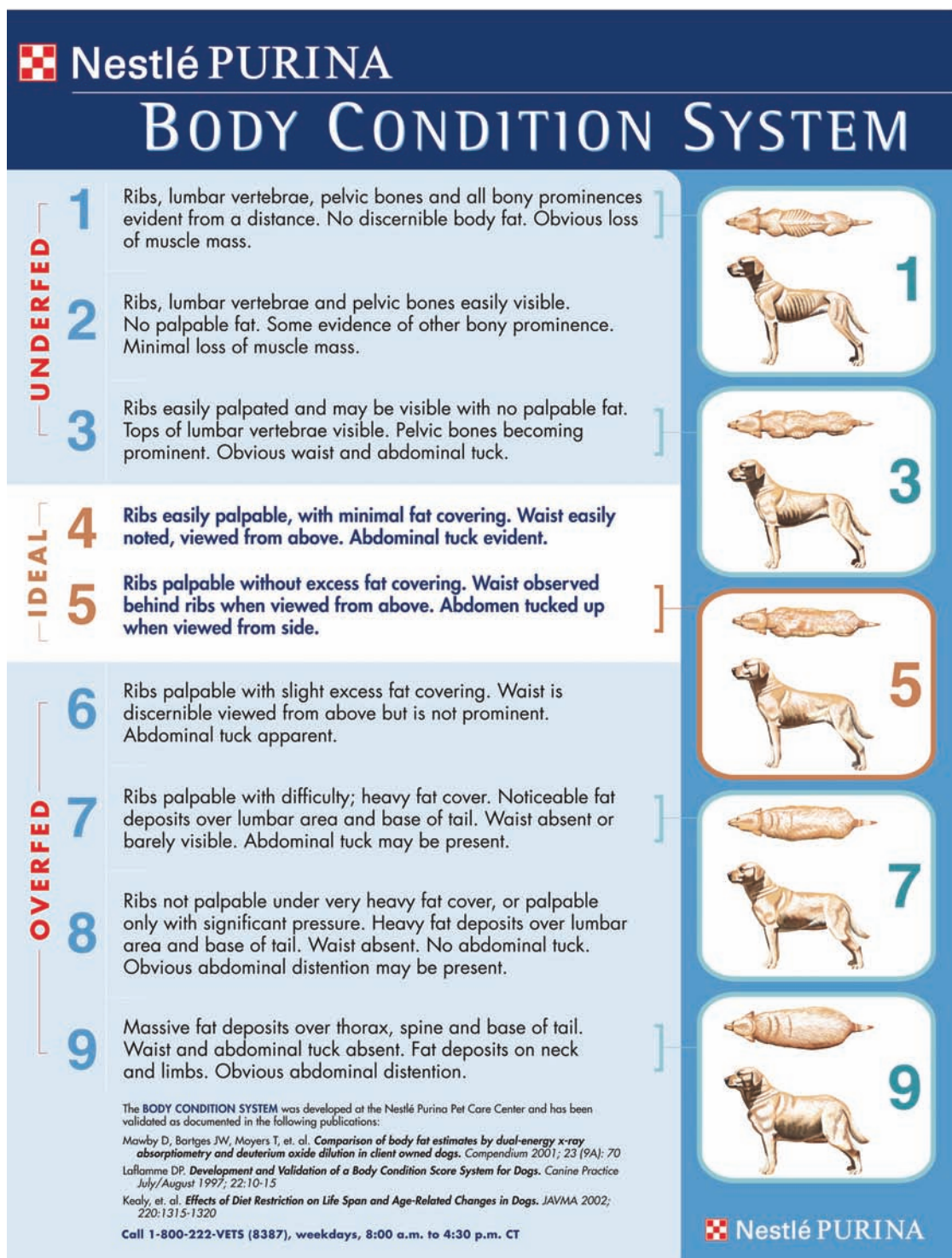


Figure 8.1. Body Condition System chart for dogs reprinted courtesy of Nestle Purina PetCare. See www.purina.com/cats/health/BodyCondition.aspx for the chart for cats.

In human medicine, there is a simple test called “Get up and go” that is used to assess performance. If a person needs to use the arms of a chair to get up, and if he or she has dyspnea or trouble walking across a room, that individual is considered to be at a low performance level and this is associated with a poor prognosis (Balducci and Beghe 2004). This simple determination test applies to veterinary geriatric oncology patients as well. If a pet struggles to stand from a laying position and if the pet has dyspnea or trouble walking to designated areas for elimination, we can consider that pet to be at a low performance level.

Frailty and Cachexia

The attending doctor should also determine if the recurrent geriatric cancer patient is frail or cachectic. Frailty is more often a chronic condition, whereas cachexia is cancer related (Repetto, Venturino, and Gianni 2004). Frail and cachectic patients have little functional reserve and are not able to endure additional stress of surgery or chemotherapy without supportive care to counterbalance their condition.

Be sure to chart the geriatric patient’s physical appearance, mentation, and performance in the medical record. These observations have bearing on treatment selection and outcome. Immunonutrition and rehabilitation techniques may help in the care and maintenance of cachectic and frail cancer patients.

Dealing with Anemia and Chronic DIC

The presence of anemia is a major factor affecting the overall prognosis of geriatric oncology cases in human and veterinary medicine. Aging patients have reduced hematopoietic capabilities that are further stressed by the progression of cancer. Surgery, radiation, chemotherapy-associated anemia, and reduced helper T-cells (CD4 cells) aggravate an aging hematopoietic deficiency. Anemia serves as a marker for recurrence in hemangiosarcoma patients.

Transfusions and/or hematopoietic growth factor therapy may be helpful to maintain the geriatric patient’s hematocrit at a level on the order of 24–30%. Erythropoietin therapy acts on late stage red blood cell precursors. As the precursor population is exhausted or the patient produces antibodies against it, the stimulatory effect of erythropoietin runs out. Erythropoietin is worth using because it may increase the quality of life, especially for patients with chemotherapy-associated anemia (Rowe and Avivi 2004). Clinicians may utilize new therapeutic developments in this field such as species-specific erythropoietin or T-Cyte[®], a thymic protein for SQ injection, which restores helper T-cells that may secondarily increase the hematocrit (Beardsley 2005).

Recurrent or highly metastatic tumors such as hemangiosarcoma are often diagnosed at advanced stages. Patients generally have anemia, thrombocytopenia, thrombosis, and coagulopathy. They may have sub-clinical, chronic, peracute, or acute DIC. The prognosis for recovery with treatment is grim (Thomason, Calvert, and Green 2005).

Other Geriatric Syndromes

The attending doctor needs to probe the patient and ask questions to determine if the geriatric oncology patient has age-related syndromes such as cognitive disorders, mentation disorders, degenerative

neuropathies, incontinence, hearing loss, visual deficits, depression, anxiety, and so forth. The family's ability to manage and/or tolerate pre-existing geriatric syndromes in their aging pet may create decision-making issues regarding treatment for advanced stage or recurrent cancer.

Diagnosing Recurrent Cancer

When dealing with the local recurrence of solid tumors or relapsing lymphoma, we first want to confirm the diagnosis with FNA cytology, incisional punch biopsy, or Tru-cut biopsy. For lymphoma, insert a 22-gauge needle into at least two lymph nodes using the standard non-aspiration technique. FNA is an excellent and reliable diagnostic tool if the primary mass is an exfoliative type of tumor such as mast cell tumor or lymphoma.

Routine FNA techniques will not confirm the diagnosis of recurrent sarcomas. To overcome this problem, we use a modified, more aggressive version of FNA. Insert an 18-gauge needle and angle it to chop off a core of tissue, then aspirate. Expel the tissue sample onto a slide and make smears for microscopic examination. This technique is described in detail in chapter 5.

It is likely that thousands of primary and recurrent local sarcomas go undiagnosed because the attending doctor accepts a negative FNA report from a non-exfoliative tumor.

If only every graduate could have “situated knowledge” from the start. Situated knowledge is subjective knowledge drawn from practical experience of dealing with clients and patients. This knowledge is the missing piece or the gap in knowledge acquired in the classroom. It exists as practical wisdom, intuition, or good clinical judgment. The clinician must have it in order to do a good job, but there is no way to study it.

The attending doctor needs to approach each and every case using practical wisdom and common sense. Practical wisdom and good clinical judgment are virtues that have much to do with on-the-spot decision making and can be studied and learned only by reviewing cases (Floersch 2002).

The attending doctor needs to distinguish each case using practical wisdom or “situated knowledge.” If we suspect recurrence of a sarcoma, textbook knowledge tells us that they are non-exfoliative, but situated knowledge (from experience) tells us not to rely on simple FNA for diagnosis.

This same situation occurs with vascular tumors such as hemangiopericytoma or hemangiosarcoma when the clinician attempts simple FNA and aspirates only blood. Practical knowledge tells us to look at the sample before sending it to the lab. The fact that only blood was aspirated from the mass indicates that you are dealing with a vascular tumor. Instead of wasting the client's time and money with a useless FNA, suggest the next diagnostic step. Confidently inform the client that you have a high index of suspicion that this particular mass may be a vascular tumor and that it needs tissue for biopsy and laboratory confirmation. The client will authorize the biopsy if a definitive diagnosis is needed for decision making.

Doobie's Case (Listen to Intuitive Caregivers)

I accepted an out of state phone consultation regarding an 11½-year-old F/S Golden Retriever diagnosed with chondrosarcoma (CSA) on the skull. The owner discovered the primary mass. An initial FNA was negative for cancer cells. Doobie's owner intuitively insisted upon surgical removal. The mass was 3–4 mm in size and, according to the histopathology report, was completely removed. The family drove 5 hours to a university for consultation about treatment options. Three options were given: (1) tumor bed excision for wider, deeper margins, (2) radiation

therapy, or (3) follow up with monthly chest x-rays and abdominal ultrasound. The family selected option #3 and took Doobie dutifully for tests every month for the following 6 months.

At 3 months, the owner felt a thickening near the primary site. An attending clinician suggested FNA. Once again, the cytology report was negative with no significant cells. Doobie was given a clean bill of health at her 6-month recheck. The client asked about the swelling, which seemed to her to be larger. The oncologist looked at the record, cited the negative results of the previous FNA, and said that the results were not significant.

One week later, Doobie had a seizure. A neurologist ordered an MRI. The study identified a brain tumor and a large nasal tumor. The attending clinicians pondered whether Doobie's tumors were new or related to the original CSA. They all agreed that it would have been reasonable to follow up Doobie's case with CT or MRI of the skull at one of the monthly rechecks. The primary mass was located on her head and the intuitive owner had pointed out a new mass effect in the area of the primary tumor. The clinicians agreed that relying on FNA for diagnosis of non-exfoliating sarcomas such as chondrosarcoma could fail to rule out the presence or absence of malignant cells. Everyone on this case learned and gained experience and they all gained much more respect for the caregiver's intuition.

Using Technology for Monitoring Recurrent Cancer

The best way to deal with recurrence is to always be looking for it. Routine physical examinations, blood work, and imaging of the geriatric oncology patient all become an essential part of the treatment and follow-up protocol. Teach the client how to palpate all of the pet's lymph nodes and carefully examine the primary tumor site. This type of hands-on monitoring for recurrence can be called "tumor watch."

The pet caregivers partner with us to remind us to perform the specific exam that their pet needs at each recheck. Ask the clients to remind you to perform rectal exams on a monthly basis for their dog with excised anal sac tumors, for example. Ask the family whose pet has an abdominal mass to remind you about the follow-up radiographs or ultrasound for "met (metastasis) checks." Ask them to measure the pet's girth once a week to monitor for abdominal distension. When the clients are in partnership with the tumor watch monitoring program, they benefit emotionally as participants rather than remote spectators in the effort to save their pet. Enlist them to prompt you to stick to the recheck schedule and do your detective work.

Ultrasound is very useful for monitoring for recurrence of abdominal tumors, for monitoring bladder tumors, and to guide FNA or Tru-cut biopsy needles into organs and accessible masses. It is also helpful to monitor recurrent pleural effusions and to guide small gauge FNA needles into peripherally located thoracic cavity masses. FNA or Tru-cut samples may fall short of confirming the diagnosis, especially in the liver, due to lack of stroma, tumor heterogeneity, necrosis, and inflammation. It is good practice to look at the FNA cells immediately. If the sample does not contain representative cells, repeat the FNA procedure until you get a worthy sample (see chapter 5).

There is a tendency toward overreliance on negative cytology reports. Consider FNA as a screening tool and depend on histopathology for the definitive diagnosis. When monitoring for recurrence, however, FNA results may fit the case history, yielding round cells or spindle cells that resemble the primary tumor.

There is good rationale to perform a second-look laparotomy (SLL) and surgical biopsy to accurately and definitively diagnose residual or recurrent tumor(s). Exploratory celiotomy is often the

only sure way to definitively diagnose some cases of hepatic neoplasia and low-volume infiltrative GI lymphomas in cats. Mortality rates range from 17% to 27% and complication rates run from 16% to 30% for cancer patients surviving a first time exploratory (Tobias 2005). However, these mortality statistics would be expected to be much greater when dealing with recurrence in geriatric oncology patients. It is reasonable to consider SLL as part of the monitoring program to evaluate the progress of treated primary or metastatic abdominal tumors, especially when secondary cytoreduction may be helpful (Stanclift and Gilson 2004).

The same residual disease monitoring consideration can be applied for patients with nasal passage cancer. MRI is used at routine checkpoints to locate residual or recurrent disease following radiation therapy (Henderson 2005).

A second look endoscopy can be very helpful for viewing and sampling treated GI tract, respiratory tract, and bladder tumors. Laparoscopy and thoracoscopy can be used to visualize and diagnose metastatic and recurrent cancer. Follow up imaging with ultrasound, CT, MRI, and PET. Radio-pharmaceuticals may be used to detect for occult cancer and recurrent tumors at early stages.

Routine ultrasound screening of the spleen is reasonable for older dog breeds predisposed to hemangiosarcoma. This might detect tumors before rupture. Frequent tumor watch rechecks looking for expected metastatic or recurrent lesions may benefit cancer patients. It is hoped that earlier intervention could increase survival time.

It would be ideal to have a non-invasive, simple, inexpensive, and accurate test to detect early recurrent cancer in veterinary patients. Serology may reliably detect biological tumor markers in the near future. Such a test is proposed by www.pet-screen.com in Nottingham, UK, where a proteomic analysis can be completed in 7 days. New screening tests such as one that detects circulating endothelial precursor cells (EPCs) may identify dogs at risk for hemangiosarcoma at sub-clinical stages (Modiano and Helfand 2005). Ask your laboratory or consulting oncologist or go online with Veterinary Information Network (VIN) to learn if new serology tests are available to detect lymphoma, hemangiosarcoma, sarcoma, and carcinoma in dogs and cats.

If the cancer patient's original tumor was associated with paraneoplastic hypercalcemia, a rise in the serum calcium level may serve as an inexpensive marker. This would apply most often for T-cell lymphoma, anal sac adenocarcinoma, and some miscellaneous tumors. Elevations in serum alkaline phosphatase levels may indicate metastatic lesions involving liver and bone. This is associated with a poor prognosis in dogs with primary or metastatic osteosarcoma. Anemia and cancer cachexia-related weight loss would also indicate recurrence.

Advanced Stage and Relapsing Lymphoma

The most common recurrent cancer in our practice is relapsing lymphoma. Our typical relapsing lymphoma patients are older dogs that were in remission for over 1 year and dogs that come out of remission shortly after their induction.

The most common advanced stage cancer patients in our practice are dogs with advanced multicentric high-grade lymphoma. The clinician can immunophenotype the patient's tumor for prognosis. T-cell lymphomas are more resistant than B-cell lymphomas. One study found T-cell lymphomas to be more prevalent in Boxers (82%), followed by Rottweilers (68%) and Golden Retrievers (50%) (Lurie et al. 2004).

Oncology clients need to know when to expect relapse. We teach our lymphoma clients to check all of the patient's lymph nodes at least twice a week. We teach our feline lymphoma clients to be

alert for warning signs of recurrence and to palpate the abdomen of their cats for recurrence. We want our clients to be alert and to detect relapse early on, before the tumor volume increases to an advanced stage.

Consultation for a relapsed lymphoma could go like this: “Simon’s first remission has ended. It does not mean that he will die right now or very soon. We do know that the duration of the second remission is generally half of the first remission and the third remission is half of the second. Therefore, we will probably gain 6 months in this second remission since his first remission lasted 1 year. Simon has a good chance of achieving a second remission and he should feel well during his second remission. We must warn you that he could experience side effects to the re-induction protocol. Remember, we cautioned you about this possibility during his first induction protocol. Our plan is to start week 1 all over again and go from there for 6 weeks as before. Please look at your old treatment calendars to refresh your memory. How do you feel about starting week 1 over again? Can you bring Simon back for a CBC and chemotherapy in 2 weeks? Will you be able to afford this round of treatment?”

Generally, the family wants to try for another remission and consents to start the re-induction protocol. In most cases, the second phase protocol duplicates the original protocol. The re-induction protocol should be modified if the geriatric patient had an adverse reaction to Adriamycin or vincristine during the previous induction. If Adriamycin was used as a single agent, the patient may be approaching the total cumulative dose range for Adriamycin (280 mg/m²). The patient may have developed heart disease, renal disease, or some other concurrent illness over the past year, which would increase the risk for side effects.

Occasionally, we use the calcium channel blocker verapamil as pretreatment to reduce the multidrug resistance phenomenon. Most of the time, we settle for using other types of chemotherapy drugs for rescue or as palliative options. Patients may achieve a stable, partial, or complete remission that may last another 2 months. The most important goal is to maintain quality of life, avoid toxicity, and comfort the family during this round of chemotherapy.

For advanced stage first time lymphoma cases, caregivers need consultation about the increased risk of tumor lysis syndrome, infections, and morbidity. Use the standard induction protocols but administer the drugs over a 3–4 day period along with IV fluids, antibiotics, intense monitoring, nutritional support, and so forth as described in the “Chemotherapy in the Management of Geriatric Cancer” section of chapter 6.

Resistant Lymphoma

For geriatric patients with resistant lymphoma, the primary treatment goals are to avoid adverse side effects, maintain quality of life, and try for another remission or stabilize the progression of disease. Multidrug resistance (MDR) is our biggest drawback. Diffusion gradients for drugs in the interstitial matrix and extracellular fluid of lymphoma tissue are variable. Drug concentration may be minimal in hypoxic underperfused areas of the tumor. There are many valid reasons to abandon or alter standard re-induction protocols. The weary pet owner may not have the financial means to support another protocol.

There are several useful single rescue drugs such as L-asparaginase given every 2–3 weeks, Adriamycin rescue every 2–3 weeks (if appropriate), or lomustine every 21 days. Rescue combinations D-MAC, ADIC, CHOP (Couto 2005), and MOPP (Vail, MacEwen, and Young 2001) are worth trying. (See the lymphoma rescue protocols used at the Ohio State Veterinary School for dogs and cats in section 1-C in Table 6.2.)

A Few Words on MOPP Rescue

The MOPP rescue protocol took a costly turn when procarbazine became prohibitively expensive. Most pharmacies will not stock procarbazine (Matulane[®]) unless the client pays \$5,500.00 for the entire bottle. Occasionally a supplier will acquire procarbazine powder and compound it for specific patients at a more reasonable price. Patients may still achieve remissions using Mustargen[®] IV at 3 mg/kg and vincristine at 0.7 mg/kg IV and oral prednisone leaving procarbazine out of the protocol. The Veterinary Cancer Society web site may help doctors locate suppliers who stock Mustargen and procarbazine at reasonable prices.

LoLuC-P Optional Low-Cost Protocol for Maintenance

In situations where there are financial constraints, I try to provide one rescue dose of Adriamycin or, at the very least, vincristine at 0.7 mg/m². Dexamethasone at 0.5–1 mg/kg may also be very helpful for re-induction on day 1. If the client can afford L-asparaginase, we prefer to give it as well. For patients that are frail, sick, or have a high tumor burden, we may recommend a reduced or a split dose schedule over 24–48 hours. We may give the vincristine on day 1 and L-asparaginase on day 2. For low-cost maintenance, a rotation of oral chemotherapy medications can be used in sequence. We have been successful in maintaining remissions for a number of relapsed lymphoma patients by rotation of oral lomustine followed by Leukeran and then Cytoxan[®].

For dogs, the lomustine dose is 60–80 mg/m² and for cats, it is 50–60 mg/m² divided into 25% fractions and given over 4–7 days. The Leukeran dose is 1.4 mg/kg divided a.m. and p.m. for 1 day given only on day 21. Cytoxan at 100 mg/m² is given with a large amount of broth, 15–20 minutes before morning urination, on day 28 and 29. This rotation cycle is repeated again on day 35 after a CBC finds the WBC to be above 4,000 with neutrophils above 2,000.

If the client allows induction with vincristine and L-asparaginase, give the first divided dose of lomustine 4–5 days later. If only L-asparaginase was used, administer the dexamethasone IV as earlier along with Benadryl; start giving the divided dose of lomustine on day 1. Divide the dose into two to four (four doses is preferable, using 10 mg capsules) equal amounts with instructions to administer 25% of the dose every 48 hours until finished.

Patients on lomustine need close monitoring for platelet counts and leukopenia and chemotherapy-induced anemia before each additional treatment. Liver function should also be checked periodically for lomustine hepatotoxicity. This protocol increases the interval between lomustine doses and, in my experience, seems to spare the platelets in the long run. Cats often need intervals up to 6 weeks apart between doses of lomustine to avoid myelosuppression.

If prednisone has some efficacy for the patient, it is given concurrently on a tapered schedule as in the original induction protocol. It is given at 5 mg twice daily for cats. Dogs are maintained on prednisone at 0.5–1 mg/kg every other day, depending on the patient.

To ensure increased water intake with Cytoxan, we instruct clients to give prednisone on the days of Cytoxan along with a large offering of broth or chicken soup slurry. Since using this strategy for oral Cytoxan in the late 1970s, we have eliminated Cytoxan-induced hemorrhagic cystitis in our practice. I prefer not to use Cytoxan IV to avoid toxicity for the geriatric patient.

This oral combination chemotherapy protocol has been helpful for achieving stable disease for many of our relapsed lymphoma dogs and cats. Patients stay in remission or in stable partial remissions

for variable periods. We may add subcutaneous Cytosar U[®] injections at 250–300 mg/m² on day 1 and 3 of each week (total 500–600 mg/m²) into this protocol for patients with CNS involvement or renal involvement, or to help sustain partial remissions in more resistant lymphomas. On occasion, I have used Cytosar U as a substitute for procarbazine in the MOPP protocol as an option.

Slim's Case (Life Was Good in Stable Partial Remission)

Slim Pancratz, a M/N Whippet, was diagnosed with multicentric lymphoma at 10 years of age. He received the modified Wisconsin protocol. Slim came out of remission at 10 months and received re-induction chemotherapy. He achieved only a partial remission. The Pancratzes needed to conserve funds and requested fewer visits and a less costly maintenance protocol. We placed Slim on a 10-day interval rotation schedule using oral lomustine, Leukeran, Cytosan, and alternate-day prednisone. The Pancratzes brought Slim in every 2–3 months for a CBC recheck and IV vincristine. Slim gained weight and became lethargic. He was diagnosed with hypothyroidism and responded well to thyroid supplementation; he went back to his normal weight and vigor. He survived a total of 170 weeks with lymphoma.

Options Beyond Chemotherapy for Recurrence

Keep in mind that the immune system ignores neoplastic cells because they are “homegrown” in the body. The mechanical and molecular signals for angiogenesis are unfolding but the trigger for lymphangiogenesis remains unknown. Researchers in the field of proteomics (analysis of proteins and effector molecules) have identified tumor-specific signaling pathways. New types of drugs can target specific proteins that regulate these pathways.

Targeted therapy may seek out and destroy cancer cells by finding a protein trigger, receptor, or switch to exploit. Inhibition of tyrosine kinase signaling, blocking growth receptors, and inhibition of angiogenesis hold promise as useful targeted therapies. New drugs may provide amazing results for relapsing and resistant geriatric lymphoma patients in the future. You may check new drugs and new protocols on the Internet at www.uptodate.com (Jain 2004.)

Adverse reactions and high cost may restrict the use of targeted therapy drugs for use in dogs and cats. Gleevec[®] provided miraculous results for people with resistant CML. Gleevec may have some efficacy in hemangiosarcoma but it causes moderate grade 3 to severe grade 4 vomiting in dogs. It may be better tolerated physiologically by cats. It would cost \$1,200.00 a month to maintain a 70-pound dog on Gleevec. It is recommended for daily use for CML patients until resistance develops.

When dealing with resistant lymphoma, the family may continue to ask if there is anything else to do. In situations like these, we educate the family about other potentially aggressive salvage therapies. Options to pursue would be to try half-body radiation therapy or bone marrow transplant (Tremayne and Sullivan 2005). At times, we recommend metronomic (low dose) therapy that involves using low doses of Cytosan, Leukeran, and lomustine concurrently. Deeply bonded clients may readily accept these options. At this point most clients have begun to accept that their geriatric oncology pet has received a noble effort by all concerned.

Metronomic Chemotherapy

Metronomic chemotherapy is the use of anticancer drugs at a lower dose and a higher frequency, aimed at inhibiting angiogenesis. It is a viable palliative option for patients with resistant, inoperable,

advanced cancer. It is especially useful for geriatric oncology patients with recurrent cancer. Often, the geriatric oncology patient's family declines standard recommendations for salvage surgery, rescue chemotherapy, or radiation therapy. They fear that their aging pet cannot tolerate further aggressive treatment. Metronomic therapy may use any combination of NSAIDs, Cytoxan, tamoxifen, and doxycycline for their reported antitumor effects.

Metronomic therapy incorporates an evidence-based and scientific method of therapy, although the exact mechanisms of action are not fully understood. It is very well tolerated (Liptak et al. 2004; Mutsaers et al. 2001).

I have frequently used low dose, increased frequency therapy as a kinder, gentler way to approach recurrence in my geriatric cancer patients. It is also helpful for frail geriatric oncology patients with concurrent illness or malnourishment and in patients with reduced renal and hepatic functional reserve. Metronomic therapy is a viable palliative option for recurrent STSs and recurrent abdominal organ tumors. With metronomic therapy, we educate the client to be satisfied with achieving stable disease rather than looking for complete remission.

Recurrent Soft Tissue Sarcoma (STS)

STSs including feline vaccine-associated sarcomas (FVASs) are the most common locally recurrent malignancies that veterinarians and oncologists grapple with. If the geriatric oncology patient received aggressive enblock specialty surgery followed by radiation therapy, the tumor-free interval is generally longer. Most STS recurrences take place within 6–8 months from first excision. If the STS patient is not a surgical cure, the mass generally appears within 1 year. Geriatric patients with hemangiopericytoma have the longest tumor-free intervals in the STS group.

Lady's Case (Not All Third Recurrent FVASs Are Doomed)

Lady O'Donnell, a 13-year-old F/S DSH, presented with her third recurrence of FVAS in the interscapular space. The O'Donnells asked me to help them save Lady. After evaluating the history, I decided that we might be able to help, even though the literature says that further surgery at the third recurrence of FVAS has no survival value. In Lady's case, her attending doctor performed her first two surgeries. Her third surgery involved a referral institution that utilized photodynamic laser therapy. But it recurred and enlarged over several months.

When we evaluated Lady, the mass was $6 \times 6 \times 4$ cm, lobulated but moveable. Thoracic and abdominal x-rays showed no metastases and no bone involvement. Blood work and urinalysis showed that Lady was in overall good condition for her old age. We used our multimodality protocol that combined surgery, intraoperative chemotherapy, and RTx. This was followed by external beam RTx and carboplatin chemotherapy. Lady had no recurrence of her FVAS for the following 3 years. She developed hyperthyroidism, malignant mammary adenocarcinoma, and GI lymphoma that were each successfully treated. Lady died of renal failure at age 16½. The O'Donnells were very grateful to have the extra years with their dear Lady.

Recurrent STS and recurrent FVAS are generally more aggressive than the original tumor. Tumor-free intervals shorten with subsequent surgeries. There is a point after which surgery is no longer helpful. Epidemiological studies conducted by Dr. Phil Kass of the University of California, Davis, found that there was no significant extension of survival times for cats with FVAS after the third surgery (Kass et al. 1993). In my experience, when the original tumor and its recurrences were previously

treated with routine surgery or other superficial techniques, then a more aggressive definitive surgery incorporating multimodality therapy can be successful in selected cases such as Lady's.

Each geriatric cancer patient's treatment history and current health status must be completely re-evaluated for restaging the recurrence. Results from radiographs, blood work, and appropriate imaging techniques, such as ultrasound, CT, MRI, or PET scans, will aid in decision making for treatment of recurrent STS (McEntee 2004). The principles used at the first approach would also apply for the second or third approach if a cure were still possible. Long-term survivors may develop other tumors and be clinically misdiagnosed as having recurrence (see Figure 8.2). The efficacy and safety of repeating a course of radiation therapy is very difficult to assess and requires individualized case management by the radiation oncologist.

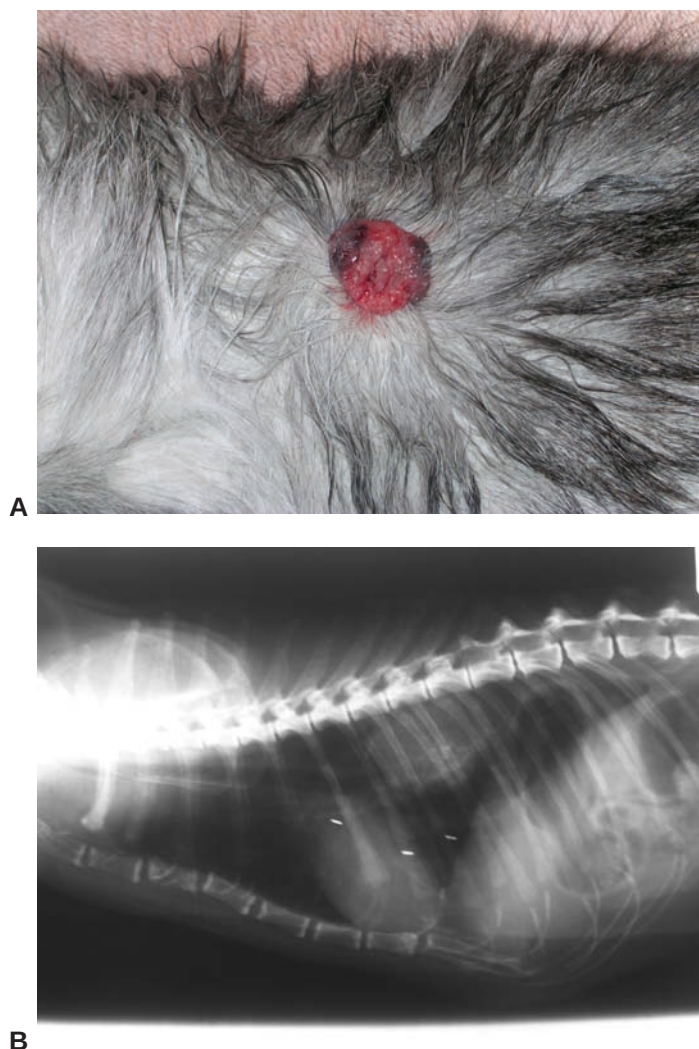


Figure 8.2. 18-year-old Hiss Clouse developed a tumor on his skin (a) suspected of being recurrent vaccine-associated fibrosarcoma, treated 4 years previously. A solitary pulmonary mass (b) was suspected to be a metastasis. The skin tumor was a hair matrix tumor and percutaneous FNA of the pulmonary mass found marked suppurative septic inflammation. This mass was also radiographically consistent with feline bronchial SCC.

Normal tissues cannot tolerate radiation therapy doses that exceed a total dose over 6.5–7 gray (Thrall 2001). In selected cases, a high dose fraction delivered to a shrinking field can target the most aggressive extension of a recurrent sarcoma's tentacles. Collaboration between the radiation oncologist and the surgeon is essential when considering surgery and additional radiation therapy for tumor recurrence at a previously irradiated site.

Tigger's Case (Don't Give Up if the Recurrent Tumor Volume Is Small)

Tigger, a 12-year-old M/N DSH, developed a second recurrence of vaccine-associated sarcoma in the left prescapular lymph node area. The recurrence followed two extensive surgeries that involved multimodality treatment, which included intraoperative radiation therapy, follow-up RTx, and chemotherapy. Tigger's owner had myelogenous leukemia and underwent a bone marrow transplant while his dear Tigger received the follow-up RTx treatments. Tigger's first recurrence was within 3 months and it was treated vigorously with wide surgical excision and intraoperative RTx. The second recurrence occurred within 2 months in the prescapular lymph node area. One of my associates told Tigger's owner that the prognosis was grim and that there was nothing else to do for Tigger.

He came to see me a month later. Tigger appeared healthy with the exception of the 3 cm mass threatening his survival. I looked into his master's soulful eyes and could tell that he was brokenhearted about the thought of giving up on his best friend. I told him that I would hate to see a small lesion like that sarcoma kill his cat, and that I would not give up on Tigger if he still wanted me to fight for his life. He said that he was out of remission too and that his doctors had not given up on him and that he wanted me to try to save Tigger.

We performed a third multimodality procedure for Tigger. It involved aggressive excisional biopsy, intralesional carboplatin, and a megadose of intraoperative RTx. Tigger survived another 5 years cancer free following that gut-wrenching decision to treat his recurrence. In fact, he outlived his master!

Recurrent Mast Cell Cancer

Mast cell tumors are the most common potentially malignant and fatal skin tumors in dogs. They are also among the most likely to recur if not removed widely. Geriatric oncology patients with recurrent mast cell tumor (MCT) require full staging of their disease before localized therapy such as surgery or radiation therapy is elected. Staging consists of FNA of the liver and spleen and local draining lymph nodes in addition to current blood work, urine analysis, and radiographs. A subset of geriatric oncology patients with previous MCTs will grow new tumors periodically. Another subset will develop numerous MCTs in the skin. Management options are most successful when each patient is carefully evaluated and given individualized cancer care.

Katie's Case (Recurrences Every 2 to 3 Years Are Treatable)

Katie Haddon, a F/S Rhodesian Ridgeback, developed multifocal cutaneous MCTs starting at age 3. She developed new MCTs that appeared every 2 to 3 years. Most of her MCTs were operable. When Katie was 11 years of age, she developed a rapidly growing mast cell tumor on her tail. Rather than amputate her tail, the Haddon's elected radiation therapy for Katie.

Jodi's Case (Cryotherapy, an Option for Mast Cell Recurrences)

Jodi Hoffman, a very high-strung 8-year-old F/S Boxer with MCT, developed new MCTs that were removed surgically every 3 to 4 months over a 1-year period. Jodi was also stressed with the rigors of dealing with a large chronic corneal ulcer. Her family dreaded the thought of more surgery every time a new MCT appeared. We offered the alternative of using cryotherapy for Jodi's next MCT. She was given local anesthesia with lidocaine and we infiltrated the area surrounding the mass with Benadryl[®] and dexamethasone. Liquid nitrogen was applied for three freeze-thaw cycles. The lesion swelled initially and then regressed over a 3–4 week period with no complications. This option spared Jodi's family the cost and emotional trauma of putting her through yet another stressful surgical procedure.

Recurrent Hemangiosarcoma

Waiting for recurrence of hemangiosarcoma in post-splenectomy patients is a dread-filled vigil. Many clients decline chemotherapy using the VAC protocol (vincristine, Adriamycin, Cytosan) or single agent Adriamycin due to the potential for adverse side effects, cost, and poor response despite treatment. Explain to clients that when hemangiosarcoma recurs, the patient will generally slow down or “crash.” Recurrence is generally multifocal and disseminated with vascular lesions that cause low-grade DIC, hemorrhage, thromboses, blood loss anemia, weakness, and pale mucous membranes. Teach clients how to assess and be ready for their geriatric oncology pet to crash.

Unfortunately, surgical intervention has been hopeless against hemangiosarcoma recurrence due to its aggressive ability to form multifocal blood channels (“auto-angiogenic”) in the abdomen, chest, and blood stream (Khanna 2004). Monitoring the patient with chest x-rays, as well as a periodic recheck ultrasound of the abdomen and heart, may occasionally detect a treatable, resectable lesion. However, without promising follow-up therapy, it would be very difficult for any oncologist to encourage a second surgery to remove one or two recurrent lesions due to the predictability of microscopic disease within a short time. The multifocal pattern of metastases with hemangiosarcoma makes treating recurrent bleeding episodes unsuccessful.

Consulting with clients at the time of recurrence and hemoabdomen should also be aimed at comforting them as they face the emotional trauma of pet loss. The family may want to take the patient home for some private last moments in Pawspice care. The patient may be very weak, anemic, and in shock. Most doctors would shun the idea of allowing a hemorrhaging cancer patient with DIC to go home in this near death condition. However, the client certainly has the right to take the family pet home to die, despite our professional reluctance to discharge such a sick patient. Many caregivers want to and are prepared to hold a vigil for their dying pet. Our job is to make sure that the geriatric oncology patient is not in pain.

We can expect and hope for better control for recurrence of hemangiosarcoma in splenectomized patients in the future with the use of multiple targeted therapy drugs. It would be ideal if we could use a combination of effective gene therapy, anti-angiogenesis agents, small molecule therapy, and possibly a histone deacetylase (HDAC) inhibitor like suberoylanilide hydroxamic acid (SAHA) (Cohen et al. 2004). Stay in touch with the use of other HDAC inhibitors such as valproic acid, which may enhance the effects of Adriamycin (Thamm et al. 2006). New technology may unfold methods to detect and enhance the treatment of this fatal vascular cancer, as well as osteosarcoma (OSA).

Recurrent, Metastatic Osteosarcoma

Most canine OSA patients originally present with appendicular lesions. If the family is willing to treat, the lesions are most often managed with amputation and chemotherapy. These treated patients are at great risk to develop metastatic pulmonary disease.

Few viable options exist to successfully manage pulmonary metastases. Metastatic clones are generally very resistant to chemotherapy. Dr. Chand Khanna benefited a small number of dogs in a study using inhaled interleukin-2 (IL-2) encapsulated liposomes. That study is closed.

Researchers are attempting to develop a clinically useful OSA tumor vaccine. A vaccine for OSA may become the favored option for future consideration. Check the Louisiana State University and the Colorado State University Web sites for updates on clinical trials using this promising therapeutic modality. These sophisticated options may become more available for dealing with recurrent OSA lesions in dogs in the near future.

The overall prognosis for dogs with OSA is better for those patients with recurrent lesions that do not have a large soft tissue component or concurrent hypertrophic osteopathy. The prognosis is worse for OSA patients with elevated serum alkaline phosphatase (Dernell, Straw, and Withrow 2001), with lesions located in the proximal humerus, and with lymph node involvement (Hillers et al. 2005).

Many caregivers decline amputation for their OSA dogs, especially if metastasis is present at diagnosis. Palliative IV chemotherapy using carboplatin along with IV bisphosphonates and oral piroxicam or radiopharmaceutical treatment with samarium may be of value to slow down the rate of growth and the painfulness of metastatic bone lesions (Dernell, Straw, and Withrow 2001). Pain control using a combination of analgesics as described in chapter 7 is the most important goal for patient care.

Pulmonary Metastatectomy

Dogs that survive initial treatment for OSA are at great risk for pulmonary metastases. There are few viable options when dealing with pulmonary metastases. They are considered more resistant to chemotherapy than the primary tumor. Periodic chest x-rays or CT scans are the mainstay for monitoring and early diagnosis. CT imaging helps to evaluate the lung fields to rule out sub-clinical metastases that are not detectable on plain radiographs. Metastatectomy holds promise in selected cases. The best results from metastatectomy are for dogs that have been tumor free for over 10 months with less than three metastatic tumors localized in one lung lobe. Although pulmonary metastatectomy is difficult and expensive, it is possible to extend the survival of selected metastatic osteosarcoma patients with a carefully planned procedure. If the patient has more than 300 days tumor-free interval, a limited number of tumors with a more than 30-day doubling time, and a negative bone scan, that dog is considered a reasonable candidate.

The surgical approach to these cases requires sternotomy or thoracoscopy. Close attention to perioperative pain control is essential. A tumor on the surface of a lung may be removed via sub-pleural enucleation. A tumor in the distal part of a lobe may be removed via partial lung lobectomy. When there are multiple tumors in one lobe or in the proximal lobe, lobectomy is required.

The median survival for 36 dogs treated with metastatectomy was 176 days ranging from 20 to 1,495 days (O'Brien et al. 1993). Pulmonary metastatectomy has been successful in controlling the painful symptoms of hypertrophic osteopathy in at least four dogs with pulmonary metastases from osteosarcoma. The surgical procedures were well tolerated and restored the quality of life for all four

dogs for 50, 51, 246, and 265 days, respectively (Liptak et al. 2004). When consulting with clients about this option, we must educate them about the fact that another wave of metastatic nodules may overtake the remaining lung lobes. There is no guarantee that the lung fields will remain clear in the geriatric oncology patient's near future.

Leaf's Case (Pulmonary Metastatectomy Helped Him Live Longer)

Leaf, a 10-year-old M/N Yellow Lab mix, had a mandibulectomy followed by four treatments of cisplatin for OSA of the mandible. One year later, Leaf's chest x-rays showed a 2 cm nodule in the right middle lung lobe. We followed the mass for another month and detected a satellite growth or a new metastatic nodule near the previous metastatic nodule. The client elected lobectomy for Leaf. He recovered uneventfully and survived another year before pulmonary metastases recurred. Although the new tumors also were amenable to a second lobectomy, the family declined the procedure.

Recurrent OSA Lesions in the Axial Skeleton

One-third of treated long-term OSA survivors may develop metastatic OSA lesions in their long bones. The patients are generally already three-legged. The new lesion is painful but the caregivers cannot consider a second amputation. They want and need more options to pursue. Palliative radiation therapy with several follow-up fractions or a full course of 18 fractions has been successful in helping to palliate and treat some cases of recurrent osteosarcoma (Dernell, Straw, and Withrow 2001). This option has the potential to extend the life for some dogs with recurrent OSA of the long bones.

Murphy's Case (Long Life After Limb Salvage for Her)

Murphy, a 5-year-old F/S Great Dane belonging to Dr. Robin Downing, DVM, was cancer free for 3 years following a limb salvage procedure at Colorado State University for OSA of her left distal radius. Murphy received two doses of cisplatin and two doses of carboplatin. She developed a low-grade beta hemolytic *Streptococcus* infection at the allograft, which was responsive to Clavamox®. Robin chronicled Murphy's treatment in her book *Pets Living with Cancer: A Pet Owner's Resource* (Downing 2000).

Three years after limb-sparing surgery, Murphy developed lameness in her right hind leg. She was diagnosed with a ruptured anterior cruciate ligament and a tibial plateau leveling osteotomy (TPLO) procedure corrected the problem. After 2½ months of rehabilitation, Robin noticed asymmetry of the right malleolus. Radiographs demonstrated a prolific lesion at the distal right tibia at the distal pin site, consistent with osteosarcoma. The lesion was confirmed as OSA with histopathology.

It was presumed that Murphy's lesion was recurrent metastatic OSA and that it would be resistant to further chemotherapy. The lesion was not amenable to a second limb salvage. Robin decided against amputation. During her struggle with decision making, Robin asked me for a second opinion. My postulate was that Murphy's new lesion was too far away from her primary to be a metastasis. I felt that this lesion was a *de novo* osteosarcoma and that it had the same odds of being responsive to treatment and chemotherapy as her primary OSA. I advised Robin to try palliative radiation therapy and treat Murphy with at least four rounds of carboplatin chemotherapy.

Murphy entered a clinical study group of 15 patients that would receive full-course radiation therapy at CSU to their OSA lesions in 18 fractions, to spare the skin. Murphy survived another 13 months, totaling 4½ years, with her original limb-sparing allograft. Murphy died peacefully in her sleep from dilated cardiomyopathy at 9½ years of age. Necropsy found three small metastatic pulmonary nodules and no viable cancer cells in her tibial lesion (Downing 2005).

In the future, other novel therapeutic options for a patient like Murphy may be available for OSA patients in your practice such as an OSA vaccine, use of a bone-seeking radioisotope called Samarium, or use of stereotactic radiosurgery.

Advanced and Recurrent Mammary Cancer in Dogs

Mammary tumors and recurrence are very common in older, intact female dogs and in dogs spayed after 2½ years of age. In such cases, take the time to educate the family that their pet's entire mammary chain has undergone "field cancerization" resulting from hormonal influence on target mammary tissues. The patient may have metastatic disease and be developing new local tumors and/or having recurrence of old tumors simultaneously. New mammary tumors have a 50% malignancy rate. They may be unrelated to the patient's previously excised tumors and not as dangerous as a locally invasive recurrence of an incompletely removed mammary tumor.

Radiographs that examine three views of the chest and sub-lumbar/iliac lymph nodes are essential to determine the stage of disease prior to radical mastectomy. If chest radiographs are negative for metastatic disease, surgery is the best procedure for advanced stage and/or recurrence of localized multiple mammary adenocarcinomas. Radical mastectomy with local lymph node excisional biopsy may be curative. If the mass is adhered to the body wall, include the body wall with the resection. Ovariohysterectomy of older mammary tumor patients does not inhibit recurrence, but it spares camouflaging recurrence with mammary hypertrophy (Ogilvie and Moore 1995; Rutterman, Withrow, and MacEwen 2001; Morrison 2002c).

Mammary adenocarcinoma in geriatric oncology dogs and cats can be treated more safely with mitoxantrone than with Adriamycin. Using dose escalation, start with 5 mg, then 5.5 mg, and do not exceed 6 mg/m² every 21 days for six IV treatments. My preference is to avoid cardiotoxic Adriamycin in aged patients unless their carcinomas are resistant to mitoxantrone.

For frail patients or clients with financial restraints or reluctance to continue IV chemotherapy, consider the use of metronomic (low dose) oral therapy. Oral Xeloda® has proven activity against adenocarcinoma. (*NEVER use Xeloda in cats because it turns into 5-FU, which KILLS cats.*) For dogs, I use an empirical dose of Xeloda at 500 mg/m² PO 48 hours and rotate this with Cytosan at 25 mg/m² PO q 48 hours. Piroxicam at 10 mg/m² can be added to this protocol as a chemoprevention agent along with selected immunonutrition supplements.

Advanced Stage or Recurrent Mammary Cancer in Cats

Because cats are independent and self-groom, their mammary carcinomas may not be diagnosed until they are in advanced stages of disease. Cats with a history of primary mammary carcinoma are at great risk for local recurrence, regional metastases, and pulmonary metastases. Educate clients that bilateral chain mastectomy is the best-known precaution for long-term survival in cats diagnosed

with primary mammary carcinoma. The patient's best opportunity for prevention of recurrence rests with your initial management strategy. By recommending bilateral radical mastectomy from the start, you may save the cat's life. Remove the tumor-bearing mammary chain first, followed by excision of the opposite chain within 4 to 5 weeks whenever possible.

When dealing with recurrence, make new radiographs that show three views of the chest and two views of the abdomen to rule out pulmonary metastases and sub-lumbar/iliac involvement. Restage the geriatric cat before attempting a second surgery or a first bilateral radical mastectomy. The second incision should include excision of the previous surgery site. If mammary nodules recur along the chain or at a previous surgery site, they may be approached surgically once again. If the mass is touching the body wall or is adhered to fascia overlying the ribs or body wall, excise at least one fascial layer below the mass or remove that section of the body wall.

If the cat received prior chemotherapy, select an agent that has not yet been used for follow-up chemotherapy. If you used mitoxantrone previously, then use Adriamycin and vice versa or use carboplatin at 21-day intervals. If the family declines IV chemotherapy, consider metronomic therapy with low dose oral Cytoxan and piroxicam, and suggest immunonutrition as an optional supportive therapy.

Recurrent Anal Sac Carcinoma Over 4 Years

Tumors arising in the last inch of the GI tract are generally not noticed until they cause local irritation, swelling, tenesmus, and abnormal passage of stool. This holds true for recurrence or metastasis from the primary mass. If the primary tumor caused malignant hypercalcemia (MH), calcium levels can be used as a tumor marker to monitor for recurrence or metastasis. Some cases do not have recurrent hypercalcemia until the recurrence reaches a certain tumor volume such as a large sub-lumbar mass obstructing the distal colon.

Some dogs are presented with deep sphincter recurrence along with enormous sub-lumbar lymphadenopathy. It was not the primary tumor that caused the clinical signs but the pressure from the lymphadenopathy pushing the colon downward and obstructing the passage of stool through the pelvic canal. The primary tumor may not recur following surgery in some cases. The patient's metastatic disease becomes clinically obvious around 6–9 months following the initial surgery. Chemistry and electrolyte panels may not show abnormalities in calcium levels.

A point to remember is that male dogs with anal sac adenocarcinomas were initially suspected to have benign hormone-dependent perianal tumors. Another issue confronting the clinician is that FNA offers no cytological help in differentiating the malignant anal sac gland carcinomas apart from the benign hormone-responsive hepatoid gland tumors. The basement membrane or wall of the anal sac must be submitted for biopsy for definitive diagnosis (Goldschmidt and Hendrick 2002).

Rosie's Case (Anal Sac Carcinomas Respond to Debulking)

Rosie, a F/S Australian Shepherd, shares her life with one of our profession's most treasured personalities, Dr. Robert M. Miller (RMM cartoons and "Mind Over Miller"). At 8 years of age, Rosie developed metastatic anal sac adenocarcinoma (ASC), manifested by sub-lumbar/iliac lymphadenopathy. Her chest x-rays were negative for pulmonary metastases and she had normal blood chemistries with no hypercalcemia.

The Millers told me, "We were given a poor prognosis for her, so we'll let Rosie go naturally." I consulted with them about the literature and my personal experience with ASC. I recommended

that they at least have the primary mass excised so that Rosie would have less discomfort. The Millers declined my suggestion for exploratory celiotomy for sub-lumbar/iliac nodectomy and chemotherapy. They elected to use piroxicam for its antitumor effects and two oral supplements selected from our immunonutrition protocol: Inositol hexaphosphate (IP-6[®]) and a full range of beta glucans from the *Agaricus blazei* mushroom.

Rosie celebrated a 1-year anniversary with a surprise: Her recheck x-rays and ultrasound did not identify sub-lumbar/iliac lymphadenopathy and there was no evidence of local disease.

Two years later, Rosie developed a new mass on the opposite anal sac. The mass was excised and diagnosed as ASC. In her third year (Figure 8.3), Rosie developed tumors that slowly encircled her entire anal sphincter. She remained relatively asymptomatic. At age 12, Rosie developed tenesmus. Dr. Miller obtained several opinions regarding surgery and radiation therapy for Rosie. The consulting surgeons felt that the mass was inoperable and would create incontinence. Other options, such as radiation therapy, did not appeal to the Millers due to the fact that her iliac nodes were enlarged. They reported that Rosie exhibited tenesmus during elimination but otherwise seemed to behave normally with an excellent quality of life. Rosie was managed with stool softeners and a soft food diet. I recommended adding an opiate pain control medication, Tramadol[®], to complement the piroxicam.

For advanced ASC cases like this, I recommend palliative radiation therapy or palliative debulking laser surgery to shrink the local mass, chemotherapy with oral Xeloda (capecytabine) at 500 mg/m² BID for 10 days on and 10 days off, 50 mg Cytoxan q 48 hours (in the morning, 15–20 minutes before urination, with a big bowl of broth), and continuation of piroxicam.

Dr. Miller's goal was to maintain Rosie's well-being for as long as possible. We entered Rosie into our Pawspice program. The Millers wanted to enjoy Rosie's cheerful life until her time came.



Figure 8.3. Dr. Robert M. Miller (cartoonist RMM) and Rosie celebrating her 3-year anniversary with metastatic anal sac carcinoma. A new mass was excised on the opposite anal sac after 1 year. After 2 ½ years, local recurrence slowly infiltrated her anal sphincter 360 degrees. Her quality of life was good on chemoprevention and immunonutrition with piroxicam, *Agaricus Bio*, and IP-6[®].

Residual or Recurrent Nasal Cancer

The radiation oncology and surgical oncology departments at North Carolina Veterinary College start out with a treatment plan for nasal tumors that intentionally addresses residual and recurrent disease. They educate clients about the shortcomings of historical treatment for nasal cancer and propose a way of dealing with the expected.

Following external beam radiation therapy to the nasal cavity, patients are followed up with routine CT scans to determine and delineate residual or recurrent tumors. When detected, these are surgically removed. Patient survival times exceed those of historical controls. This multimodality approach uses a combination of radiation, imaging, and surgery to enhance survival times (Henderson 2005).

Rufus's Case (a Chondrosarcoma Responded to Chemotherapy)

Rufus Gleason, a M/N 9-year-old Black Labrador Retriever, had epistaxis and stridor due to nasal passage chondrosarcoma. The family declined definitive radiation therapy for Rufus but elected aggressive palliative chemotherapy with carboplatin, piroxicam, and immunonutrition. The epistaxis and stridor regressed for 2½ years. Rufus regained his energy and entered numerous 10K walks. Recurrence manifested as progressive stridor with swelling of the muzzle that enlarged steadily, causing facial deformity. It was resistant to further chemotherapy.

Rufus entered Pawspice care as cheerfully as he had handled his other treatments. The family even took him cross-country for a family reunion. He survived with a surprisingly good quality of life for 4 additional months (Figure 8.4).



Figure 8.4. Rufus Gleason at recurrence of nasal chondrosarcoma after 2½ years of remission with carboplatin and piroxicam chemotherapy. His recurrence caused extensive nasal deformity and was resistant to carboplatin.

Multiple Primary Malignancies

What if the geriatric oncology patient develops a second, third, or fourth cancer? Some scientists propose that cancer should be considered another geriatric syndrome (Ershler 2004). One of my patients, a 13-year-old black Cocker Spaniel named Ruben, developed seven types of cancer over 4 years. Ruben started out with lymphoma at 9 years of age. He responded well to chemotherapy. Along the way, he developed sebaceous gland adenocarcinoma, ceruminous gland adenocarcinoma, sweat gland adenocarcinoma, bladder cancer, and malignant melanoma. Ruben responded well to treatment for these new primary neoplasms and maintained a good quality of life. Finally, he developed SCC deep in the nasal septum.

We helped the family understand that Ruben had experienced a failure of his innate immune system. His repair genes and tumor suppressor genes, which normally suppress the genetic mutations that lead to cancer, were dysregulated in the process of senescence. We also explained that chemotherapy has a negative effect on the immune system. The family understood that Ruben developed his cancers due to a decline of his normal immunosurveillance system. This explanation helped the family in their decision making. It was the challenge of the SCC that caused Ruben's caregivers to surrender his battle against cancer.

The Role of Integrative Medicine in Advanced Stage and Recurrent Cancer

Many pet owners want to leave no stone unturned, especially when facing recurrence, relapse, or metastasis in their geriatric pet. They appreciate having options to pursue when conventional medical technology can no longer help their pet. Some caregivers observe that their pets feel better when a combination of supportive alternative therapies is provided alongside conventional protocols. Some clients with pets in chemotherapy feel that the drugs cause too many side effects and make their pet sick. They shun conventional therapy in preference to holistic therapy, hoping that it will cure their pet without side effects.

According to a survey by the American Animal Hospital Association (Moore 2005b), the percentage of clients seeking alternative therapies went from 6% to 21% over the past decade. When the attending clinician loses patience with the client or gives up on the case, caregivers often feel that they have nowhere else to turn. If caregivers feel that the doctor is unable to help their pet, they will often seek out alternative, complementary, and integrative medicine with or without your blessings. They seek solutions to the problems with alternative therapies such as nutritional therapy, acupuncture, chiropractic, homeopathy, herbal medicine, massage therapy, magnet therapy, aromatherapy, and so forth. Many pet owners feel that blending alternative techniques along with a doctor's conventional orders could potentially benefit their pet's quality of life.

When clients ask my opinion about trying alternative care for their pet's recurrence, the first thing to I do is take a moment to praise their love and devotion for their pet because it is their special love bond and anticipatory grief that are motivating them to keep searching for a "cure."

Regardless of efficacy, one very important ingredient that alternative medicine offers is hope. This is in contrast to the evidence-based paradigm of our conventional western medicine that generates statistical data on response rates, disease-free intervals, and survival times. Western medicine shares some aspects of the herd health care system, treating large groups of patients with A or B and analyzing the results with statistics, percentages, and survival charts. Holistic medicine focuses on the

patient as a whole, unique individual and is one-on-one oriented. This approach can be very comforting and nurturing for the weary family of a geriatric cancer patient.

A working definition for hope is to wish for something with expectation. Alternative therapies are ministered to the patient with hope. The promise of hope is alluring and very difficult for a caretaker to resist when a geriatric pet has recurrent cancer with comorbidities, discomfort, and a poor prognosis.

Point out that researchers have examined a number of the most efficacious remedies offered in holistic and alternative medicine and that some techniques do have merit and efficacy while others are unsubstantiated or questionable.

As a rule, if an integrative technique seems to alleviate pain and adverse conditions or improve the patient's well-being and survival, then it is good to continue. If there are no benefits after four visits or treatments, then it makes sense to stop the treatment unless the effect is expected to be long range, as with immunonutrition.

Nutrigenomics, Immunonutrition, and Chemoprevention

Today's scientists have a greater understanding of how nutrients affect health. The new field of nutrigenomics studies the molecular alterations of gene activities after specific dietary nutrients with specific genomes are consumed. It explores the mechanisms of how nutrients affect genes by turning them on or off to benefit the patient (Moore 2005a).

Immunonutrition is the mainstay of my integrative approach toward supporting cancer patients. Clients want to provide the best possible nutritional support at all stages of their pet's cancer (see Table 6.9). Combining immunonutrition, chemoprevention, and metronomic therapy helps to support and palliate geriatric cancer patients struggling with recurrence. At times, this is the only type of therapy that the family is interested in or will allow.

After a considerable amount of investigation, I selected a limited number of scientifically researched and trustworthy supplements from a plethora of available products for our immunonutrition protocols. We select supplements for each individual geriatric cancer patient's specific needs. In the selection process, it is imperative that the product be prepared by an ethical company. They have high standards for quality control. There are thousands of products available on the market, but approximately 38% of the products misrepresent contents with inaccurate information on the product label. This variability creates chaos, is responsible for variable results, and validates skepticism about supplements and nutraceuticals.

The highest quality supplement companies undergo rigorous self-inspection standards that parallel the regulations of the pharmaceutical companies. At times, immunonutrition and chemoprevention are the only supportive therapies that are safe and nurturing for the geriatric patient grappling with recurrence.

Summary

There is a great deal of uncertainty in decision making for geriatric pets with advanced stage, recurrent, and relapsed cancer. There are no age-based studies from which one may extrapolate helpful information. Veterinarians need to rethink their overall reluctance to working with geriatric cancer patients. Advanced stage cancer and recurrence in older dogs and cats finds the veterinarian ministering

to a very heterogeneous group of complex geriatric oncology patients. These cases may help readers gather “situated knowledge” and practical wisdom for clinical judgment in the emerging area of geriatric oncology.

Every doctor has a horror story where the outcome was far from the intended purpose of therapy. Geriatric oncology patients are complex and challenging and they can be fragile and unpredictable. Dr. Patricia Olsen, PhD, president/CEO of Morris Animal Foundation, during a 2005 interview with *Veterinary Medicine*, said, “In life, we are responsible for our efforts but not the outcome. You have to expend considerable effort, but also remember that you can’t always be responsible for the outcome” (Olsen 2005).

We must ponder over the most difficult emotional, ethical, economic, and medical issues inflicted upon us by cancer’s recurrence, relapse, or metastasis in our geriatric oncology patients. Once we make a decision that we feel is right for the patient and family, we should be able to live with that decision, no matter what complications come afterward. If we blame ourselves for all the failures that oncology will inflict upon us, we will slip into compassion fatigue and wither.

Paternalistic decision making must be replaced with decision-making partnerships. When facing recurrence, many of your clients will be willing to jump into the heart of battle once again to keep an elderly pet even longer. They will enter round #2, 3, or 4 as long as they are enabled by your practice team to help them maintain a good quality of life for their geriatric pet. If you cultivate an optimistic attitude toward treating recurrence in geriatric oncology, you will be prepared to freshly assess each patient’s unique situation.

Reach out to help those heartbroken caregivers who are stumbling down the difficult road of relapse and recurrence. The recurrent cancer is gnashing at their pet’s survival and their personal happiness. Clients intuitively look to their veterinarians as healers. You have the power and knowledge to help clients negotiate the hurdles on the bumpy road to their pet’s next remission and, when all else fails, you can help them find their way at the end of the road.

Patient evaluation using the body score, performance level, and quality of life assessment add up to an impression of the overall condition of the recurrent geriatric cancer patient. These factors have a direct impact on prognosis and creating an individualized viable treatment plan to help and, most of all, not harm the geriatric patient.

Be supportive, whether clients choose the high road or the low road. Help them to pass through that difficult threshold of re-evaluation and decision making, when recurrence strikes their pet. Provide the client with satisfactory options for dealing with the recurrence and pain control, while maintaining a good quality of life. Consider metronomic therapy, especially for geriatric patients with reduced functional reserve.

Suggest chemoprevention with currently proposed agents or COX-2 inhibitors, when appropriate and safe. Provide immune support with immunonutrition using currently proposed immune enhancement agents. These are viable options for pet owners to pursue if they feel they must decline standard therapy. Help the family go forward with their decision, offering encouragement and validation to help them maintain their pride and confidence.

Treat recurrence in geriatric oncology patients as a geriatric syndrome that involves physiologic stress and pain. Presume that cancer causes stress and immunosuppression on the body. It is also safe to presume that the cancer was caused by the biology of aging and its related stresses with free radical damage, exposures to environmental carcinogens, and decline in immune function. Therefore it makes sense to support the immune system and to scavenge free radicals whenever feasible.

Treat the pet for cancer pain by presuming that cancer hurts by its mere presence, even if overt pain is not obvious to you or the caregiver. Use the proposed pain scoring system at

www.colostate.edu/depts/lar/Pain_Assessment.doc. Teach clients to assess quality of life using criteria similar to the proposed HHHHHMM Quality of Life Scale described in chapter 10 to monitor and assist the patient's needs on a weekly or monthly basis. Give your clients the working knowledge and the tools to bravely and competently assist their geriatric pet in round #2, 3, or 4 in the battle against cancer.

You can offer the major helping hand during decision making, treatment, or palliation. Pet caregivers will always be grateful for your kindness and helpfulness. For me, the task at hand is to pay homage, time after time and case after case, to the amazing human-animal bond, as each heartstring is plucked one by one. This goal bestows a greater and sublime purpose to the art of practice.

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Chapter 9

When and How to Decide That a Geriatric Cancer Patient Is Terminal

To be a scholar is not enough. . . . We must realize that we live in an imperfect world, but that we are here to make it better. We should . . . respect . . . the ethic of reverence for life.

Leo Bustad, DVM, PhD

The anguish inflicted upon pet owners when they learn that their pet is terminal is heart wrenching. When you say there is nothing further that can be done to medically help their pet, the family feels helpless. Clients rightfully want to know when you think their pet's death will occur and what conditions will lead up to the death, but they need to hear this with sensitivity and regret in your heart. Let them know that you do not want to be right about the statistical prognosis and that there can be exceptions. We need to respond with kind, compassionate words when our clients' hearts are breaking.

One of the most frustrating problems in oncology is uncertainty. Science and literature tell us which cancers are incurable and allow us to quote the published survival statistics with and without treatment. Looking at statistics, we can only estimate approximately how much time a terminal geriatric patient has to live. Our educated guess is only a supposition because the literature does not provide us with focused information about the prognosis of geriatric oncology patients or the particular patient at hand.

Clarification of Terminology for Terminal

In addition, to say a cancer is terminal is different from saying that the pet is in the terminal stages of the disease. We must distinguish how we are using this powerful and hopeless word to help guide the family in the decision-making process. Veterinarians who use the word "terminal" when speaking to the caretaker should be careful to explain the expected survival time. You can say, "Terminal doesn't necessarily mean tomorrow or imminently. The statistic we have is an average. Some geriatric pets die sooner, especially if they have concurrent illness or if they don't tolerate or respond to treatment, others outlive the expected survival time." Using the word "terminal" when speaking to the client makes the most sense when the geriatric patient is in the advanced stages of cancer, or when the pet is ready to enter Pawspice care. At THAT point, it makes sense to use the word "terminal."

Criteria for Terminal Decision Making

The criteria most commonly used to decide if a geriatric cancer patient is in the terminal stages of cancer are based upon cancer type, stage of disease (tumor burden), histologic grade, and clinical

assessment of the patient's performance and biological age by the attending doctor (Repetto et al. 2004). Stage and grade factors do not always apply across the board to all tumor types. In a retrospective study of 38 cats with lymphoma, the only factor that influenced survival was initial response to treatment. Cats with complete remissions enjoyed median survival times of 654 days, while those with partial and no response had only 112 and 11 days, respectively (Milner et al. 2005). Treatment intensity may yield superior overall responses but cause more age-related or breed-related toxicity such as the vulnerability of Doberman Pinschers to Adriamycin cardiotoxicity (Stone, Goldstein, and Cotter 1991).

The interactions between aging and cancer and its treatment may have a positive or negative influence on quality of life and life expectancy and how we evaluate if a geriatric oncology patient is terminal. Oncology applied on top of geriatric medicine is not an exact science. This uncertainty may lead the attending doctor and client to come to the shared decision that favors no treatment, which in itself classifies the geriatric oncology patient as terminal.

Animals age with great variability and vulnerability. It is useful to refer to the comparable aging charts for species and weight. Clients need to understand how old their pet is in human years (Table 1.3). The geriatric oncology patient may be physiologically young when compared to other animals the same chronologic age. Other important factors to consider would be the geriatric patient's functional performance assessment, the impact of morbidity from concurrent conditions, and quality of life issues as discussed in chapters 8 and 10. External factors that have a direct influence on the veterinary cancer patient's survival include access to specialty care and new technology, the degree of emotional attachment of the caregivers, and the finances allocated by the family for their geriatric pet's care.

Objective data regarding evaluation of these criteria, which are germane to veterinary geriatric oncology, are currently not available. Veterinary geriatricians are enabling pets to live longer, healthier lives with antioxidant and co-factor enriched nutrition and high-tech medical care (Roudebush et al. 2005). The increased frequency of tumors in aging animals is largely due to senescence of the immune system and carcinogenesis via initiation, promotion, genetic mutations, and environmental exposure and age-associated changes in susceptible tissues (Lyman 2004).

The growing population of aging companion animals will provide us with more tumor-bearing geriatric patients. Veterinarians who are willing to multitask through these complex cases have the opportunity to expand the boundaries on the frontier of clinical geriatric oncology for companion animals.

Initial Presentation of a Terminal Case

Most veterinary patients do not exhibit obvious preliminary warning signs during the sub-clinical phase of malignancy. Senior and geriatric animals are less likely to exhibit clear warning signs of cancer due to the mingling of coexisting conditions and the physiological changes associated with aging (Table 2.2.), including obesity, which may camouflage cancer and shorten the pet's lifespan (Kealy et al. 2002). Geriatric pets are often presented to their local attending clinicians when they exhibit obvious symptoms due to advanced stages of cancer. Many are rushed to emergency clinics with an oncology-related crisis, which may need surgical intervention (Salisbury 2002). Initial assessments may presume or conclude the presence of cancer or an associated paraneoplastic syndrome. This prompts the need for further evaluation to establish a definitive diagnosis. The bad news often comes as a shock to the unsuspecting family, who may then be caught up in the spirit of battle against the cancer (Butler et al. 1991).

Clients may notice that their geriatric pet has some degree of gagging, coughing, or respiratory compromise or weakness. If the signs persist or worsen, they present their pet for examination by appointment or as an emergency. Initial x-rays may find widespread pulmonary metastatic disease, pleural effusion, or a globoid-shaped heart. This may immediately indicate the terminal nature of the patient's cancer.

It is important to confirm the diagnosis of cancer. Although fungal disease, anterior mediastinal lymphoma, thymoma, and lymphomatoid granulomatosis may appear as terminal cancer, these conditions may be responsive to definitive treatment. Pericardial effusion causing a globoid-shaped heart and muffled heart sounds was due to a benign or inflammatory process in 44% of 42 cases reported (Berg and Wingfield 1984). Occasionally, some patients maintain a tenuous but apparent well-being despite extensive pulmonary involvement.

There will always be surprises and exceptions to a prognosis. A geriatric dog collapses. Initial evaluation in the emergency room finds hemoabdomen with hypovolemic shock. Hemoabdomen is most often due to ruptured splenic hemangiosarcoma, hepatocellular carcinoma, and lastly adrenal carcinoma (Salisbury, Lafond, and Morrison 2002). Clinical and radiographic findings such as organomegaly, ascites, carcinomatosis, abdominal lymphadenopathy, and cardiomegaly require further imaging with abdominal and cardiac ultrasound to determine the cause and extent of disease. Ultrasound findings may show multifocal visceral lesions in multiple organs, consistent with terminal stages of metastatic disease. Splenic hematomas generally appear as solitary lesions with less cavitation.

Many clinicians suggest immediate surgery for all patients with hemoabdomen. Please note that it is not entirely necessary to operate on those patients who can be stabilized with aggressive supportive care. This dramatic scenario creates some regret for caregivers who were hastily advised that the only options for their pet were emergency surgery or euthanasia. Many pet caregivers would prefer to pursue the opportunity for stabilization and take their pet home for Pawspice care.

Cells and/or tissue samples are needed to establish a definitive diagnosis. If the findings are consistent with hemangiosarcoma, sarcoma, carcinoma, or malignant histiocytosis involving multiple organs in a susceptible breed, decision making may be straightforward. To date, systemic treatment provides only a low rate of response for aggressive multifocal visceral soft tissue sarcomas, carcinomatosis, or histiocytosis. A number of clinical trials are evaluating the use of immunotherapy, anti-angiogenesis therapy, small molecule therapy, and gene therapy (Helfand 2003; London 2004). These agents may prove helpful as adjuncts and permanent maintenance therapy when clinically available to bolster response rates.

Radiographic bone lesions that exhibit lysis and proliferation, characteristic of osteosarcoma, allow a working diagnosis of bone cancer for decision making. The Veterinary Cancer Society (VCS) has accepted radiographs showing bone lysis and proliferation at typical sites in large-breed dogs to be sufficient evidence for making the presumptive diagnosis to accept patients into bone cancer protocols. The protocols require histopathology of the lesions following amputation or limb salvage for definitive confirmation of the diagnosis.

The attending clinician often makes an immediate decision that a patient is terminal, based upon facts and figures provided on the minimum database examination. Therein lies the problem. We can't be right all of the time, even when things look obviously grim. We can advise clients that "Cats with extreme neutrophilic leukocytosis due to cancer are 14 times as likely to die unexpectedly within 30 days than cats with leukocytosis due to other diseases" (Lucroy and Madewell 2001). Nevertheless, there are patients who defy the prognosis and outlive our expectations.

Advising Deeply Bonded Clients in the End Phase

How do you converse with clients who want you to try to help their terminal geriatric cancer pets against all odds?

This is the time to set aside personal biases against age and cancer, which *dishonor* The Bond. Avoid fatalistic thinking that puts old clichés in your mind, such as, “The fat lady has sung. Let’s drop the curtain on this case.” Offer flexible options to people until they make the choice that fits their wishes.

How do you speak to clients who are clearly not comfortable with the options you suggest? Some pet owners feel that they were rushed or pressured by the attending doctor or emergency clinic doctor. They felt pressured to make a final decision, given the choices of euthanasia or definitive care at a costly estimate. The veterinarian’s role in pressuring clients to agree to euthanasia before the client is ready to do so has created a generation of caretakers who suffer for years, sometimes for the rest of their lives, from intense guilt.

There is a third option that many owners accept gratefully when the other two are not acceptable. Some pet caregivers want their pet to come home and pass away there, either by house call euthanasia or by natural death. Neglecting to offer this option puts our ethics and our ability to respect The Bond in question.

Dealing with deeply bonded caregivers in terminal situation decision making can be emotionally draining and difficult for the doctors and staff. This emotional trauma is called “vicarious traumatization” and appears as burnout, indifference, negativity, or depression (Norton and Cooper 2001). See the section on compassion fatigue in chapter 11.

Cecilia’s Case (A Deeply Bonded Caretaker Wants to Share Each Step of the Emotional Journey to the End)

Cecilia Corbin, an 11-year-old F/S Golden Retriever, recovered uneventfully following emergency splenectomy for hemoabdomen. Her owner, Julie Corbin, authored a PhD dissertation that I had reviewed the previous year.

Corbin wrote: “Cecilia’s biopsy confirmed hemangiosarcoma. One or two of the tumors on her spleen were benign but the rest, including the one that ruptured, were malignant. It was also confirmed that the small masses on her liver were cancer and it looks as though the cancer has already metastasized. We are in shock at that news, as her presentation is so very normal and her athleticism remains intact. I understand the seriousness of her condition.

I want to look at all options that will honor her spirit, will to live and most importantly her quality of life.”

Cecilia recovered quickly, but 10 days later, she collapsed. Corbin wrote: “Her hematocrit was 18%. Our doctor gave her supportive treatment. The next hour, her hematocrit went up to 20 and stabilized there. We stayed with Cecilia from 1:30 A.M. till 8:30 A.M. By morning, her hematocrit was 27%. We made the decision to take her home. You know how I feel about that. The hospital staff is getting a deeper understanding of the human-animal bond and the power of love and intention. The Hospital Administrator is a former pet bereavement client of mine. She gave us an exam room to stay overnight at the clinic and arranged for one of the Dr.’s to be on call. They were truly wonderful and not only tended to Cecilia but to us as well. That was such a Godsend to us.”

For bonded caretakers, it’s important to time the end of their pet’s life properly. Simply pulling the plug because it’s close to the end is not acceptable. These caretakers walk a thin

line and walking that line requires vigilance and careful timing. They do not want to deprive their pet or themselves of those last days, hours, or minutes, while still ensuring that euthanasia is not delayed past the point where the pet will be in pain or suffering.

Corbin wrote: “If Cecilia recuperates from this episode, would chemo still be an option or is she just too close to the end at this point? I understand the fragile nature of her condition and know that she could appear ‘perfect’ one day and the next be bleeding out, but she is showing us such a strong will to live. Any thoughts? Again thank you for ‘supporting’ us through this time. I wish Cecilia could meet you, but in a way I believe she already has.”

In reply, I commented that palliation with carboplatin in a split dose fashion four to seven days apart might help Cecilia (as it did Wheaty; see later in this chapter) and to stay on 24-hour vigil in case she develops DIC during her Pawspice. A few days later, Julie wrote: “Just wanted to give you an update on Cecilia. I NEVER thought I would see her acting her ‘normal’ self again. Less than two days after her near death experience, she is prancing around as if nothing ever happened. We are all stunned. She must be wonderdog! They really did not think she would make it—I had my doubts as well. . . . I sensed that our doctor thought she would not pull through (we even considered euthanasia that evening) and that she was coming home to pass on. I know that the tides could turn at anytime, but I am amazed at her ability to come back from this.”

Two weeks later, Cecilia was euthanized. On that day, Julie wrote: “Yesterday I took her for a walk on the trails and today I gave her peace—she was in pain and that is where I draw the line. I will call you when I have a bit more clarity. I am not able to even walk into our home, and we are at a hotel tonight. I miss my girl so much and was with her till her last breath—she is with me now in a different way but somehow right now that brings no comfort. I have never loved anything or anybody as I do her—this will be a real tough one.

The following illustrates what I call the “woulda-coulda-shoulda” stage of grief, where many people who experience pet loss are stuck. Even when the ending is handled perfectly, caretakers will still go through the stages of grief and will often want to put blame or fault on themselves, the doctor, or the clinic. Some will obsess about the final decisions and actions and question every little decision and action. A week later, Corbin wrote: “Hello Dr. V, I was wondering if you might be available for a phone consult. I would like to get your input on a few things. Cecilia’s doctor was not in on that day and the treatment protocol was much different. Cecilia’s hematocrit level that morning was 36 and they did not want to keep her at the hospital. I took her back later that day because she got weak. Her hematocrit dropped down to 30 in 6 hours. Forty five minutes later, we put her down based on the attending doctor’s recommendations and comments that Cecilia was in pain, uncomfortable and not getting enough oxygen. Could that be so at 30?

I have a few other very valid explanations as to why she was panting—one being her phobia of thunderstorms and we had a huge one making its way to us. When I was told she was very uncomfortable and would only get worse, I made what I believe was the correct but too quick of a decision. I should have demanded supportive treatment. If she were bleeding a major bleed, would her hematocrit levels drop faster and more drastic? 30 is not that bad, is it?

When I asked, the Dr. said that anytime from that point on was the right time. She said it will only get worse and that she will become increasingly uncomfortable. I should have contacted you to get your opinion. . . . I feel that in my panic driven state I made a decision without demanding more medical facts and options. I just did not want Cecilia to be in pain. She did not appear to be in pain that day at home or in the ride there—though she did collapse.

They had her in the back treatment room for 25 minutes but never began any sort of treatment to help stop the bleeding. Instead, they brought her back into the exam room where I was and she got weak and collapsed down again. Now, I wonder what were they doing with her during that 25 minutes she was back there?

I would like your medical opinion on some of my questions and would be happy to get you copies of her chart and blood work for that day. I am not looking for blame—I know of her grave condition . . . I am just trying to understand and gain more clarity.”

In answer to haunting questions like this, it is appropriate to validate the caregiver’s emotions over their loss and grief and point out that it is natural to sift over every moment of that final day asking, “woulda-coulda-shoulda.” The validation was all that Julie needed to hear as she struggled through the grief process.

Attend to the Caretaker’s Needs

We need to expect a display of attachment and sorrow when a geriatric pet is terminal. We need to respect the end of life issues regarding when, where, and how the family wishes their terminal pet to pass. Understanding the human-animal bond means understanding attachment and people’s reactions and behavior when that love bond is threatened with terminal cancer.

With proper client education and counseling, we can and must allow deeply bonded clients who want to take their terminal pet home to die, to do just that. In the end, caregivers given this opportunity are much more satisfied with how their pet passed away. The clients that I have worked with who wanted to take their terminal pet home were sincerely grateful for the precious time and privacy that they shared with their terminal pet.

Terminal patients need a special allowance from normal hospital procedure. The attending doctor can sign off patient responsibility and arrange for that terminal cancer patient to go home to die without faulting or judging the client’s wishes. This would parallel the human hospice movement. Doing the same for pets creates a new perspective on expanding the options we can offer clients for dealing with the final moments for their terminal pets as a member of their family.

In this situation, we as veterinarians have a dual loyalty and a conflict to resolve. We are taught not to discharge a sick animal that is unable to stand or unable to function. When dealing with terminal geriatric cancer cases, such as intra-abdominal bleeding from hemangiosarcoma or advanced metastatic disease, we need to rethink the situation. We must be loyal to the patient’s physical needs and the client’s emotional needs, we must honor the human-animal bond, and we must heed our oaths.

In end of life situations when the client wishes to bring the pet home, provide a client consent form. The form should acknowledge that the patient is terminal and is going home at the bequest of the family for end of life Pawspice care.

We also have a responsibility to spare our geriatric cancer patients in Pawspice care from pain, to keep within our personal ethics and honor the veterinarian’s oath to avoid suffering in our patients. Attending veterinarians need to have the confidence and willingness to deliver enough pain control for all terminal cancer patients (Gaynor 2001). Alleviate cancer pain by placement of a fentanyl pain patch or by teaching the caregivers to administer subcutaneous injections of nalbuphine at 0.2–0.4 mg/kg every six to eight hours as needed. If death comes peacefully and painlessly for the cancer patient, then our job has been done well.

When Do You Use the Word “Terminal”?

The word “terminal” is misunderstood, poorly defined, overused, and unintentionally abused in cancer medicine. “Terminal” in cancer medicine is defined as close to causing death from progressive advanced disease with vital organ involvement in the absence of any useful further therapy. In human medicine, terminal generally means that the person has less than six months to live. However, in veterinary medicine, terminal is used on a more arbitrary basis. When one doctor uses the word “terminal,” he or she may mean the pet is dying from this disease within hours, days, or weeks. Another doctor may mean that the pet will die of this disease some day. Yet another doctor may feel that the pet is too old to treat or has too many complications, and euthanasia is the easy way out. In some hospitals, the pet’s disease might be considered terminal because the hospital doesn’t offer definitive care. What is the real meaning of “terminal”?

Hemangiosarcoma and lymphoma are considered by most veterinary clinicians to be “terminal.” For dogs presenting with anemia and weakness due to intra-abdominal hemorrhage from hemangiosarcoma, splenectomy is routinely elected even though the patient’s mean survival time is limited to 86 days (Wood et al. 1998). While doctors readily perform splenectomy for stage I and stage II hemangiosarcoma, they abdicate or discourage combination chemotherapy for stage IIIa lymphoma patients when the survival time for treated lymphoma patients is comparable to patients with renal or cardiac disease—clearly much longer than for dogs with hemangiosarcoma.

Some doctors are more comfortable with abdominal surgery than they are with the rigors of administering chemotherapy. The problem is that the medicine and options that their clients receive is based on that doctor’s personal bias instead of facts. There are doctors who urge clients to “do it now” for the hemangiosarcoma dog, yet say, “I wouldn’t put him through it” for the lymphoma dog. There is a lot of variation from one practice to the next.

Oncologists, and a growing percentage of veterinarians, feel that lymphomas are very treatable. Most commercial laboratories now have antibodies against CD3, the pan T-cell marker, and CD79a, the pan B-cell marker. The doctor can order immunohistochemical stains on submitted FNA cytology slides, to determine whether the lymphoma is a B- or T-cell immunophenotype. This information can better define a prognosis and may help with decision making.

Many veterinarians are not comfortable using chemotherapy agents in their hospitals and do not encourage referrals for chemotherapy. The core of this reluctance to administer chemotherapy is lack of education and lack of familiarity with handling the drugs and associated hazards. The contemporary veterinarian seeks this education. Chemotherapy is now being emphasized in the veterinary school curriculum as well.

Combination chemotherapy protocols create a high percent of responses, complete remissions, and high-quality survival for B-cell lymphoma patients. First remissions, ranging from four to 14 months, are achieved in over 80% of all lymphoma patients. T-cell lymphoma patients are less responsive and have shorter remissions. Doxorubicin-based protocols provide the longest first remissions and various rescue protocols may improve survival (Rassnick et al. 2002). A sub-group of fortunate responders remains relapse free for the rest of their lives.

The meaning of the word “terminal” should not be conditional, yet in daily practice, terminal is often a conditional state of being. A geriatric cancer patient with grade III mast cell tumors, concurrent heart disease, diabetes, hypothyroidism, Cushing’s disease, and obesity may be conditionally terminal in one hospital but not another. If you carefully multitask for that patient, you may find a nice response. There is useful chemotherapy for mast cell and lymphoma patients who must avoid steroids, cardiotoxic, and nephrotoxic drugs. Age by itself should not be a contraindication for comprehensive cancer treatment.

Two new lymphoma cases presented for consultation on the same day. Each family was told that their dog was terminal by their attending doctors. One patient was an 8-year-old Boxer with painful bilateral renomegaly and hepatomegaly. The other patient was a 7½-year-old Bernese Mountain Dog (BMD) with stridor, anorexia, and enormous peripheral and sub-lumbar/iliac lymphadenopathy. Both dogs were diagnosed by their attending doctors with high-grade lymphoma. In no way would I, or any oncologist, overtly disagree with the attending doctors about their prognoses. Both dogs were very sick and dying from untreated lymphoma. They did appear terminal. However, if given the opportunity to undergo induction with combination chemotherapy and supportive care, they could achieve remission and enjoy a quality of life for a significant period.

After consultation with the families, they both elected induction therapy for their dogs. The Boxer did not respond to induction therapy while the BMD did. This may be because Boxers have a high rate of T-cell lymphoma, which is less responsive than B-cell lymphoma (Lurie et al. 2004; Ponce et al. 2004).

The Tumor Is Inoperable, or Is It?

The word “inoperable” is also conditional. If an attending doctor says the tumor is inoperable, that may be true in his or her hospital. However, the same tumor may be successfully addressed by a board certified surgeon at another hospital or referral center.

“Terminal” and “inoperable” are two very negative words, and they have the effect of quashing any hopes that a client may have of obtaining help to battle the cancer in a geriatric dog or cat. Upon hearing these words, many people now go to the Internet and may find that help is available for their geriatric cancer pet at a different animal hospital or referral center, using conventional, integrative, or alternative treatments.

A contemporary veterinary geriatrician thoroughly examines each patient’s medical and functional condition, researches the options, and makes recommendations for the pet owner to consider. Individualization of the older patient’s treatment plans, based on the diagnosis, staging, and comprehensive geriatric assessment, may yield a surprising benefit.

If the patient has overtly terminal disease, then this bad news must be gently communicated to the pet owner. Highly bonded pet owners will take your advice and look into useful therapeutic options that may restore the pet’s ability to eat and function. If you offer to provide good pain control and nursing instructions for the patient, you will be surprised that many pet owners will gratefully pursue end of life Pawspice care instead of opting for premature euthanasia.

The Long Problem List and Polypharmacy

The attending doctor must perform a full evaluation of the geriatric cancer patient. Veterinarians wear the hat of a geriatrician, dentist, dietician, surgeon, internist, oncologist, pharmacist, and consultant. We must assess the combination of the acute or terminal cancer condition and the chronic diseases and geriatric syndromes, along with the drugs the patient is receiving and any complications. The patient’s problem list may be long and complex. Many age- and disease-related changes can cause multivariate effects on a drug’s pharmacokinetics and pharmacodynamics (Hoskins 2004).

It requires more time to think about cases that have polypharmacy for a long problem list. It takes extra research, caution, and work to negotiate interactions with polypharmacy and design a feasible

treatment plan. Most veterinarians receive patients and clients alone in the exam room, without much of a support team, yet they must think on a multidimensional level for these complex cases. The doctor must identify the patient's problems and develop a plan to resolve the problems if possible.

When the patient is not in an emergency situation, it would be better for the attending doctor to say to the client, "I'd like to evaluate all facets of Poopsie's complex case and perhaps consult some specialists. Can I call you tonight/tomorrow with a plan that might help her?"

Unfortunately, geriatric cases like this are often viewed as terminal due to the complexity of concurrent conditions and their morbidities. If each comorbidity problem can be improved by at least 50%, the complex geriatric oncology patient may improve. Consultants from other disciplines may help provide more viable management options than those available at your facility. Geriatric oncology cases are more likely to need a multidisciplinary approach in order to have a positive outcome. A full range of options should be made available for the client to consider as you partner with the client during the decision-making process.

Healer or Executioner

An inherent problem that erodes the emotional stamina of veterinarians is that we are asked to practice at both ends of the spectrum as the healer or the executioner. Some clients don't even want basic services for an old dog or cat. Some, like Corbin, want to obtain as much time as possible with their pet but draw the line at any sign of pain or suffering. Others want us to perform heroic services beyond that line because they can't let go of a failing pet or accept the inevitability of death. Our job is to find a balance and provide patient services for every client's comfort zone. At the same time, we must clearly but gently inform clients, in adherence to our oath, when we feel that the line has been crossed.

The key to providing Pawspice care is to offer the best medicine, pain relief, and nursing support possible, to the client's satisfaction level. Another key is to realize when and if you are personally having trouble with the emotional responsibility of caring for your terminal patients and their caregivers (see the section on compassion fatigue in chapter 11).

Luna's Case (She Wasn't Too Old to Treat at 26 Years of Age)

Luna, a 26-year-old F/S white cat, had extensive squamous cell carcinoma (SCC) involving the right temporal area, the entire full thickness of her pinna and ear canal. Her fungating lesion was large, ulcerated, and looked terrible. The family took Luna to a veterinarian for an annual exam once the lesion appeared at age 21. They went to different hospitals each year and asked the doctor for advice on how to best manage the growing lesion. Each year, the family received conservative advice from the various attending doctors due to reservations regarding Luna's advanced age.

At her 26th-year exam, the fifth attending doctor recommended a consultation with our oncology service. Our geriatric evaluations found Luna to be a good candidate for surgical ablation of her right ear and surrounding temporal tissue. Luna had surgery on the same day as two other (less healthy) 18-year-old cats. Luna was discharged from the hospital before either of the 18-year-old cats and she lived cancer free until age 27½, when she passed away from renal failure.

Marty's Case (A Collie's Hemoabdomen Was Not Terminal at 19 Years of Age)

Marty Lloyd, a 90-pound M/N Collie, was 19 years old when Gary Lloyd admitted him for acute weakness and pallor. Hemoabdomen was diagnosed and abdominal ultrasound identified two masses in the spleen. His database panel, U/A, and chest x-rays were normal. We counseled Mr. Lloyd about the increased risk of anesthesia and surgery and the prolonged recovery in the oldest geriatric patients. We advised him that 80% of dogs in this situation are diagnosed with terminal hemangiosarcoma that yields less than 4 months survival. Mr. Lloyd said, "Do you mean that you can stop the bleeding now with surgery, and maybe give him 4 months to live, and maybe a 20% chance he could be cancer free?" I said, "Yes, you have the picture." He said, "Dr. Alice, why would I not want to do it?"

Marty recovered uneventfully from surgery. Histopathology diagnosed the splenic lesions as nodular splenic hyperplasia. We presented Marty's case and applauded Mr. Lloyd for his decision with a card for Marty's 20th birthday at the 1999 Bustad Awards ceremony. Marty enjoyed an excellent quality of life with the help of acupuncture until he was 22 years of age.

Bear's Case (A Big, Ugly Tumor May Not Always Be Inoperable and Hopeless)

Bear Smith, a 110-pound, 12-year-old intact male Akita, developed anal sac carcinoma over a two-year period. Bear did not receive treatment due to the incarceration of his master. When help was requested, Bear's tumor was enormous, ulcerated, infected, and involved 360 degrees of the entire anal sphincter. The family reported that Bear was able to pass stool without much trouble. The Smiths asked two veterinarians to operate and both doctors felt that Bear had inoperable disease and recommended against surgery due to the extensive nature of the lesions (Figure 9.1a).

A third doctor told the family that in his opinion, the mass was inoperable and that Bear was probably filled with cancer internally. He said that surgery would do no good. Someone at Mrs. Smith's local pet store referred her to Dr. Rachel Jones for laser surgery. Dr. Jones performed a minimum database exam, which found a normal blood panel, normal sub-lumbar/iliac lymph nodes, and normal chest films. The laser procedure was very helpful in debulking the mass (Figure 9.1b). Dr. Jones referred Bear to our service for oncology management. Bear appeared bright and alert despite his post-op anal sphincter issues. He was able to defecate without straining and had a normal performance assessment and a good quality of life. Our job was to help shrink residual disease and stay within the strained family budget. We placed Bear on oral piroxicam, 10 mg BID, and oral capecytabine (Xeloda®) at 500 mg twice daily for 10 days. This schedule was repeated every 21 days. Bear's 360 degree anal sac adenocarcinoma mass continued to regress over a six-month period (see Figures 9.1c and 9.1d) and was lost to follow-up.

The next case helps to remind us that aggressive dogs and cats can be treated, even at the end stage of their lives. Do not decline to treat them out of hand. Aggressive geriatric oncology patients can be safely sedated for their treatments, although they are at greater risk for complications. A few might surprise us with a response, as in Wheaty's case.

Wheaty's Case (It's Not Over until It's Over)

Wheaty Rowe, 12-year-old M/N Wheaton Terrier mix, was diagnosed with metastatic hemangiosarcoma involving the spleen and right ventricle. It was 4:30 p.m. on New Year's Eve



Figure 9.1. Bear, a 12-year-old male Akita with advanced anal sac carcinoma, was considered terminal according to several clinicians (a). After debulking laser surgery (b). After 3 months on oral Xeloda and piroxicam (c). After 6 months of treatment (d).

when his family called me in desperation. Mr. Rowe said that they had been turned down by two different surgical specialty clinics. Each said that they could not help the family save Wheaty. The Rows wanted my opinion ASAP because Wheaty was having trouble breathing and his abdomen was bloated.

The Rows said their doctors recommended euthanasia, but they had faith in me since I had helped them 10 years previously. They were an hour away. I cautioned that Wheaty could expire on the way over. Wheaty presented with signs of right-sided heart failure due to a 6 cm mass in his right ventricle, organomegaly, and ascites. He did not have the expected hemoabdomen from the 4 cm mass in his spleen.

Wheaty had enough energy to lunge at me every time I got near him. His body condition was good but his recent performance level was compromised. The family begged me to do whatever I could for him. During the consultation, we discussed the possibility of medical management and chemotherapy and the VAC protocol for soft tissue sarcoma (STS). Adriamycin would be contraindicated and risky because of Wheaty's heart condition. I recommended carboplatin, since it has activity against some sarcomas.

Wheaty required sedation for the chemotherapy treatment. I thought he might die every step of the way but we all survived the procedure. One week later, Mr. Rowe returned with a seemingly different dog. Wheaty was 100% improved. The ascites was resolved; he was eupneic and more aggressive than ever. We treated him every 21 days, and to the joy of his family, old Wheaty survived with a good quality of life for 4 more months.

Chemotherapy for Advanced Stage Geriatric Patients

When treating advanced stage disease in geriatric patients with chemotherapy, select drugs that bypass any known compromised organ function. For instance, if the patient has kidney disease or CRF, never use a highly nephrotoxic drug such as cisplatin, and modify the dose by 25–50% for drugs that rely on renal excretion. If a terminal canine patient has a heart condition or is a breed that is prone to cardiomyopathy, avoid using Adriamycin.

Management using oral and subcutaneous chemotherapy and support medications vs. IV medications is preferred for advanced stage and terminal geriatric oncology patients. This approach is appreciated if the patient is fearful, stressed, or malnourished. This keeps the caregiver and patient at home and may avoid unnecessary side effects.

It is advisable to avoid using Adriamycin in very old patients because they have a greater prevalence for myocardial and renal compromise, dehydration, and malnourishment. Cisplatin should be excluded in geriatric oncology due to the high incidence of renal fibrosis and dehydration in older animals. Cisplatin is inherently nephrotoxic and using it in geriatrics creates an unjustifiable renal insult. The attending doctor needs to offer more supportive help for advanced stage and terminal cancer patients to ameliorate dehydration and malnourishment. Terminal geriatric oncology patients in Pawspice care would clearly benefit with enteral feedings and SQ fluids directed at nutritional rehabilitation and rehydration (see Quality of Life Scale, Table 10.1). If we can improve the terminal geriatric patient's nutritional status and hydration, the pet may be able to handle palliative therapy more readily.

Metronomic (low dose) chemotherapy, chemoprevention, or conventional drugs used at the lower end of the therapeutic dose can minimize the risk of side effects. If the patient tolerates a conventional chemotherapy drug at the initial low dose range, then it is appropriate to escalate the dose on subsequent treatments (Balducci 2004). If there is no indication that the patient has received benefit from the initially selected drug, it is appropriate to try another drug using the principles of dose escalation.

When using the longer-acting chemotherapy drugs that are more toxic in geriatric cancer patients, I often split the dose. This precaution is especially important for geriatric patients with renal or hepatic compromise and obese geriatric patients. The lean body weight is determined. In addition, we reduce the traditional dose by 25% if there is renal or hepatic compromise. We then administer 50% of the dose on day 1 and day 8 of each cycle instead of giving a traditional dose on an every 21–30 day schedule. We employ the split dose method most often with Adriamycin, especially for older medium, large, and giant breed dogs. It's generally thought that the m^2 Body Surface Chart

under-doses large-breed dogs and overdoses cats and small dogs weighing less than 20 pounds. By spreading the dose out over four to seven days, the patient has fewer toxicity problems.

For example, the split dose schedule that I use for Adriamycin is 20 mg/m² on day 1 and day 8 given over 15–20 minutes for large to giant breed dogs. I use Adriamycin in this split fashion for breeds at risk for dilated cardiomyopathy, such as Doberman Pinschers. In this way, we can reduce the risk of cardiac and GI toxicity to a minimal degree while gaining a higher total dose for the geriatric patient. For geriatric dogs between 20 and 55 pounds, I use 20 mg/m² for day 1 and 10–15 mg on day 8, depending on the size and condition of the patient. Geriatric cats and dogs under 20 pounds generally do not receive split Adriamycin doses because they experience minimal toxicity at the reduced dose of 20 mg/m² every 21 days.

Palliative Radiation Therapy for Terminal Patients

Some terminal geriatric cancer patients may benefit from palliative radiation therapy (RTx). The normal rigorous treatment schedule that involves daily or alternate-day anesthesia is reduced to once a week for three or four weeks. The dose fraction is much higher and the tumor response time is reduced. Palliative RTx offers the patient a reasonably effective total therapeutic dose while minimizing the number and frequency of anesthetics. This schedule minimizes the stress on the compromised, terminal patient. In some cases, we maintain regression of oral masses in terminal cancer patients using monthly fractions of RTx.

If you are not sure about a case, consult a radiation oncologist to help you decide if the terminal cancer patient has a radiation-responsive mass. If anesthesia is deemed a reasonable risk, the client may consider either an aggressive palliative schedule or a basic palliative schedule (see the section on palliative radiation therapy in chapter 6).

Schniffer's Case (How "Terminal" Is "Terminal"?)

Schniffer Gore, a 13-year-old F/S German Shorthaired Pointer, presented with acute onset signs of fever, anorexia, and depression. On physical exam, the temperature was 106 degrees Fahrenheit and a 3 cm mass in the left anal sac was palpated. Minimum database exam found an elevated white blood cell count and normal organ function and urine values. Chest and abdominal x-rays revealed extensive metastatic disease with nodules throughout the abdominal and chest cavity. After two days in the hospital on symptomatic treatment, Schniffer was ambulatory and regained her appetite.

The Gores wanted Schniffer to come home for Pawspice care. They were sad that their infant son would never know their beloved Schniffer. They wanted to keep Schniffer comfortable until the time came for her passing. They declined chemotherapy but accepted our suggestion for immunonutrition. Schniffer amazingly survived with good quality of life for one year, befriending their son as he grew into a toddler.

Client Consent Forms

Veterinarians routinely use a client consent form before anesthesia and surgery. Nevertheless, when dealing with fragile, sick, malnourished, vulnerable, and terminal geriatric cancer patients, it is reasonable to

Figure 9.2. Client Consent Form for treatment of a terminal patient with a poor prognosis.

for advanced cancer in geriatric patients will be more commonly attempted in the future. It is prudent to clearly apprise the client of your treatment goals for improving the quality of life of his or her pet, and of your concerns as well.

Via the signed notation in the pet's chart, the client acknowledges an understanding of the prognosis with or without treatment and the potential side effects of therapy. It is also important to convey your willingness and enthusiasm to give the patient your best effort in the event that the client elects to try to save his or her pet.

The cases selected for inclusion in this chapter are dramatic ones, involving the "oldest of the old." An essential component of practice in geriatric oncology is having finely honed decision-making skills. We need to use objective methodology to decide if a cancer patient is truly terminal or conditionally terminal. If there is a decent chance that the patient can survive a definitive or palliative surgical procedure or handle a chemotherapy protocol or palliative radiation therapy, the client may elect to proceed with treatment. If the patient's cancer has no useful therapy that can extend life, then offer pain control and support in the form of end of life Pawspice care. Give the client assurance that euthanasia can and should be used to help the cancer patient pass peacefully, but only after all other methods are considered.

Summary

When to declare a cancer patient "terminal" is not always a clear-cut clinical decision. Offer supportive options, especially pain control, for the terminal patient until instructed otherwise by the client. Also, provide sincere respect for The Bond—the deep attachment that the primary caregiver has for his or her geriatric cancer pet—during every step of the decision-making process. Some terminal geriatric cancer patients may benefit from aggressive palliation, cytoreductive (debulking) surgery, feeding tubes, cystostomy tubes, palliative radiation therapy, nutritional therapy, and general palliative and supportive care. Decision making should be a special partnership between you and your clients, with the terminal geriatric cancer patient's needs foremost in mind.

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Chapter 10

Palliative Care: End of Life “Pawspice” Care

Palliative care should not be the last resort . . . or about giving up. It’s about increased quality of life and enhanced coordination of care. It is not about dying. It is about living with cancer. It’s not less care. It’s more care.

Fred Meyers, MD, University of California, Davis School of Medicine

In a broad sense, most of the oncology treatments that we can offer for pets of any age that develop aggressive, recurrent, or advanced stage cancer are truly palliative in nature. Idealism and/or clinical arrogance may tempt us to characterize cancer treatment otherwise, but it continues to humble us with its millions of victories.

Defining the work of veterinary oncology as palliative, rather than cure-oriented, need not connote lower expectations. In palliation, our primary goal is to stabilize a tumor and keep it from enlarging or metastasizing. One day we may turn cancer into yet another chronic disease. We may list certain cancers as concurrent illness. It’s important for practitioners and caretakers alike to understand that pets “cancervive” (can survive) with a reasonable quality of life on long-term palliative therapy.

I like the word “palliative” because it has the word “pal” in it. Most clients have never heard this long word before, yet they may be entering their pet into this thoughtful and supportive type of management. Palliative care can be explained to clients as finding ways to help their sick pal feel better by reducing pain, slowing down the cancer, relieving an obstruction, or improving or restoring a vital function. Palliative care is not aimed at or expected to cure. The primary goal of palliative care is to provide supportive care and comfort for the patient.

Aggressive palliation is emerging as a very acceptable course of therapy in human medicine for geriatric cancer patients. Its goals are more optimistic than those of traditional palliation, while remaining less toxic than traditional treatment. It is used to treat advanced stage geriatric cancer patients who have a reasonably high performance level. Geriatric oncology patients who can perform daily functions and still enjoy a high quality of life may be candidates for aggressive palliation.

You have an increasing opportunity to provide both aggressive palliative care and/or “comfort” palliative care as viable treatment options for your geriatric cancer patients. The field of geriatric oncology for pets is wide open for many combinations of palliative care. Together, caregivers and the cancer care team can be very creative. The arena of comfort care requires resourceful thinking, and imagination is the only limiting factor.

All forms of cancer therapy discussed in chapter 6 can be modified and specifically tailored to reduce toxicity and fit into a palliative care program for an end of life cancer patient. The attending clinician must reassign the purpose of the treatment to be “treatment with palliative intent.” Furthermore, the clinician should modify the treatment dose and schedule to deliver therapy with minimal risk to

the patient, as in metronomic therapy. Above all, palliative therapy must primarily be supportive. Ideally, palliative therapy would also be devoid of adverse side effects, but this is an impossible wish.

Geriatric patients are fragile and prone to reacting negatively to any type of drug or conventional treatment modality. Sedation or anesthesia is required for salvage surgery, placement of feeding or ostomy tubes, palliative radiation therapy, imaging, or other delicate procedures such as interventional radiology. Many sophisticated palliative and ancillary procedures may place the geriatric cancer patient at some risk for accidental death. The problem is magnified when the patient has concurrent illness and debilitating comorbidities. We should confer with the patient's caregivers to determine if they want resuscitation for their geriatric pet undergoing palliative care procedures. I often write a sentence stating the client's wishes regarding resuscitation in the medical chart and ask them to initial the statement for clarification.

One of the most dramatic areas for palliation has come to us from radiation oncology. There is radiobiological rationale for accelerated fractionation of radiation therapy to treat stubborn tumors and to palliate advanced painful lesions. Old cats with CRF and ulcerative inoperable nasal planum squamous cell carcinomas were the first cases that we palliated. We used four accelerated fractions given at day 0, 7, 14, and 28. Old dogs with nasal cavity tumors may also benefit from accelerated radiation protocols and combination treatment. Caregivers may be more likely to give consent for a less time-consuming, less demanding radiation protocol, utilizing CT-enhanced treatment planning.

If the family is reluctant to subject their geriatric oncology pet to a three-week radiation protocol, the next best option is to offer a palliative accelerated fraction schedule. In this way, the geriatric patient receives a therapeutic radiation therapy regimen with fewer treatments over a reduced period.

Today, we add piroxicam to the palliative radiation protocol. In addition, the client may be given the option of using mitoxantrone for their squamous cell carcinoma (SCC) cats and carboplatin for nasal tumor dogs. These two drugs are well tolerated as palliative chemotherapy for geriatric patients as long as we are able to keep the patients well hydrated. Metronomic chemotherapy and immunonutrition may also be applied to further palliate geriatric cats and dogs with a variety of tumor types. Tomorrow, we may add small molecule therapy into our palliative protocols for cancer patients with a wide variety of tumors.

Informed Consent and Informed Refusal

Dr. James Wilson, veterinarian and attorney, led a popular session at veterinary meetings titled "Paw & Order." Wilson recommends that veterinarians use improved methods and documentation to acquire client acknowledgement and compliance. Every veterinary hospital office staff is already trained to routinely have clients sign a standard consent form before anesthesia and surgery. Wilson recommends the addition of an "informed refusal" form for clients who decline the veterinarian's recommendations.

Some clients fail to recognize the benefit that their pet would gain from a certain proposed therapy. A stubborn or fearful client may be reluctant to initial the pet's chart or to sign any type of form. If this is the case, the client's lack of compliance should be noted in the medical chart.

Informed refusal may also be used on a conceptual basis for cancer patients who will not be receiving conventional treatments. For instance, if a client declines induction therapy for a treatable cancer like lymphoma, I ask them to sign the pet's medical chart or an ancillary note of acknowledgement or an informed refusal form. The notation in the chart states the prognosis without treatment in order to qualify for an informed refusal. Choosing a modality of aggressive palliative

cancer therapy or comfort palliative therapy for a pet of any age is a very personal decision. The client should not be made to feel judged or intimidated by your request for acknowledgement and documentation.

If the client is not likely to initial or sign the chart, I let him or her know, in a gentle and non-threatening way, that I am signing it in the person’s presence for verification. This makes the client a witness to your entry into the medical record. It helps to have this documented in the event that there is a misunderstanding down the road. Unfortunately, some clients feel that they should only have to pay for veterinary services if the outcome is successful. Explain to clients that our work, especially in the area of palliative care, has no guarantee of successful outcome. Remind clients that there is a potential for treatment-related adverse side effects.

Taking care of the geriatric oncology patient is a partnership. You can say something like this: “The decision that you are going to make for your geriatric pet must be very difficult. We know that you love your pet. We are also aware that you may have other priorities or philosophies that may force you to decline standard therapy that we could use to treat the cancer. Some cancers respond with a certain percentage of remissions and even cures, but we cannot guarantee a remission or a cure for your pet. Remember, you can always change your mind.”

For cases where the client elects no further conventional treatment, or when further treatment is considered hopeless, too toxic, or too risky, we encourage clients to enter the patient into a supportive end of life Pawspice program. This concept, as an option, validates the client’s bond for his or her pet and restores pride in the difficult decision. We often ask clients to initial their pet’s medical chart when entering their geriatric cancer pet into the end of life Pawspice program.

When planning to administer any type of drug therapy to frail, sick, malnourished, or terminal geriatric cancer patients, discuss the concept and value of informed consent. Then ask the client to sign an informed consent form or initial the medical chart. By signing, the client actively acknowledges the severity of the pet’s specific situation. Clients entering their pets into Pawspice care must be fully aware of the prognosis of their pet’s cancer and of the potential side effects that palliative and supportive medical therapy may entail. Rather than using a harshly worded legal document (Figure 9.2), I write a line or two in the pet’s medical chart regarding the poor prognosis despite treatment, including the risks associated with treatment. I read it to the client while writing and then ask the client to read the entry and sign beneath it right in the chart. This personal acknowledgement of risk and prognosis is very helpful to keep pet caregivers cognizant of the purpose of palliative therapy and the reality of the situation.

Aggressive Palliation and High-Risk Procedures

High-risk procedures and aggressive palliation for advanced cancer in geriatric patients will be more commonly attempted in the future. It is prudent to clearly apprise the client of your treatment goals for improving the quality of life of the pet, along with your concerns. The client needs to acknowledge and understand the prognosis with or without treatment and the potential side effects of therapy. Convey your willingness and enthusiasm to give the geriatric cancer patient your best effort in the event that the client elects or demands that you try to save his or her pet.

In advanced stage cases that have a poor prognosis for successful induction or for cases that require risky anesthesia or technically complex and difficult procedures, I say, “Your decision permits us to use our best medical knowledge to help your pet. We hope that we can gain a remission and that there is a favorable outcome despite the poor prognosis and risk of side effects and possibly

death.” I always suggest to clients that they say goodbye to their pet before the procedure in the event that the pet passes away during the procedure or in the post-operative period.

Pawspice Care for Geriatric Cancer Patients

Although this book encourages veterinarians to treat cancer more effectively and innovatively, our geriatric cancer patients are at maximum risk for death. Cancer ravages over 50% of our senior and geriatric companion animals. Our geriatric cancer patients are often pre-burdened with other concurrent morbidities such as dental disease, degenerative arthritis, organ failure, incontinence, and cognitive dysfunction. The level of morbidity caused by concurrent conditions confounds the decision to treat a geriatric pet’s cancer. Some cancers are insidious and can be very occult in the geriatric oncology patient. Many cancers are not discovered until the companion animal is already in very advanced stages. Some cancers are discovered or suspected only after causing a seizure, collapse, or acute pain, or by causing a rapid destabilization of the compensated aged pet.

Patients needing palliative, in-home hospice (“Pawspice”) care often have management issues such as relapse, resistance, recurrence, obstructions, functional disabilities, uncontrolled pain, and reduced quality of life. There may also be other extenuating arbitrary issues with owner disillusionment, reluctance to continue conventional aggressive therapy, and budget concerns.

Most caregivers and their veterinarians are burdened with old wives’ tales, myths, and preconceived notions about cancer and its treatment. Previous experiences may have created erroneous biases and negative ingrained emotional reactions regarding cancer. This creates a fatalistic approach toward treating cancer in younger and middle-aged pets and leaves no alternative for geriatric pets. Caregivers come to us with this dichotomy every day. They love their geriatric pets but they can’t rationalize treating their pet for cancer. Case by case, attending clinicians and their professional staff must overcome the defeatist attitude about the aging process, cancer therapy, palliative therapy, and end of life supportive care. We must try to dispel the old mindset and look at a new way of thinking about these issues. It is best to ask clients if you can help them examine their negative notions and myths. Negative thinking no longer serves The Bond that clients shared with their aging pet before the cancer was diagnosed.

Veterinarians must rid themselves of the old utilitarian knee-jerk impulse to rank euthanasia as the second or third best option for pet caregivers. Instead, we can implement end of life care programs such as Pawspice for every client’s dear pet. People come to us for advice and present their pets to us as patients; they do not expect us to prematurely terminate their pets’ lives without exhausting reasonable home care options. Our profession can, with solidarity, offer pet owners supportive, palliative options for comprehensive home care and attention to their pet’s special needs when they are going down that final road toward death.

Many clients have complained to me that their initial veterinarian was too quick to recommend euthanasia if their pet’s disease was incurable, their senior pet had concurrent conditions and treatment would be too complex, or the pet was “too old.” Refrain from suggesting or insisting on euthanasia as the next best option if the client declines the treatment plan that you recommend. Instead, say you are ready to provide pain relief for the pet and ensure the pet’s comfort while the owner makes a decision regarding therapy.

Others complained that their veterinarian seemed to insist that the recommended procedures be done as an “all or none” policy. Some clients complained that they felt pressured to comply with procedure A or B, even though the pet’s overall prognosis was poor. They complained that their

veterinarian did not give them alternative choices, and if procedure A or B were not followed, their pet would suffer and need to be euthanized. Yet somehow the consultation ended and their pet was discharged from the clinic without being offered adequate pain control and supportive care for the ongoing condition at home. Pet caregivers felt abandoned, unsupported, and disappointed.

Emma’s Case (It Ain’t Over till the Fat Lady Sings)

Emma Moon, a 14-year-old F/S German Shepherd Dog mix, was the only pet of a childless, vibrant film-business couple. One day, a very upset man entered our busy reception room. He asked our receptionist, Jennifer, if we had time to give a second opinion. That day, two different specialists had told Mr. Moon and his wife to euthanize their beloved dog, Emma. The doctors said that Emma had two types of advanced cancer, was very old, and needed to be euthanized. Jennifer comforted him and told him that she would ask me to see if we could do anything to help. Meanwhile Mr. Moon sat on the floor with tears running down his face.

I asked him to tell me what was going on. He managed to tell me that Emma had been diagnosed with bone cancer a few months ago. Then she rapidly developed a large tumor in her groin, which was diagnosed as mast cell cancer. He said that today’s x-ray of the diseased leg looked like the bone cancer would fracture. Both specialists agreed that Emma should be put to sleep that day or very soon thereafter. Mr. Moon said that he and his wife were tormented over this advice. They were not ready to let Emma go because she still wanted to eat and be with them. The clients in our waiting room and my staff empathized with his distress. I emphatically told him, “Your dog does not have to die from euthanasia today if you are not ready.” I told him that we could enter Emma in a Pawspice program. I said, “If you are this conflicted and not ready yet, then it is not the right decision.” I told him to bring his wife and Emma and all of her medication to me at the end of the day.

Sure enough, Mr. Moon returned at dusk with his wife. He carried Emma on a big soft pad into exam room #3. Emma’s paws never touched the ground. She had pink mucous membranes and a pleasant interested look on her face. Mrs. Moon was puffy-eyed and looked at me with hope. We examined Emma. She was breathing comfortably and had no heart murmur. She had a large swelling of her left humerus that had been diagnosed as osteosarcoma. Referral x-rays showed a large osteosarcomatous lesion with lysis and erosion of cortical bone.

The lesion appeared to have a hairline fracture present but there was no displacement. A huge, bright pink soft tissue mass extended along Emma’s left caudal mammary chain. The mass was $16 \times 8 \times 8$ cm. Fine needle aspiration cytology had diagnosed mast cell tumor earlier that day. Emma’s abdomen was normal on palpation with no organomegaly. The couple said, “Look at her, she isn’t ready to die yet. She still gets up to do her business and she eats and wags her tail and likes being at the center of things. We want help to keep her with us until we feel she is ready to go.”

I described Emma’s pain response to the Moons, saying that, “Dogs and cats don’t exhibit their pain in ways that we completely understand. Dogs, by their very nature, want to stay with their pack and will fake wellness despite their pain. A pet’s pain may not be recognized as such by their caregivers, even when they know their pet very well.” I concurred with Emma’s doctors and verified that Emma indeed had pain.

The sheer volume and location of the mast cell tumor warranted a poor prognosis for any dog. Emma’s mast cell cancer added a negative factor to the bone cancer. The pathological

fracture and the fact that she was on NSAIDs for bone cancer yet needed steroids for the mast cell tumor, compounded by her advanced age, all added up to a very poor prognosis for Emma.

I had no disagreement with her doctors' opinions yet could not disagree with the Moons, either. Emma was bright, alert, and responsive, and she seemed to be quite content. We offered palliative Pawspice care. I said, "Look at Emma with your questions and she will tell you and communicate in some way when the time is right."

We designed a special home care calendar with scheduled pre-emptive pain control for the bone tumor and palliative treatment for the mast cell cancer. We started Emma on Duragesic[®] pain patches every 72 hours for osteosarcoma pain control. We administered IV dexamethazone and vinblastine for the mast cell cancer along with famotidine and Benadryl[®] injections, and SQ fluids with vitamins B, C, and B-12. We reviewed the calendar schedule with its specific instructions for oral prednisone, chlorambucil, benadryl, and Pepcid A/C[®] along with supportive supplements from our chemoprevention and immunonutrition protocol. The Moons were instructed to discontinue all NSAIDs and recheck with us weekly for vinblastine injections and to assess Emma's quality of life.

To our amazement, Emma's mast cell tumor regressed completely, and she survived with good quality of life in her loving home for an additional eight months in Pawspice care.

If a pet's illness cannot be treated due to financial constraints or a logistical problem, it is still a matter of good professional service to compassionately provide advice and meticulous home care instructions. When a treated pet's cancer has repeatedly recurred, metastasized, or is resistant to treatment, or if the pet is in the terminal stages of cancer, Pawspice care is a wonderful next step that keeps both pet and caregiver comfortably close to their nest. A well-conceptualized, creative Pawspice plan for pet owners may be the very best care that our profession can offer a terminal patient to support the people-pet bond.

In Pawspice, veterinarians and their staff can kindly and respectfully help the caretaker sustain a quality life for terminal pets during the very last days and hours before The Bond must be physically and emotionally severed. Clinic staff members can be trained in family practice skills (Table 8.1) and be prepared to support the emotional needs of family members. This service allows the family an opportunity to enjoy the benefits of the long farewell that Pawspice offers with their beloved geriatric pet. Encourage the family to focus on enjoying the private moments with their Pawspice pet and to treasure the good parts of each day. Help worried caregivers realize that their Pawspice pet is still very much alive and present right there with them at home, holding court during this special Pawspice time.

The pet's caregivers—your clients—are also bonded to you and your staff. They are accustomed to the ritual and the idea of purpose and being welcome into your facility and interacting with you and your receptionists and nursing staff in an intimate fashion. All of this "social contact with purpose" ends for them abruptly with the passing of their geriatric oncology patient. Therefore, Pawspice can be more than a long farewell. It can also be a transition away from a routine that includes very meaningful connections and supportive relationships with you and your staff. It is a passage into the enormity of the at home caregiving routine for the geriatric oncology patient.

When a pet is injured, becomes ill, ages, or has arthritis, degenerative myelopathy, or cancer, the question of home care always comes up. How much care is a pet owner willing to provide for an ailing pet? After 35 years of experience in treating veterinary cancer patients, I can state with authority that the answer to this question is very personal. For some pet owners, the willingness to provide palliation and Pawspice care for a pet has no limit, while others are either unable or unwilling. Each owner has his or her unique personal lifestyle considerations and tolerance levels that will support or preclude the owner's ability to provide Pawspice care for a pet.

The human-animal bond for geriatric pets may be quite fragile or very intense and occasionally not rational. This variability in the bond depends upon the pet caregiver's personal bias, philosophy on aging, and loyalty toward his or her elderly pet. Some pet owners have been saying their good-byes for years before their geriatric pet has even developed any form of illness. When cancer strikes, some caregivers feel that their pet's time is up. They are not willing to make the personal or financial investment to challenge fate.

Other caregivers may feel protective or fearful of distressing or disturbing their geriatric pet. Some clients seldom or never allow their geriatric pets to have anesthesia for dental care. The periodontal disease becomes a source of infection and a roadblock in the face of palliative chemotherapy, surgery, or radiation therapy. This situation along with other extenuating circumstances may be why some clients elect to pursue only supportive Pawspice care and decline available types of palliation.

After an initial consultation regarding options for curative treatment or palliation of their geriatric pet with cancer, the family must struggle with decision making. Issues to be weighed include personal finances, the logistics of getting to and from the treatment center, and scheduling for visits and home care requirements.

Re-evaluation of Attachment

Caregivers must face how they feel about their attachment for their pet's compromised status. They deal with feelings of guilt and remorse and they examine their sense of duty as their geriatric pet encounters problems and the disability progresses. Initial willingness to participate in a Pawspice program may wane after the pet encounters side effects from treatment. Caregivers often find themselves re-evaluating their commitment with the changing status of the Pawspice patient.

Many pet owners are emotionally overwhelmed by anticipatory grief over the impending loss of their pet. They don't realize that they are cheating themselves out of the real benefit of Pawspice—final days or weeks of enjoyment with their pet—because they are so upset. Based upon the personality type, marital and financial situation, family commitments, and other personal issues that you may or may not be aware of, pet owners may respond with a wide range of emotions from panic all the way to an emotional shutdown. If at any time you suspect that a client is emotionally unstable, encourage that client to seek professional counseling.

When you outline a Pawspice plan for a pet, the owners will weigh their specific issues and then either accept the challenge to treat their pet's illness with your recommendations or decline. When a client declines an aggressive treatment plan, the battle is not necessarily over. They may seek a palliative therapy that is not offered at your practice. They may pursue alternative treatments and they may do so without your knowledge or guidance because they don't want to hurt your feelings, because they are embarrassed, or because they think you will be angry with them and/or disapprove of the treatment they have chosen.

Veterinarians must refrain from being judgmental or from interpreting a client's decision not to provide a particular recommended treatment as personal rejection. Continue to educate the owner and offer options that the owner can incorporate into his or her treatment or Pawspice program. If the only contribution the owner will accept from you is comfort and support for the pet, offer that. Create a protocol for supportive care and this becomes a very palatable and viable option while keeping your client's confidence into end of life Pawspice care and showing respect for his or her choices.

Home Care for the Pawspice Patient

When preparing caretakers to provide Pawspice care at home, always speak in a tender, unhurried fashion. They are most likely under a tremendous amount of personal, financial, and emotional stress. A trained nurse, technician, or doctor can make house calls to assist and coach caregivers for a desensitization period. The family should be able to establish their own home care routine within a reasonable amount of time.

Pet caregivers may feel trepidation at the thought of using needles and syringes to give injections to their ailing pet. They might be upset at the thought of using a feeding tube. The use of a feeding tube may sound like heroics to one person and make perfect sense to another. Cats are more likely to need feeding tubes to provide them with proper nutrition during recovery from hepatic lipidosis, after oral surgery, or during radiation treatments to the oral cavity. Many Pawspice patients require SQ fluids to maintain hydration, especially if there is concurrent renal disease, hypercalcemia, or other electrolyte imbalances.

You and your staff can address a client's fear of needles with a cheerful approach. One technique is to ask the owner to look at a pen. The pen's function is to transfer information to the chart. Explain that the syringe and needle are like a pen; they transfers medications to the patient. Consider the syringe to be a tool, like a pen, and nothing to be afraid of. Teach caregivers to give mock injections with saline at the clinic and at home until they acquire the skill of handling needles and syringes. Suggest injecting teriyaki sauce into chicken or Grand Marnier into strawberries. Provide a practice needle in the gauge that will be used for their pet, and suggest they use this to inject water into an orange. Piercing the orange rind will prepare them for the sensation of piercing the pet's skin. When it comes time to give their pet an injection, caregivers will be more confident.

Many pet owners want to nurse their terminal cancer pet at home. They need their veterinarian and the nursing staff to teach them how to care for their pet and maintain hygiene while working within their inhibitions and concerns. Home care for a pet with incontinence or paresis is a task certain pet owners elect with the help of pet wheels, hoisting straps, harnesses, ramps, extra soft bedding, egg crate mattresses, and loads of towels and diapers.

Some pets will need frequent bandage changes. Some will need their bladders expressed. Some need diapers. Incontinent pets need frequent bathing to avoid urine scald and fecal contamination. If the pet has a resting place outdoors, it needs to be protected from flies and ants. It doesn't take long for maggot infestation to develop in a decubital ulcer. Some pet caregivers want to provide oxygen therapy for their pets with compromised respiration. Advise them to purchase portable oxygen tanks and a stethoscope so they can routinely listen for troubled breathing and fluid sounds.

Some people get upset with a growing tumor, thinking it might rupture and cause their pet to die. We comfort them and tell them that this would be unusual and that at worst, the wound might drain or have a discharge similar to a sliced tomato.

Some people react with a paralyzing fear or nervousness at the sight of blood or oozing wounds. They may have trouble providing wound care. They may feel squeamish looking at, touching, and treating wounds from radiation therapy mucositis or desquamation, IV slough sites, ulcerated tumors, or decubital ulcers. Others cringe if they have to watch our nurses give injections or provide medical procedures. We solve this problem with frequent rechecks or hospitalization.

Most pet owners have great fortitude and interest in learning how to administer injections and medications and nursing care to their geriatric cancer pets for Pawspice care. They truly want this level of care for their pet's convenience and they are willing to make the sacrifice. Others may be less eager but need to master technical home care procedures to save money.

Pet Aversion to the Caregiver

When a pet in Pawspice shows aversion to the caregiver’s attempts at medication or other care, we run into a problem that may erode the home care equation. This very problem hit me broadside when Alaska, my aging Great Pyrenees in Pawspice, started to avoid me. She no longer greeted me with her usual cheer because she knew that I might have a pill, a syringe, or some SQ fluids for her. It only took one week to solve this problem. One of my assistants came to my home every day to give Alaska her injections and SQ fluids. Alaska was once again happy to see me all the time.

Sinji’s Case (She Refused to Cooperate but Needed Help)

Mr. Citroen told me that he just could not torture his 12-year-old cat, Sinji, with pills or injections. Her mesenteric lymphoma responded well to the first chemotherapy treatment but he could not justify her aversion toward him when he approached her with the prednisone tablets. She would not accept any liquids or compounded medications or transdermal preparations. He called my clinic in frustration, to terminate treatment. We offered the option of visiting his local veterinarian once every two weeks for SQ injections of L-asparaginase, Cytosar-U[®], and Depomedrol[®]. We also recommended that the doctor give her a 10 mg capsule of lomustine every six weeks following an acceptable CBC. Mr. Citroen realized that Sinji might die without the proper medication and he was grateful for a flexible modification in her palliative chemotherapy and Pawspice program.

The essential ingredient for Pawspice care is willingness. Look for willingness in yourself, in the hospital staff, and in the geriatric oncology patient’s caregivers. When you hold staff meetings, ask the question, “Do we want to be a compassionate veterinary caregiving facility with a Pawspice program? Will our nursing and reception staff members be able to provide the necessary support?” Ask who would like to be the “Pawspice support person” for the clinic or for a special client. Ask clients to direct phone calls and concerns to their designated nurse or to members of the clinic’s cancer care support team. The nursing staff can handle questions regarding home care problems. The doctor evaluates Pawspice patients on a regular basis as outpatients. At those rechecks, the pet is weighed and checked for hydration and nutritional status. The caretaker’s questions are answered and changes in the patient’s health status, medications, and quality of life assessment are addressed.

The Evolution of Pawspice Philosophy

Companion animal medicine is relatively young. Our profession’s founding philosophy was forged from a utilitarian stewardship of livestock and epidemiology when animals were not generally thought of as family members or pets. It is only in the last 25 years that companion animal medicine has emerged into the pediatrician–family practice model.

Wellness and hospice communities across the country have revolutionized how Americans care for people who are sick and dying. It is time for the veterinary community to take a lesson from this movement and to stop delivering the euthanasia speech over every old, sick pet. Veterinarians must move away from the reflexive response of suggesting utilitarian or premature euthanasia. This action greatly undervalues and diminishes the moral status of the pet owner in the human-animal bond (Tannenbaum 1985). The veterinary profession will gain more stature when practitioners learn to emulate the philosophy of the hospice movement in honor of that special bond that connects people to their pets.

Veterinarians who offer a Pawspice program as an alternative to euthanasia dignify the profession by expressing respect for patients and their caretakers and for The Bond. Bioethicists hope that companion animal professionals will be able to cultivate sensitivity and keep a courteous, caring balance with life and death, yet be vigilant against the owner going too far at the expense of the animal's quality of life. (Rollin 2006; McMillan 2005). As the veterinary community begins to embrace the hospice philosophy in the form of Pawspice care for pets, we must maintain a sense of balance. We must be careful not to head in the direction of the mindless machinery of medicine, insensibly keeping non-sentient patients alive who are clearly beyond hope. Our efforts to provide Pawspice care are justified in honoring the human-animal bond and attachment, as long as the patient has what we must define and defend as a good quality of life (Wojciechowska and Hewson 2005).

The Pawspice option gives pet owners more time to let go of their geriatric cancer pet slowly and peacefully. Many tender private moments of quiet emotion and sweet conversation are shared between the family members and their dying pet.

Education of Home Caregivers

In exam room consultations, attending veterinarians and staff can gracefully provide the education and support needed for efficient home care of ailing pets on a fee-for-service basis. Pet owners will gladly pay for education that alleviates pain and provides good nutritional, hydration, and medical support for their dying pet. These consultation and demonstration sessions give the caregiver the ability to care with expertise.

The most important factors to educate home caregivers to confidently monitor are quality of life; minimal pain; adequate nutrition, hydration, and respiration; and detection of sepsis. When properly prepared by the veterinary staff, caretakers can provide end of life Pawspice care for a dying pet with all of the benefits of hospital care while allowing pets to remain in the comfort of their own home. Ask yourself, "If this pet's owners were trained to take the pet's temperature, administer subcutaneous fluids and proper pain control medications, provide food, and maintain hygiene, might this pet live more comfortably with better quality of life and perhaps live longer at home?"

A Pawspice program should include moments of pleasure or fun and joy for the pet. Owners can be overwhelmed by their pet's imminent passing and by their new tasks, such as medicating, cleaning, and providing special diets. It's important to help them avoid becoming so focused on caretaking that they forget to appreciate their pet during the additional time that Pawspice creates.

Creative caregivers can always find fun things to do with a pet in Pawspice care, regardless of the pet's limitations. This can be as simple as giving massages, gentle brushing and grooming, playing with toys or a laser light, or taking short walks with a dog that is able to still enjoy sniffing favorite spots. If going for walk is a dog's favorite activity, recommend short walks more often. If the pet is not able to get up or walk without assistance, instruct the owner to provide assistance with straps or harnesses or to use a pet stroller, cart, or wagon. Cats and small dogs can be carried in a pack or in a padded bicycle basket for a gentle ride. The bonded owner and Pawspice pet both benefit greatly from the continuation of happy moments and the continual creation of new happy memories to cherish later.

Benson's Case (Serum Fun Factors and Survival)

Benson Copeland, a 10-year-old M/N Newfoundland, was my first real Pawspice case. Benson belonged to Jack and Kathy Copeland of Mammoth Lakes, CA. Jack brought him

down from Mammoth when his local vet, Dr. Mehrhof, palpated an abdominal mass and ascites. He was treated the previous year for malignant melanoma of the buccal mucosa.

Benson was incontinent and in some mild discomfort due to abdominal distension. However, his mucous membranes were pink and he was bright and responsive. Chest x-rays were negative for metastases. Abdominal ultrasound found numerous hypoechoic lesions in his liver and large hypoechoic lesions in his spleen consistent with hemangiosarcoma or metastatic malignant melanoma. The abdominal effusion was a modified transudate, typical with non-exfoliating abdominal tumors.

We informed Jack that surgery was not an option for Benson and that his prognosis was poor. We recommended euthanasia but Jack said that his wife, Kathy, wanted Benson to come back home for one last goodbye. I had recently heard a seminar on the beneficial effect of increasing serum fun factors for women with breast cancer. Using this information, I told Jack to do all the fun things that Benson loves to do. Jack said that Benson loved to swim at Horseshoe Lake. He asked me if Benson was strong enough to go. My answer was, “Let Benson make that decision. If he stops along the way, let him rest.”

Six months later, we were in Mammoth for a ski trip. The Copelands held a dinner party in honor of Dr. Mehrhof and myself and Benson. Benson had a miraculous response to serum fun factors. Old Benson was still around enjoying his swims at Horseshoe Lake! Benson looked more like a black Gordon Setter due to cancer cachexia. He still had moderate ascites, but he was cheerful and alert. The Copelands took my advice literally. They accommodated Benson’s situation by getting a ramp for their trailer and parking it closer to the lake. They also took Benson swimming twice a day instead of once or twice a week. This new schedule for fun raised Benson’s serum fun factors. The weightlessness of swimming twice a day seemed to have made Benson so ecstatic that he put off dying for six months. Dr. Mehrhof and I looked at each other and at Benson in amazement, wonder, and respect.

Assessing Quality of Life

There is a real need for assessing quality of life for aging, ailing, and terminally ill pets and especially for the cancer patients under our care. Most companion animals have one or more abnormal conditions that developed in their senior years and these conditions generally worsen with time. One-third of our pet population is overweight and/or obese. When these pets become burdened with cancer and its related treatment issues, their pre-existing conditions complicate matters and limit their owner’s choice of treatment options.

Veterinarians are frequently asked, “When is the right time to euthanize my beloved pet? How will I know?” I tell them, “One day, you will just know it is the right time because your pet will tell you with a look or a gesture, a sign or a series of bad days.” A quality of life scale helps everyone, especially those in denial about the gravity of the pet’s situation and those who feel unable to make the assessment objectively. Caretakers use this itemized scale to decide whether or not their pet is being humanely maintained in Pawspice. Every animal has certain needs and desires that must be recognized and respected. If we can meet these basic needs and desires at a satisfactory level for our ailing companion animals, then we are justified in preserving the life of the ill pet during the steady decline toward death.

The basic needs and desires innate to quality of life for terminal geriatric cancer patients should not and cannot, in good conscience, be ignored. It is up to the veterinary professional and to the pet’s individual caretaker to design an end of life program. The Quality of Life Scale provides guidelines for the assessment of a pet so that pet owners can maintain a rewarding relationship that nurtures the human-animal bond while being confident that the pet is well enough to justify prolonging life. This

Quality of Life Scale will relieve guilt feelings and engender the support of the veterinary team to actively help in the care and decision making for Pawspice patients.

The program needs to address each factor that deals with quality of life openly and honestly. We can be very proactive in helping pets achieve an improved score on their evaluations. The scale for each factor runs from 1 to 10, where 10 is the best and highest quality rating for each factor. Since there are seven basic factors in this proposed scale, 70 would be a perfect score. If the terminal geriatric cancer patient scores at least 5 on each issue, the quality of life is considered reasonably good. We could say that a score of 35 means that the caregiver is justified in continuing Pawspice. Each factor needs to be monitored by both the attending doctor and caretaker with careful attention.

The factors in this Quality of Life assessment tool can be easily remembered as “HHHHHMM,” or “five Hs and two Ms.” Every Pawspice program should strive to satisfy each of the factors: Hurt, Hunger, Hydration, Hygiene, Happiness, Mobility, and More good days than bad days. A score above 5 on each factor can be considered acceptable for the decision to begin or continue a Pawspice program. A concise format is adapted for client use (Table 10.1).

Table 10.1. Quality of Life Scale (The HHHHHMM Scale)

Pet caregivers can use a quality of life scale to determine the success of Pawspice care. Using a scale of 1 to 10, patients can be scored.

H: 0–10	HURT: Adequate pain control, including breathing ability, is first and foremost on the scale. Is the pet's pain successfully managed? Is oxygen necessary?
H: 0–10	HUNGER: Is the pet eating enough? Does hand feeding help? Does the patient require a feeding tube?
H: 0–10	HYDRATION: Is the patient dehydrated? For patients not drinking enough, use subcutaneous fluids once or twice daily to supplement fluid intake.
H: 0–10	HYGIENE: The patient should be kept brushed and cleaned, particularly after elimination, avoid pressure sores, and keep all wounds clean.
H: 0–10	HAPPINESS: Does the pet express joy and interest? Is he responsive to things around him (family, toys, etc)? Is the pet depressed, lonely, anxious, bored, or afraid? Can the pet's bed be close to the family activities and not be isolated?
M: 0–10	MOBILITY: Can the patient get up without assistance? Does the pet need human or mechanical help (e.g., a cart)? Does he feel like going for a walk? Is he having seizures or stumbling? (Some caregivers feel euthanasia is preferable to amputation, yet an animal who has limited mobility but is still alert and responsive can have a good quality of life as long as his caregivers are committed to helping him.)
M: 0–10	MORE GOOD DAYS THAN BAD: When there are too many bad days in a row, quality of life is too compromised. When a healthy human-animal bond is no longer possible, the caretaker must be made aware the end is near. The decision needs to be made if the pet is suffering. If death comes peacefully and painlessly, that is okay.

Over 5 is acceptable in each category. A total of 35 points or greater is acceptable for a good Pawspice.

Adapted from Villalobos, A.E., Quality of life scale helps make final call, *VPN*, September 2004.

The HHHHHMM Quality of Life Scale

1. Hurt: 0–10

Adequate pain control is first and foremost on the scale. This includes the pet’s ability to breathe properly. In human medicine, not being able to breathe is ranked at the top of the pain scale. Attention to the pet’s ability to breathe properly is a top priority. Cases with pulmonary effusion need thoracocentesis on an as-needed basis. Pet owners need to be trained to monitor the pet’s respirations and comfort level and to identify labored breathing so they won’t wait too long to provide relief. Some families are willing to provide oxygen therapy at home for their ailing pets. The veterinarian can prescribe oxygen through a medical supply house. Pain control may include oral, transdermal, and injectable medications and be given pre-emptively.

2. Hunger: 0–10

Malnutrition develops quickly in geriatric oncology patients, especially if they have lost their lean-muscle reserve. Caretakers need to be educated about how much their pet needs to eat to maintain body weight. Help the owner assess if the geriatric cancer pet is marginal or severely malnourished. A “rule of thumb” would be to start nutritional support with 250 kcal/day per 10 pounds if a pet exhibits three days of total anorexia or has lost 10% of its body weight (Ogilvie and Moore 2001; Remillard et al. 2000). Many Pawspice pets will live much longer if offered wholesome, flavorful foods that appeal to their dwindling appetite.

My own Great Pyrenees, Alaska, went from a life of consuming only dry food to canned food and then to hamburger, fresh baked turkey, chicken, various types of sausages, venison (thanks to Dr. Jack Stephens), pastrami, cheeses of all types, and gourmet cut and marinated meats. She liked parmesan cheese, smoke flavor, Alfredo sauce, and cheddar cheese soup mixed into her food along with lots of encouragement and coaxing and hand feeding. It takes patience and gentle concentrated coaxing to get some Pawspice pets to eat. It is hard not to be disappointed when such specially prepared food is rejected. Suggest to your clients that if their Pawspice pet rejects an offering, they can come back with another offering with a different flavor a little later and that meal may be more appealing to the pet.

If the pet is not taking in adequate calorie-dense nutrition willingly or by coaxing or force-feeding, then placement of a feeding tube should be considered. Cats do very well with esophageal feeding tubes. Gastrostomy and jejunostomy tubes also have a role in Pawspice care. Instruct owners to use a blender or liquid diets to help their best friend maintain proper nutritional and caloric intake if they elect to use assisted tube feeding.

3. Hydration: 0–10

Educate the pet owner about adequate fluid intake per pound (10 ml per pound per day) and to assess for hydration by the pinch method. SQ fluids are a wonderful way to supplement the fluid intake of ailing pets. Provide demonstration sessions in which the veterinarian or a staff member will teach a pet owner how to administer SQ fluids. Giving SQ fluids regularly can improve the Pawspice pet’s quality of life tremendously.

4. Hygiene: 0–10

Good hygiene is a must! Can the pet be kept brushed and cleaned? Is the coat matted? Is the pet situated properly so that it won’t have to lie in its own soil after eliminations? Many Pawspice pets, especially cats with oral cancer, cannot keep themselves clean as they have their whole lives and they may become demoralized quickly when unclean. The odor associated with necrotic oral tumors can be offensive and cause social rejection by family members.

Prescribe antibiotics to help reduce foul-smelling infections. Also teach owners to dampen a sponge with a highly diluted solution of lemon juice and hydrogen peroxide. They should gently

stroke the face, paws, and legs of the patient with the saturated sponge. This action is similar to a “mother tongue” and helps to clean the fur while soothing the unkempt cat. Dogs love this type of facial and paw grooming too!

5. Happiness: 0–10

Happiness is important for both the caregiver and the pet. Does the patient have desires, wants, and needs? Are they being met? The Pawspice pet’s bed can be moved close to the family’s activities and not left in an isolated or neglected area.

Is the ailing pet willing to interact with the family and be responsive to things going on around him? Is the Pawspice cat able to purr and enjoy being on the bed or in one’s lap? Is there a response to a bit of catnip? Can the cat bat at toys or look and follow a laser light? Can the ailing pet enjoy upbeat greetings from and petting by loving family members? Is the pet depressed, lonely, anxious, bored, or afraid? Do you have a routine fun time that the pet looks forward to?

6. Mobility: 0–10

Is the pet able to get up and move around enough to satisfy normal desires? Does the pet feel like going out for a walk? Is the pet showing CNS signs, seizures, or stumbling? Can the pet be taken outdoors or helped into a litter box to eliminate with assistance? Will a harness, sling, or cart help? Is medication helping?

The answer to the mobility question has viable and variable scenarios. The scale score for mobility is acceptable anywhere from 0–10. I have met some utilitarian pet owners who are very rigid in their requirements for mobility of their pets. They may be regretful but willing to sacrifice their pet’s life rather than elect amputation of a limb. Some pet owners feel that amputation is a mutilation and is not fair to the pet. Instead, they allow the pet to bear a painful limb for months before euthanasia.

7. More Good Days than Bad Days: 0–10

Ask your clients to estimate if their pet has more good days than bad days in a week. When there are too many bad days in a row, the quality of life is compromised and Pawspice may not be appropriate. Bad days may be days filled with undesirable experiences such as vomiting, nausea, diarrhea, frustration, falling down, seizures, and so forth. Bad days could be caused by a progressive condition such as cancer cachexia, profound weakness from anemia, or the discomfort caused by gradual tumor pressure or obstruction or a large, inoperable tumor in the abdomen. If the two-way exchange needed to communicate and maintain a healthy human-animal bond is absent, then the pet owner must reconcile or be gently told that the end may be near.

Krash’s Case (He Was a Very Happy Pawspice Patient)

Krash Pancino, a 12-year-old male 90-pound Golden Retriever of Orange County had compromised mobility when he entered our Pawspice program with osteosarcoma (OSA) of his left distal radius. His history precluded amputation because of severe degenerative joint and disk disease and degenerative myelitis. Krash had severe osteoarthritis of both his knees, along with moderate to severe degenerative joint disease from bilateral hip dysplasia. Krash’s cancer leg was splinted for visits to the dog park and at playtime to offset a potential pathological fracture. His life was happy and full of joy and love for three months (Figure 10.1).

Dr. Robin Downing wrote thoughtfully about the mobility issue in her book, *Pets Living with Cancer: A Pet Owner’s Resource*. Dr. Downing wrote, “Because Murphy is such a big dog—150 pounds and very tall—her ability to get up and down and to walk under her own power are very



Figure 10.1. Krash Pancino at home with family. His OSA leg was splinted for visits to the dog park and at playtime to offset a potential pathological fracture. His Pawspice was full of joy and love that lasted for 3 months.



Figure 10.2. Dr. Robin Downing with Murphy, her 3-year OSA survivor. Murphy had limb-sparing surgery at Colorado State University and was featured in Downing's book, *Pets Living with Cancer*. Murphy developed another OSA lesion in her right tibia at 8 years of age.

important benchmarks in my personal ‘bottom line.’ She would be impossible to pick up and carry around” (Downing 2000) (Figure 10.2). “For the same reason—her size—her ability to control her urine and stool output is important.”

In my opinion, the mobility scale can have a variable score from 0 to 10. The need for mobility seems dependent on the species and breed. Cats and small lap dogs can and do enjoy life with

much less need for handling their own mobility than large and giant breed dogs. If the pet is compromised and is only able to lie in bed, teach the owner to create a schedule to change the position of the pet and rotate the body at least as often as every two hours.

Atelectasis and decubital ulcers must be avoided. The nursing care necessary for large immobile dogs is very demanding. Is the bedding material soft enough? Can an egg crate mattress be used and set up properly to avoid decubital ulcers? Is there a role for a pet mobility cart or an Evans standing cart? These items make a difference in the quality of life for the pet that has limited mobility yet is still alert and responsive.

Sometimes clients are not sure how to assess quality of life issues when the end is near. It can be made more clear to them if a standard scale for quality of life is explained and measured ahead of time and re-evaluated every couple of weeks. Quality of life may need to be assessed every few days or hours, as the situation requires. What many pet caregivers want is for their pet to pass on “naturally” at home, in their arms, in their own bed. In some cases, the veterinarian providing Pawspice care for a pet can realize this dream, as long as the pet is peacefully weakening and not suffering. As veterinarians, we need to understand that it is a very personal and natural wish when our clients request us to help their pet to die naturally at home. We are the ones they turn to for help because we took the Veterinarian’s Oath: “I solemnly swear to use my scientific knowledge and skills for the benefit of society through the protection of animal health, the relief of animal suffering . . .”

Guarantee that the pet is pain-free during the final phase of Pawspice by using the most powerful pre-emptive pain medications during the last days and hours. This will also help clients to better weather pet loss later. Refer to graduated scale for analgesia using the World Health Organization (WHO) pain ladder (Figure 7.1). Help your clients learn more information about pain control at www.colostate.edu/depts/lar/Pain_Assessment.doc. Suggest the option of home euthanasia and, if your hospital does not offer home visits, refer the family to a house call veterinarian.

Use the conceptualized user-friendly HHHHHMM scale for quality of life to facilitate the heart-wrenching decision that euthanasia truly is. Your professional guidance and kindness will help relieve the angst and regret about a beloved pet’s death that too often haunts pet owners for the rest of their lives (see Table 10.1).

Satisfaction: An Important Ingredient of Pawspice Care

Ask the pet owner if he or she is satisfied with the Pawspice arrangement. At times, there is conflict within the family about how attached the main caregiver is to the pet. Some family members feel inconvenienced with the soiling, the odors, the sacrifice, the sadness, or the diverted attention and devotion of the caregiver. This issue creates a double-edged sword for the patient’s main caregiver to deal with on a daily basis. Address these issues directly with the family to help them come to a supportive consensus. If this issue goes beyond your personal counseling ability, suggest a family counselor.

One recommendation that I have found very helpful for planning ahead is suggesting to clients that they visit a pet cemetery. In this way, the pet caregiver is introduced to all the options of after-life services and items, before the geriatric pet passes away. They will know where to go for a memorial stone for their backyard or an urn for their pet’s cremains.

You and your staff play a vital role in the Pawspice care of the geriatric oncology patient. Discuss each case to learn if the preservation of The Bond between this person and this pet will be a rewarding experience. If so, then Pawspice will be a good experience for all involved.

Veterinarians can win client loyalty by respecting and preserving the special bond that connects pet owners to their pets. If the veterinary team helps to control pain and provide nutrition in a peaceful hospice way, client-caregivers gain confidence. They will gain courage as the caretakers of their Pawspice pets and will later look back at the Pawspice experience with satisfaction.

U.S. Pawspice Programs Are Metastasizing

Many house call practitioners tell me that a significant percentage of their home visits are made to provide supportive care of animals with end of life care needs. Dr. Tami Shearer has a non-profit pet hospice practice in the Columbus, Ohio, area. She provides second opinions, pain control, and rehabilitation services for patients, along with instruction and workshops for caregivers.

End of life care is being taught in many veterinary schools as an active part of patient care. The pet hospice program at Colorado State University (CSU) is staffed and run by veterinary students, and supported by faculty advisors in the College of Veterinary Medicine. Animal hospitals in the greater Fort Collins area refer terminal patients to the Veterinary Teaching Hospital Hospice Program. Every patient and caregiver is required to have a relationship with a local DVM, and that veterinarian is constantly updated about the health status of the animal and the emotional needs of the owners. The referring veterinarian also ensures that the hospice case managers understand the patient’s medical needs. Many local veterinarians who work with the CSU Hospice Program will perform home euthanasia.

The goal of the CSU hospice is to create the best end of life experience for both patient and family in their home, when the pet can be made comfortable at home. They teach students that when a terminal pet’s medical needs can be met at home, that’s where the pet should be. If the family feels that they need extra time to say goodbye or if an animal is diagnosed with a terminal illness but has good general health, hospice can help by confirming that the pet’s needs are being met in that environment. Student participant Christie C. Long, Professional Veterinary Medicine Class of 2007, says, “We find ourselves in many situations providing extensive emotional support to owners, especially in helping them determine when it’s time to euthanize their animals” (Long 2005).

Practical Ideas for Some Specific Disease Conditions

Renal Failure Patients

Pets with renal failure that are fed special modified diets such as Hill’s k/d[®] or Select Balance Modified Diet may survive with a better quality of life if they are supported with educated home care. This may include subcutaneous fluids, Tumil-K[®], pepcid, Amphogel[®], vitamins, and fatty acids (safflower oil or fish oils). Regularly scheduled recheck exams, laboratory profiles, and CBCs can monitor renal function, acidosis, and anemia.

Erythropoietin may be used to bring low PCV levels back to normal. One cat in my practice survived six happy years at home on daily subcutaneous fluids, finally passing away at the age of 22.

Senior Cats with Feline Triad Disease

Cats with concurrent liver, pancreatic, and intestinal inflammatory disease may be palliated with fluids and oral potassium gluconate, vitamin E, prednisolone, metronidazole, Actigall[®], pancreatic enzymes, L-carnitine, glutathione, lactulose, S-Adenosylmethionine (SAMe), and SQ vitamin K-1, according to Dr. Johnny Hoskins (2000, 2004). Animals with severe liver failure may be helped with Hill's new diet l/d[®], actigall, vitamin K-1, and milk thistle. Products that contain a combination of supplements to assist the function of the liver are available.

Diabetic Pets

When a diabetic pet's owner is reluctant or needle-shy, the veterinarian can offer oral hypoglycemic medication. Good clinical results can be expected with oral medication in one-third of diabetics that have no ketones in the urine. Clients feel that their veterinarian is trying to help the pet while prioritizing their own concerns. If hyperglycemia cannot be controlled by oral medication, the owner may be more inclined to then try injectable insulin as a second choice.

Anorectic Pets

Anorectic pets often need to be hand fed. People need to learn the proper technique to best hand feed their ill pet. Cats generally like food warmed to body temperature. Squamous cell carcinoma of the tongue in cats renders the tongue stiff and useless and causes early starvation despite efforts to eat. When a pet can't or won't eat, the placement of a percutaneous esophageal feeding tube may be performed under a short anesthetic with minimal risk. The procedure has been described by Rawlings (1993). After the esophagostomy feeding tube is in place, be sure to feed the pet successfully in the hospital several times before releasing him to the owner.

A discharge appointment must be scheduled, during which the doctor or a nurse will demonstrate feeding technique and instruct the owner about how and what to feed the pet at home. The owner should be invited to call for further instructions. The diet and supplements for feeding must be spelled out to avoid clogging the tube and to ensure that the pet is getting enough calories and liquid to maintain body weight. If the tube gets clogged, instruct the owner to use Coca-Cola[®] to dissolve the clog. Create a schedule that spells out morning and evening times for medications, chemotherapy, amounts of fluid, feeding volumes, and supplements on a written daily calendar. This written schedule helps to clarify the day's work order for the home caregiver.

Nasal Cancer Patients

Pets with facial deformity and night stridor may be palliated with combinations of NSAIDs such as piroxicam or carprofen, deracoxib, and so forth. Most dogs with nasal tumors have little to no trouble with stridor while they are awake and panting but have trouble sleeping at night. Most end of life nasal cancer patients will sleep more comfortably and with less stridor if given evening sedation with butorphanol or valium or a combination.

BJ's Case (An Engineer Helped Reduce Her Stridor)

Mr. Shelton, an engineer, devised a plan to help his 12-year-old Lab, BJ, breathe more peacefully at night. BJ had trouble sleeping due to stridor and obstruction of her nasal passages. She loved to play ball and chew on bones. Mr. Shelton punched holes in a tennis ball for air passage. He taught BJ to sleep with the ball in her mouth. BJ got similar relief when she

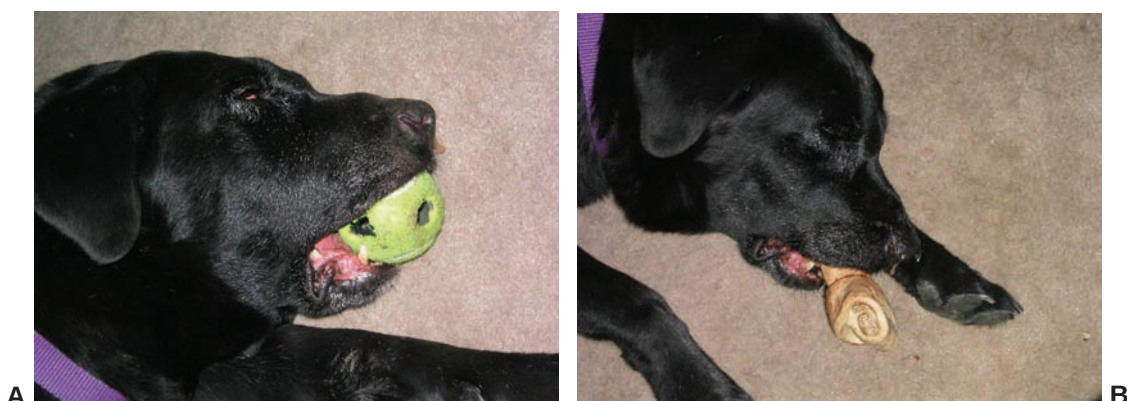


Figure 10.3. BJ Shelton, a geriatric Labrador Retriever with nasal cancer, was more comfortable when she was taught to sleep with a toy, ball, or bone to keep her mouth open. This alleviated nasal stridor.

fell asleep with a large rawhide bone or any object that was big enough to keep her mouth open. This simple adjustment was a joy for Mr. Shelton as a caregiver because it provided so much palliation for BJ. Be sure to keep this concept in mind for the next case you see like BJ. Most caregivers can teach their dog to sleep with a toy, ball, or bone keeping the mouth open, to allow air to flow freely in and out of the trachea (Figure 10.3).

Osteosarcoma Patients

Pets with bone cancer who do not undergo amputation are in great pain and at risk for pathological fracture. These patients can be palliated with pain alleviation, and walking casts to prevent pathological fractures, if necessary. Their quality of life is benefited with the use of ramps to get in and out of the car and the house and on and off the bed.

The use of piroxicam at 0.3 mg/kg once daily not only palliates bone cancer pain but also may actually yield a rare remission on a sporadic basis as shown by Knapp and workers at Purdue University School of Veterinary Medicine (Knapp et al. 1992). Carprofen, deracoxib, meloxicam, firocoxib, and other newer selective NSAIDs may also be used for bone cancer pain palliation with this optimistic goal in mind. All NSAIDs need to be used with great caution to avoid vomiting, gastric ulceration, hemorrhage, nephrotoxicity, and hepatotoxicity in geriatric, frail, debilitated, or dehydrated patients. Tramadol[®], a synthetic opioid, is very helpful when combined with NSAIDs for palliation of bone cancer pain. Fentanyl (Duragesic) transdermal opioid pain patches are very helpful in combination with NSAIDs for bone pain palliation.

Use the highest level of combinations of pain control drugs suggested by the WHO pain control ladder (Figure 7.1) to treat bone cancer pain. Adjunctive drugs such as gabapentin may be needed to provide adequate ongoing pain control.

Degenerative Myelopathy or Paresis/Paralysis

These cases benefit from a wide range of resourceful home care items such as runner rugs for a slippery floor; ramps for the stairs, bed, and car; slings for assistance while walking; chest and rump lifts to help larger dogs stand up; canvas suspension hammocks; wheel carts; soft bedding; and so on. Physical therapy pools, massage, acupuncture, chiropractic, and rehabilitation techniques may help

to palliate these special patients. Always recommend foot covers (booties) made with cloth or canvas to prevent scraping and ulceration of the metatarsals, metacarpals, and toe pads.

Decubital Ulcers

With thoughtful planning, decubital ulcers must be intentionally avoided for all recumbent animals. Instruct caregivers to shop for items such as soft bedding, foam rubber pads, egg crate mattresses, doughnut pads, and waterbeds, all with washable covers. Frequent inspection of pressure sites and complete cleaning of the geriatric oncology patient's coat and skin is important. If the patient is soiled with urine or feces, it is important to completely bathe the contaminated area for maximum hygiene.

If the pet needs or likes to be situated outdoors, extreme caution must be taken to prevent fly strike and maggots. Patients with long hair may need to be shaved to allow more convenient bathing and inspection of the skin and orifices.

Transitional Cell Carcinoma (TCC) Patients

Dogs and cats with TCC often survive for many months with conventional chemotherapy using mitoxantrone and NSAIDs. It will be a tremendous help to the family if you make several simple suggestions in advance. First, suggest that they use diapers for those patients with pollakiuria and incontinence while the pet is in the house. Second, suggest frequent trips outdoors for the patient to void. Third, they can move the TCC patient's day bed close to the doggie door to help the family endure the frustrating problems associated with house soiling.

To palliate severe hematuria and avoid extreme blood loss, a weekly visit to the veterinary office for a flush can be very helpful. Mix a 1% solution of formalin with a vial of the topical ear solution Synotic[®], which contains DMSO. Instill this solution into the bladder with a urinary catheter. Keep the solution in the bladder for 10–15 minutes. Then void the bladder and flush out the blood clots. This palliative procedure may reduce the hematuria for seven to 10 days and may be repeated as needed.

Some TCC cases develop tumor obstruction of urine outflow at the trigone or in the urethra. Prostatic carcinoma patients may develop obstruction of urine outflow due to extension of malignant tissue into the prostatic urethra. Some patients benefit from placement of a permanent urinary catheter. Unfortunately, the patient can easily remove these catheters, necessitating hospital visits for recatheterization.

For geriatric cancer patients with a potential for long-term palliation, the surgical placement of a prepubic low-profile cystostomy tube is helpful (Stiffler et al. 2003). Caregivers are instructed to void the patient's bladder four times a day. The stoma provides immediate life-saving palliation by diversion of urine and bypassing the obstruction caused by the tumor. Cystostomy may reduce hydronephrosis and allow the TCC patient to maintain a good quality of life for a variable time period. Stiffler et al. reported on three dogs with TCC that lived for three, 13, and 30 weeks and one dog with uterine carcinoma that lived four weeks following cystostomy. One elderly cat under my care lived one year following cystostomy for prostate cancer.

Quality of life is an important objective for pet owners who want their cancer patient dogs to be able to participate in as many of their normal activities as possible. Stiffler et al. placed low-profile cystostomy tubes for TCC patients in palliation. No bandaging is required and patients have unhindered mobility with no signs of discomfort. Stiffler reports, "Owners of the dogs began their grieving process during the period of cystostomy tube placement, and their confidence in the quality of life provided by the low-profile cystostomy tube was key to their emotional comfort with their treatment decision."

Brain Tumor Patients

Brain tumor patients that experience periodic seizures may be palliated at home with confidence and with few emergency visits. Caregivers can be instructed to squirt injectable diazepam into the nasal passages or into the rectum for seizure control. Steroids, lomustine, and OM-3 fatty acids and fish oils are reasonable components of a palliative care program for pets with brain tumors. If seizures are not under control with medication, the pet’s quality of life is ruined and the pet owner must yield to hospitalization for IV anesthesia. After two to three days with IV medications, if the patient is not stabilized, then the kindest option is to provide the relief of euthanasia.

Severe Refractive Vomiting

Pet owners have great anxiety and frustration when pets experience severe refractive vomiting. If the normal first line antiemetics fail to control vomiting, go to the drugs that control the chemotherapy trigger zone. The pet may need to be hospitalized and given IV Zofran[®] or Anzamet[®]. For home care, large dogs (60–90 pounds) may be given one-half of a 1 mg Kytril[®] tablet, crushed and dissolved in salty water. The solution can be gently dripped on the pet’s lips. Zofran injectable solution can also be given orally or mixed in yogurt. Anzamet can also be given orally.

On one rare occasion, I dispensed injectable atropine to help a Great Dane that had unresponsive vomiting and salivation due to pressure exerted by a tumor. The tearful pet owner could not afford the more costly antiemetics but was absolutely not ready to make the decision for euthanasia—he just wanted me to stop the vomiting on his slim budget. He was very thankful for the relief from vomiting that his dear dog received with the inexpensive injections of atropine. Be sure to provide liquid tears for pets given atropine in this fashion, especially in breeds susceptible to kerato conjunctivitis sicca.

Severe Pain

Injectable nalbuphine is an inexpensive generic drug that offers pain control without the typical sedation effects that accompany most of the powerful analgesics. Nalbuphine doses range from 0.5 to 1 mg/kg SQ every three to four hours in dogs and 0.2 to 0.5 mg/kg in cats SQ every three to six hours as needed. This pain medication is not registered under the controlled substance regulations and may be of great value in pain control at home for end of life Pawspice care patients.

Managing Soft and Loose Stools

Terminal geriatric pets in Pawspice care are often plagued with soft, loose stools. Abnormal stools may result from illness itself, the treatment, or an imbalance of intestinal flora, or from eating whatever seems palatable from one day to the next. Many Pawspice patients have a diminished appetite and will need to be hand fed. This variable appetite and food intake may cause soft or loose stools and irregular elimination times. It is difficult for some caregivers to manage their pet’s loose eliminations. The soiling problem is magnified for recumbent patients unable to get up and use their normal toilet area.

Practical suggestions make a big difference. Instruct caregivers to feed the patient tasty, bland food. They can feed a prepared diet or use barley, millet, rice, potato, or pasta cooked with chicken broth, garlic, parmesan cheese, and hickory for flavor. Adding more fiber to the diet is helpful. Clients can use canned pumpkin, metamucil, Benefiber[®] powder, oatmeal, oat bran, and high fiber bread as sources for fiber. Symptomatic treatment with Flagyl[®], Azulfidine[®], or Tyolsin[®] powder

may also help. For bland protein, we recommend yogurt, egg, cottage cheese, broccoli, spinach, kale, ground chicken, or turkey cooked in broth and flavors.

If the patient has anorexia or cancer cachexia or has a feeding tube, supplement the diet with high-quality glutamine and whey protein powders such as GlutImmune[®] and ImmunoPro[®] from Biomolecular Sciences, Inc. (www.genomicWhey.com). Glutamine supports intestinal health, helps prevent muscle breakdown, promotes healing, and is a precursor in the synthesis of glutathione. ImmunoPro contains undenatured whey proteins such as lactoferrin, immunoglobulins, and active peptides that can benefit Pawspice patients.

You and your staff should give caregivers all the comfort and encouragement they need. Offer them a supply of hospital towels for frequent bed changes. Help them establish good hygiene for the patient and encourage frequent bathing. If each one of the patient's problems can be addressed and improved by at least 50%, the Pawspice patient's quality of life improves greatly.

Technician house calls may be set up for caretakers who are unable to administer injections and fluids to the Pawspice pet. The reception staff can be made aware of which pets are on Pawspice programs so they can be sensitive when family members call in for information, updates, appointments, or emotional support.

Immunonutrition and Chemoprevention as Palliative Care

Carefully selected supplements play a major role in palliative care for Pawspice patients. Providing support for the "whole patient" has added more to my practice than I thought possible. Dr. Philip Bergman (1999), while at MD Anderson Memorial Cancer Center in Houston, presented an enlightening lecture on chemoprevention. This involves the use of natural or synthetic compounds that may reverse or suppress the process of carcinogenesis, metastasis, and recurrence. Nutritional advice and nutraceutical supplementation programs can be geared to play a role in cancer prevention for treated, untreated, or terminally ill companion animals. Chemoprevention and immunonutrition may be professionally and sensibly supervised at your clinic. This service creates further client confidence that the veterinarian is addressing the pet's immune system and supporting the pet's organ function as much as possible.

Most geriatric cancer patients who undergo surgery, chemotherapy, or radiation therapy are considered to be at a moderate-to-great risk for recurrence of their cancer. These older cancer patients are definite candidates for entry into a Pawspice program. The expectancy rate for recurrence and death from metastases or complications is 50–90% within four to 12 months. Dogs with osteosarcoma, hemangiosarcoma, adenocarcinoma, and lymphoma as well as cats with breast cancer, vaccine-associated sarcoma, oral tumors, and lymphoma are also at very high risk. Cats with IBD, chronic gingivitis, stomatitis, inflammatory disease, and feline triad disease are at greater risk of developing illness or cancer. Cats infected with FeLV and FIV are at risk for retroviral-associated neoplasia. Cats exposed to cigarette smoke and dogs exposed to agricultural herbicides and pesticides are also at greater risk for cancer. When these at-risk conditions are addressed with immunonutrition and chemoprevention, the pet may benefit.

Provide Additional Support for Caretakers of Pawspice Pets

If caregivers need help to cope with pet loss issues the UC Davis Veterinary Teaching Hospital has a pet loss support line that answers questions at 1-800-565-1525. Caregivers may find it helpful to

network with other caregivers who have a geriatric pet with terminal cancer in a similar Pawspice program. With permission, you can provide telephone or e-mail contact information to promote networking between your Pawspice clients. The experienced caregiver has the opportunity to share his or her knowledge with the newcomer.

Internet support groups exist for people who have pets with any specific ailment. There are chat rooms for pets with cancer in general or with lymphoma, osteosarcoma, feline vaccine-associated sarcoma, and many other types of cancer. I was once a guest consultant at a Friday night chat in an online support group for people who have pets with cancer. After receiving information and support at the veterinary office, many caretakers find it invaluable to exchange information and support with other caretakers. Helping clients to network brings them comfort and can be a wonderful staff time saver.

Keep several of these helpful books in your hospital lending library or for sale: *Pets Living with Cancer: A Pet Owner's Resource*, by Robin Downing, DVM, is a very helpful book to orient pet caregivers about the ins and outs of cancer treatment for pets. Dr. Downing tells about her own dog, Murphy, and her battle against osteosarcoma with limb sparing at CSU. The insightful book *Help Your Dog Fight Cancer*, by Laurie Kaplan, educates readers about canine cancer medical treatment and home care, provides encouragement for caregivers of dogs with cancer, and includes illustrated instructions on preparing meals for cancer dogs (2005). This wonderful book is available at www.helpyourdogfightcancer.com.

Some Pawspice pets benefit from day care services provided by the primary care veterinarian's facility while the owners are at work. This service may include taking the pet's temperature and weight, bathing and brushing a soiled pet, providing SQ fluids, injections, and hand feedings. This service can be the key to sustaining a quality Pawspice for the working pet owner. Convenient monthly billing and drop-off and pickup times that revolve around the owner's schedule may be pre-arranged with attending staff members before and after routine receiving hours.

After chemotherapy or radiation therapy or a long battle with illness, pet loss evokes a special kind of grief. Much of the time during Pawspice, we see clients dealing with anticipatory grief. When the battle is over and the pet is gone, there is a big letdown. See chapter 11 for information about grief after the loss.

Because we are a referral practice, we also inform the referring veterinarian about potential problems with the client's grief. We ask the doctor to alert the staff to provide as much comfort and support as possible to the grieving pet owner during Pawspice. The attending local doctor should make an effort to contact and encourage the pet owner to seek counseling and should document this effort in the medical record.

Zorba's Case (Pawspice for Old OSA Survivors)

Zorba Tuck, a 13-year-old M/N German Shepherd Dog, had been treated for osteosarcoma two years previously but was lost to follow-up. There was a sad voice mail message from Susan Tuck, Zorba's caregiver. She was in tears. Her wilting voice thanked me for the gift of Zorba's life for the past two years. Zorba had won his battle against osteosarcoma. He had an amputation of his left hind leg followed by chemotherapy. Carboplatin and Adriamycin were given initially for two cycles, followed by five treatments with carboplatin at three- to four-week intervals over nine months. Zorba had concurrent severe arthritis and was on carprofen and injections of Legend® and Adequan® from his orthopedic surgeon. Zorba needed assistance with a support sling to get up and walk as he reached his one-year metastasis-free anniversary.

He swam every day for exercise. Susan's phone message said, "It's not Zorba's cancer that is going to kill him. It's his arthritis. It pulled the rug out from under him." As Zorba approached 13 years of age, he had more difficulty with his front legs until, finally, he could no longer stand.

When I called Susan back, her phone was on call screening. She said that she wanted to speak only to her husband or to me. She did not want to take calls from her friends because they did not understand and would say hurtful things like, "Well, Zorba has had a long life." and "When will you come to your senses and let him go?" In response to this type of complaint, I generally say, "Forgive your friends. They mean well and they are sad to see your heart breaking. They don't understand how much Zorba means to you. They don't understand the depth of the human-animal bond that you share with Zorba."

When I asked Susan about Zorba's quality of life, she said enthusiastically, "He is fine, Dr. Alice, he just can't stand. He plays, he eats, he barks, he is happy. He has always been just fine lying around because of his arthritis." I asked her if she was able to keep him clean and she said, "Oh, it's not a problem and I don't mind that at all. We have a routine. Of course, I quit my job to be home with him 24/7. My husband is very supportive." Her voice cracked with grief and sorrow. I said, "If Zorba is happy, he must sense your sadness and wonder what he has done wrong." I pointed out that she seemed too sad right now for the Pawspice that she and Zorba were sharing and that she was ruining their precious moments together with anticipatory grief. She said, "That's it, Dr. Alice, I knew you would understand!" I said something like this: "Susan, you need to reconfigure your emotions. Enjoy the precious days that Zorba is giving you. He is still very much alive and with you! When you smell a rose, the fragrance gives you pleasure for that instant even though you know the rose will wilt in a few days. Zorba is like a flower. You need to inhale Zorba's fragrance and his presence today even though he will wilt tomorrow. Zorba is there with you right now. He is not dead yet. You need to focus on the moments of joy and share the happiness of your bond."

Susan thanked me for helping her to think more clearly and stay in the moment and to "Think the way Zorba did." I told her, "Look into his eyes and focus on the wellness that was right there in front of you and count your blessings about how well he is today. When more functions get subtracted from Zorba, he will tell you when the time would be right to give him back." Susan told me that she felt better and thanked me again for being so supportive.

Susan clearly needed to use a Quality of Life Scale as a guideline for future decision making. At the end of our conversation, I promised to fax articles about Pawspice, quality of life, and anticipatory grief as well as the phone number for the Pet Loss Hotline at the University of California, Davis. Susan left a message the next day. She said, "Thank you Dr. V. After reading the mobility section in the quality of life article, I knew that I was doing the right thing for Zorba. He is happy and playful." Susan felt validated with her choice for Pawspice care for Zorba. It has been over three months since Susan's tearful call, as I write. Susan hopes that Zorba will celebrate his 14th birthday and a three-year anniversary with osteosarcoma.

Summary

The Bond between pets and their human caregivers is a celebrated and cherished attachment relationship (Voith 1985). When it is time for the physical departure of the pet, The Bond grows even stronger. The pet's death is heartbreaking for the entire family. Pet owners may express emotions that are uncomfortable for the doctor and staff to witness and deal with (Cohen and Fudin 1991). Many

pet caregivers suffer from severe anticipatory grief. They often want to spend as many last days as possible with their pet at home before their inevitable loss.

Being old, having more than one concurrent disorder, and having cancer are associated with shortened survival times. Keeping all of this in mind, it is time for contemporary veterinarians to rethink how our profession can improve the attitude and delivery of end of life services for terminal patients. We can improve our willingness and demeanor when discussing options for palliative care and turn up the level of supportive care that we offer. We can very professionally help pet owners face the final days with their best friend. We can better equip our clients with the knowledge, support, and resources they need to successfully forge ahead into the final phase of their beloved pet’s life.

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Chapter 11

Euthanasia for the Geriatric Cancer Patient

Euthanasia is a time when you can do more for the family than at any other time in the pet's life. That is why veterinarians must sensitively respect the bond that exists between the pet and caregiver.

Cathy Adams, DVM

A Philosophy and Principles

Many pet caregivers hope that someday, when the time is right, their beloved pets will pass away at a ripe old age in the privacy of their loving homes. We would all prefer to have our geriatric cancer pets pass away peacefully and painlessly, but that is seldom the case. The slow decline of a sick geriatric cancer patient can be a bumpy road. Many pet caregivers say they want their old pal to have a “natural” death without understanding that their pet may suffer unnecessarily (Feldman 2004). The pet's quality of life and freedom from pain must be regarded as most important. Cancer is a merciless and relentless disease. Our geriatric oncology patients are stoic and unable to comprehend sacrifice for extra life. This combination leads to unrecognized suffering. The attending doctor, as the pet's advocate, should assist the caregiver in every way possible and be vigilant to assure that the pet will have a peaceful and painless death (Rollin 2006). It may be too difficult for the family to accompany their pet all the way to the end. They need to be prepared for the process of euthanasia.

Emergency-Related Euthanasia

Unfortunately, many geriatric pets develop cancer quietly without notice and wind up in an unfamiliar emergency clinic instead of your hospital, among the doctors and staff that they have known their whole lives. Occult cancer often reaches a threshold that precipitates an acute symptom. Geriatric dogs are commonly presented to emergency rooms for cancer-related illness such as hemoabdomen, weakness, epistaxis, seizures, pathological fractures, syncope, dehydration, vomiting, diarrhea, anorexia, pain, metabolic problems, and so forth. Geriatric cats with occult cancer commonly present with dyspnea, dysphagia, vomiting, diarrhea, dehydration, anorexia, cachexia, and so on. The emergency room clinician is often the first to diagnose cancer in the geriatric patient. Many geriatric pets diagnosed with cancer by emergency room doctors are euthanized within hours of the emergency visit, while others undergo emergency treatment and surgery.

Geriatric patients are at greater risk of death and surgical complications. Aging causes increased susceptibility to sepsis, poor organ system functional reserve, and a decreased ability to cope with

the stress of anesthesia, surgery, tissue damage, and pain. The risk for complications and poor response to cancer therapy increases for the oldest of the old, especially if they are obese or have concurrent disease and chronic debilitating conditions (Balducci et al. 2004).

Geriatric oncology patients are at risk for more oncologic emergencies than younger cancer patients receiving similar therapy. Oncologic emergencies related to treatment toxicity commonly involve vomiting, diarrhea, leukopenia, sepsis, thrombocytopenia, renal failure, heart failure, hepatic toxicity, tumor lysis syndrome, drug and radiation therapy related reactions, and so forth (Ogilvie and Moore 1995). Caregivers of geriatric oncology patients receiving therapy may feel they must give up if their pet becomes extremely ill. They may feel guilty about stressing their old pet and for making the decision to treat the cancer in the first place.

When consulting with clients who are seeking alternative care for their terminal pet, the first thing to do is take a moment to be sincere and praise their love and devotion for their pet. Of course, their special love bond and anticipatory grief is motivating their search for a “cure.”

Cabo's Case (Love Blindfolds Some to Hope Against Hope)

During one of many phone consultations with Elaine, I said, “I know that you love Cabo very much and that she means everything to you. I know that you would do anything if it would help make the renal cell carcinoma in her abdomen and the lesions in her lungs go away. Her tumor burden is too high to expect that any more chemotherapy would be able to help her. At this point, chemotherapy would most likely burden her one functional kidney and make her very sick. Furthermore, chemotherapy in the face of the huge tumor burden that she has would offer little or no benefit. There are some experimental small molecule therapies being developed but we don't have access to them as yet. My job as Cabo's doctor is to make sure that we do no harm to her in these final days. Just slow down your quest for a cure, and stay home with Cabo and try to enjoy her final days of wellness until she crashes.”

When deeply bonded clients like Elaine keep asking if there is anything else you can suggest to help Cabo and make the tumor shrink, they need to know what you know about the cancer and its impact on the patient's body and what to expect. They also need to know what you don't know. They need all the emotional support you can give them, along with as much palliative care that you can recommend for the terminal patient.

If the client feels you are a dead end for the pet, he or she will often seek out alternative, complementary, and integrative medicine with or without your blessings. I point out that researchers have examined a number of the most efficacious remedies offered in holistic and alternative medicine and that some techniques do have merit, while others are unsubstantiated, unproven, and even questionable.

The one ingredient that alternative medicine offers its patients is hope. This is in contrast to the evidence-based paradigm that our conventional western medicine generates on response rates, disease-free intervals, and survival times. A working definition for hope is to wish for something with expectation. Alternative therapies generally require one prerequisite, and that is to be ministered to the patient with hope.

As a general rule, if an integrative technique seems to alleviate pain or adverse conditions or improves the recurrent geriatric oncology patient's well-being, then it is good to continue. If there are no benefits after four visits, then it makes sense to stop the treatment. Many of my clients take their geriatric pets to holistic doctors for detoxification, acupuncture, and massage after receiving chemotherapy at our office.

Elaine's bond for Cabo was very deep. She consulted with our service, another oncologist, a holistic practitioner, and a health foods store from the start. She acquired some last-minute supplements at her health food store and opted to try interferon therapy under the direction of her other oncologist in a last ditch effort to help Cabo. Elaine told me that she knew that she was hoping against hope. She felt that it was all she could do. This happens to pet owners who can't face the fact that their pet is terminal. They still prefer hope against hope, to hope with little reason or justification.

When Cabo went into respiratory failure, Elaine wanted the emergency room doctors to resuscitate her. After 20 minutes, she finally let Cabo go. Afterward, Elaine second-guessed herself at every step of the way. She asked me about harmful side effects from interferon. She was moving through the typical stages of grief. I comforted her by helping her recognize that she was going through the "woulda-coulda-shoulda" phase of grief. She told me that she felt compelled to do all that she could for Cabo and that she would miss her forever.

Emergency-associated euthanasia is generally an emotional shock to the pet's family. They have had no time to prepare emotionally for the loss and to make matters worse are required—sometimes pressured—to make the decision to euthanize. Understandably, they may have intense guilt. They may blame themselves for not knowing or for procrastination—for letting some small innuendo or symptom slide. Some pet owners feel that they abandoned or gave up on their best friend. Self-doubt haunts some caregivers, causing angst, sleep disturbances, weight loss, and depression. They sift over every moment of the visit asking "woulda-coulda-shoulda" about each step, each action, and every decision. Their feelings of guilt may persist for a long time. Some caregivers feel that no one understands their sorrow and that they have no one to talk to about their feelings of loss.

Cecilia's Case (Self-Doubt Follows Even Good Decisions)

Many clients need emotional support following their decision. You may recall Cecilia, the Golden Retriever with hemangiosarcoma in chapter 9. Corbin wrote the following letter seven days after Cecilia was euthanized:

"When I was told she [Cecilia] was very uncomfortable and would only get worse, I made what I believe was the correct but too quick of a decision. I should have demanded supportive treatment. If she were bleeding a major bleed, would her hematocrit levels drop faster and more drastic? 30 is not that bad, is it?

When I asked, the Dr. said that anytime from that point on was the right time. She said it will only get worse and that she will become increasingly uncomfortable. I should have contacted you to get your opinion. . . . I feel that in my panic driven state, I made a decision without demanding more medical facts and options. I just did not want Cecilia to be in pain."

Planning for Death

Caregivers with a geriatric pet with terminal cancer in Pawspice care may have many questions and great fears about death and euthanasia. "How will I know when the time comes? What do I do? I can't go through this." The answer to the first question should rest with the pet. Advise the family that their old pal will give them a clear sign. The signs may be physical, such as unresponsive vomiting, uncontrollable diarrhea, dyspnea, crying, and loss of mentation or slipping into a moribund state. Some geriatric cancer pets decline to the point where the caretaker notes that

they are having more bad days than good days. Use the proposed Quality of Life Scale (Table 10.1) as a guide to help in decision making about euthanasia. When counseling caregivers, you might say, “Look into Stormy’s eyes and he will tell you when it’s the right time for him to go. The message will be clear and you will know.” The eyes usually tell the story: pupils are dilated, the cornea appears glossy, the third eyelid may be prolapsed, and the pet may be squinting (Cohen and Sawyer 1991).

The answer to the second question, “What do I do?” is more logistical. When the time approaches for the pet to be humanely euthanized, the emotional pain for the family may be softened if they know that euthanasia can be performed at any time of the day or night. Arrangements must be made in advance to cover the patient’s needs 24 hours a day. Referrals to a house call doctor or an after-hours emergency room facility need to be set up so that the decision about the right time for euthanasia is made on behalf of the pet, not the doctor’s office hours.

When the time comes for the emotional pain that is unavoidable with the euthanasia of a companion pet, caregivers whose pets are in Pawspice care are empowered to make the best decision for the pet. Advise the client to have several plans in mind. Plan A may be their ideal wish, for their terminal pet to pass away peacefully at home. Plan B may be with a house call doctor who will perform home euthanasia. Plan C may be euthanasia at your hospital during regular office hours. Plan D may be euthanasia at a specified emergency clinic in the event the need comes after hours.

Pye’s Case (Leave Room for Every Caretaker’s Plan A)

“Dearest Dr. Alice:

My beloved Pye passed away Friday evening. I write this note of thanks to acknowledge that it is by cause of your good work and guidance of Pawspice that we were afforded a long, peaceful goodbye. I had the time to say all the things that I wanted to say to him and also tell him that I know how much he loved me, too. Pye was home with his brother Joie and I when he passed. I am confident that he was exactly where he would have chosen to be.

As I was armed with your knowledgeable counsel regarding Pye’s particular type of cancer (hemangiosarcoma), I was able to see him through his several ‘incidents,’ and rather than have him euthanized prematurely (as I had contemplated more than once prior to learning of ‘Pawspice’), I was able to provide Pawspice care at home for him and we were afforded the most loving of farewells. I could not have designed a more beautiful end of life for him and I pray that when his brother’s time comes, he too, will be able to remain at home with me caring for his end of life (Pawspice) and a safe, loving, slow return to his brother. Fifteen years has been far too short a time together and I selfishly wish my beloved pets could live with me forever. But I remind myself that ‘the death of an OLD and BELOVED man (pet) can NOT in any manner of honesty, be called a tragedy.’

In loving thoughts,

Ginger Atkynes

Many pet caregivers make the statement, “I can’t go through this.” We should not ignore this cry for help. We can be supportive and say something like, “You are doing a wonderful job caring for Scooter right now. She is depending on you to do the right thing. When the time comes, it will be as if you have a curtain call. You must go out on stage, like an actor, and go through the motions. You may not feel that it is real, but you know your role and what you have to do and say, as a farewell to Scooter. When you get back home, you can have your breakdown and cry.”

Euthanasia at the Hospital

Many families plan to bring their geriatric oncology pet to your facility for euthanasia. This is a sad and very difficult occasion for caretakers but with just a little effort, you and your staff can make it as pleasant as possible. Comfort your clients. Encourage them to bring their pet's favorite blanket, toys, candles, and music. Let them know that they can bring their children, other pets, and close friends as well. Alert your staff that there is a euthanasia service going on and that they should keep their voices down to show respect for the grieving family.

Many new and remodeled hospitals have added a comfort room or rainbow room furnished with a couch and carpeting for a warmer atmosphere. If your facility lacks a comfort room, it helps to create a gentle atmosphere in one of your exam rooms. Turn off or dim bright overhead lights or use a small room lamp.

At our clinics, we shut off the overhead lights in the exam room, turn on the x-ray viewer, and bring in blankets. This subtle change in lighting works well to soften the harshness of the room. We light candles for ambiance and symbolism, and to show reverence and respect at this sad time. We place flowers and leafy greens nearby on the pet's blanket.

Next, we explain to the family that you have a two-step process for euthanasia. The first step is to give a sedative to the cancer patient and the second is to give the final injection. Now we ask if the family is ready for the first step.

Giving the patient a deep sedative allows the stressed caregivers to relax while their beloved pet gently falls into a relaxed state and loses consciousness. We always keep the terminal pet in the presence of the owner. I use a 27-gauge needle and give a deep intramuscular injection of Domitor® with butorphanol to prevent nausea. The patient seldom feels it but if there is a struggle, I apologize immediately.

Some doctors prefer to use Telazol®, SQ, or IM injections of butorphanol-acepromazine. It helps family members to know that Domitor is reversible in case they change their mind. To avoid emesis, we give an SQ injection of butorphanol as a pretreatment five to 10 minutes before the sedative or along with it. The presedation allows that big first step of physical separation to be an easy step for the family to witness. I tell them to say goodbye as they watch their beloved pet slowly falling into a relaxed sleep. Caregivers often comment that they sensed that their pet seemed very peaceful with the sedative. I let clients know that the sedative provides powerful control against cancer pain (De Lorimier and Fan 2005).

We leave the room to give the family privacy, placing a marker on the door so staff will not enter. We return in five or 10 minutes. At this time, we ask if each person in the room wants to stay for the final injection. Some family members feel that they can't be present for the "final" procedure. They are content to leave their pet in the sedated state. Many caregivers want to be present for the injection and their pet's last breath. This is the time to assure the family that the next step will be the euthanasia injection and that it will be painless and fast.

The next step in this protocol is to place a towel over the pet's body and cover the chest area up to the neck. We explain that the final injection is an overdose of a barbiturate. It can be given into any vein or into the heart. It will cause the heart to stop beating, but some reflexes are powerful enough for the pet to gasp or sigh after death.

Gently lift the towel, palpate for heartbeats, and give the euthanasia solution directly into the heart while directing the family to lovingly stroke their pet's head. Since we started using this procedure, we found that it eliminates staff pressure. The nursing staff does not have the stress, worry, and struggle of

trying to place a catheter into a hypovolemic, dying companion animal. Some house call doctors prefer to give the final injection intraperitoneal. The patient takes longer to pass but the passing is peaceful.

A number of house call veterinarians have found this two-step method of sedation and euthanasia to be of great relief to them. A house call doctor is often the provider of Pawspice care services and has the sad task of performing many home euthanasia visits. The chore of placing an intravenous catheter in the home environment can be overwhelming. One doctor told me horror stories of trying to get an IV catheter into a hypotensive cat or into an obese dehydrated nasty dog that urinated and defecated on the family living room carpet. Afterward, she and her assistant had to carry the pet's body to her car for cremation service pickup at her home office.

At the AVMA Human-Animal Bond Session in 2000, Bonnie McKinley, my long-time oncology nurse, co-presented a lecture with me on Pawspice. We ended the lecture with this two-step method of letting pets go. House call doctors were relieved to learn that they could bypass the ritual of placing IV catheters into stressed, fearful, near-death pets. They welcomed our protocol of presedation and delivery of euthanasia by IV, IC, or IP injection according to preference. House call doctors can inform clients that they will leave large deceased pets in the home. This gives the family the opportunity to hold a wake for their deceased pet. A list of private cremation services can be provided to pick up the pet's body for specified cremation or burial. Some of my clients will invite friends and family over to visit their pet to say their final goodbyes before the house call doctor arrives. If euthanasia is to be performed at the hospital, the very last thing that we want to do is to take near-death geriatric pets away from their grief-stricken caregivers, even for one minute. Many institutions teach that the euthanasia solution must be given as an IV injection through an indwelling IV catheter. Often, the pet is taken out of the exam or comfort room and away from the family, into a treatment room where the IV catheter is placed into the patient's vein as the first preparatory step before euthanasia. This runs counter to the definition of a sensitive and caring enactment of euthanasia. Catheter placement can be traumatic for a dying, dehydrated, hypotensive geriatric oncology patient and the patient might struggle. Near-death pets may be in extreme discomfort. They may have pulmonary or abdominal effusions, dyspnea, dehydration, anemia, and/or cachexia. That struggle would be too difficult of a scene for the pet owner to witness.

Taking a pet that is about to be euthanatized away from their pack, the tearful family, dismisses and violates qualities of their special attachment (Voith 1985). Placement of an indwelling catheter in a back room is done purely for the doctor's convenience and is disrespectful to the pet and the family. If we want to be the geriatric oncology patient's advocate, ideally, this scenario would never happen. If we honor the human-animal bond, separation of the geriatric cancer pet from family for catheter placement is avoided at all costs. Nurses get frustrated, even though the pet owner is not present. They feel that placing the euthanasia catheter is a behind-the-scenes betrayal to the pet and to the client. For all of these reasons, contemporary bond-centered veterinarians should redesign their old standard euthanasia protocol.

Think only about making the very last moments of life easiest for the patient and family. Use SQ or IM heavy sedation as step #1. While the sedation takes effect, allow private time for the pet to fall asleep comfortably on familiar bedding, surrounded by the loving faces and soothing voices of the family. Then give the final injection IV, IC, or IP.

Suggest a Wake

Family members may want reassurance that their pet is truly gone. Offer them the use of a stethoscope to hear that their old pet's heart has stopped beating. There is not enough reverence, service,

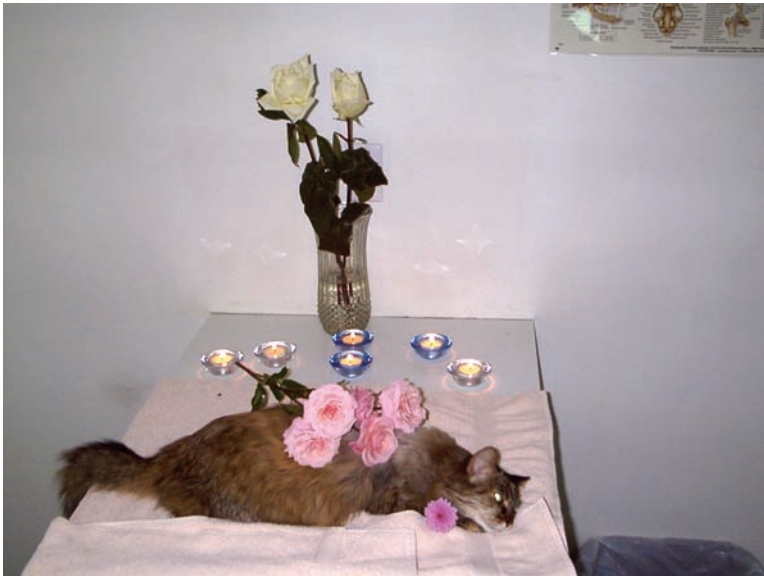


Figure 11.1. Create reverence at the time of euthanasia by suggesting a wake with flowers, candles, and soft lights. Console the family and encourage them to stay for a while to view and reflect beside their deceased pet.

ceremony, or emotional support offered by our profession and society as a whole to caretakers on the occasion of a dear pet's death (Villalobos 2002; Corbin 2004). Encourage the family to stay for as long as they need to, to view and reflect beside their deceased pet (Figure 11.1). The special bond that connects clients to their veterinarian is severed when the geriatric oncology patient dies. The clinician who learns to make the euthanasia experience an enriching one will not lose that bond with the family.

One very special way to validate and enrich the experience of a beloved pet's passing is to encourage the family to have a wake. This is a special time for the pet's family to grieve, read poems, and talk about how important and sweet their beloved pet was. Suggest writing a poem or a story about who this pet was to friends and family and what made their relationship so special.

Offer the family a lock of fur. Gently clip the fur from a familiar site and place it in a windowed envelope with the date and the pet's name on it as a remembrance. This is also a good time to make a plaster imprint of the pet's paw as a memorial (available from the Argus Center at Colorado State University).

As part of the wake, you or one of your staff can sit on the floor next to the pet and read the special poem "Rainbow Bridge." If time permits, select a few short poems from *Angel Pawprints* (for dogs) or *Angel Whiskers* (for cats). These two books are wonderful anthologies of poetic reflections on loving and losing a canine or feline companion edited by Laurel E. Hunt. My favorite reflection from *Angel Whiskers*, titled "The Last Will and Testament of Silverdene Emblem O'Neill," was written by Eugene O'Neill. It has thoughtful humor and helps one to think of forming new attachments in the near future. Another book titled *My Personal Pet Remembrance Journal*, by Enid Samuel Traisman, MSW, helps caretakers to weather the difficult days of pet loss that lay ahead of them. You might find such a book and personalize it by writing a message to the family on the inside cover.

The grieving family should feel welcome to stay in the comfort room as long as they need to. Give them private time to cry and grieve alone with their deceased pet. Every five or 10 minutes, check in on the family and see if they need a cup of water, new tissues, or any other assistance.

After the wake is over, ask who is driving home and confirm that, in your judgment, the person is competent to drive. After such an emotional experience, it can be difficult to focus. If you have any doubts, recommend that the family sit or take a walk outside the clinic for a few minutes to get fresh air and regain their composure before leaving.

Many caretakers create a shrine for their pet at home, containing photographs, candles, the pet's favorite toys, a collar, and other keepsakes. When bidding farewell to the family, mention once again that they may want to write a story or a few paragraphs about their dear pet to help in the grieving and closure processes. Ask them to send you a copy of this tribute to so that you can share it with your staff.

Compassion and After-Life Services

When a geriatric cancer patient dies in the hospital or at home or is euthanatized under a veterinarian's medical care, the family may ask about after-life services. The family may expect the hospital staff to provide information and guidance about what to do and where to go. Veterinarians can improve and update procedures and protocols concerning how the hospital staff offers the bereaved family this sensitive information. The staff should conduct conversations of this nature in a private room—not at the front desk. They should offer condolences and should compassionately offer comfort and console the caregiver during this emotional time.

Veterinarians play a complex role at death time. We wear many hats when a geriatric cancer patient is in the process of dying and after the pet has passed. Clients frequently ask, "How do you it, Dr. Alice?" I say, "I know that I am helping you step over a very difficult threshold and I'm holding your hand. By helping you say goodbye to Stormy, I can help you go through the cycle of love, joy, and grief."

Veterinarians provide the services of the attending doctor, the grief counselor, and the funeral director. Physicians in human medicine routinely disconnect with the family upon the death of a patient. They may not ever see that family again. A human body is quickly transferred to a cremation service or funeral home. Funeral home personnel are trained to help with arrangements and prepare the deceased for either cremation or burial. After a person dies, the family spends a great deal of time at the funeral home making the arrangements, picking out memory cards and poems and writing an obituary for their loved one, deciding what clothes to bring back for the service, and many other related activities. These activities help with closure, but pet caregivers have very little ritual to help them deal with their loss.

We accept that there is a need to grieve the loss of a companion animal but provide no formal outlet service. Regardless of the circumstances surrounding a pet's death, the caretaker is always in a time of need. Any support offered by the veterinarian at this sad time deepens the doctor-client relationship. The attending veterinarian, if willing, can become the provider of supportive care for the client's emotional crisis. Do not recoil from this responsibility; do not neglect to offer solace.

A well-trained, compassionate staff will also play an important role in consoling bereft caretakers. Staff can comfort grieving clients by offering professional emotional support and information. It takes caring, planning, teamwork, and coordination to make the euthanasia experience as pleasant and sensitive as possible for the geriatric oncology patient's caregivers. Half of clients who elect euthanasia question themselves after the pet has died and feel extreme guilt (Adams and Shaw 2006). "Humane euthanasia is a time when you can do more for the family than at any other time in the pet's life. That is why veterinarians must sensitively respect the bond that exists between animals and their caregivers" (Adams 2005).

Dealing with the Pet's Body for High-Need Clients

When a geriatric cancer pet dies, the human-animal bond remains precious to the caregivers and is often symbolized by loyalty and respect for the pet's body. The family is generally unprepared for handling a deceased pet's body. They depend on their attending veterinarian's kindness for counseling and recommendations to pet crematories or cemeteries. Some clients elect the traditional in-house "disposal" service if they can't afford or don't want specialized private arrangements. Others will be grateful for information about other options.

The Bond may have been very intense due to the pet's special training. The pet may have been a service dog, a show dog, or an unconditional loving companion to a "high-need" person or a person who lives alone and has no other pets. The sense of loss can be overwhelming for some pet caregivers. They may feel emotionally drained, vulnerable, and unable to make any after-life decisions without your help.

The family may expect that your hospital will cremate their pet's body. They may not know that private cremation or private burial is available. They may ask you what they should do. Instead of saying what they should do, you might share with them what you have chosen to do. I tell clients who ask, "My pets are all cremated." Their ashes are in containers on top of a high cabinet at my house. It is in my will that their ashes go with me, wherever I go, up or down, whenever the time comes."

One of my current responsibilities is being a board member for the Los Angeles Pet Memorial Park. The park itself is beautiful, with lovely memorial benches under large trees for people to sit and look at hundreds of headstones. The park offers private cremation services on site, burial services, and a pet mausoleum for those who can't afford a full burial due to land fees. There is a little Rainbow Bridge Park on the grounds. This park is a wonderful place for people to visit before and after their pet has passed. Members get a newsletter and a yearly invitation to a fund-raiser at the park. Pet owners have an open invitation to visit their pet's gravesite. The staff at the park is very sympathetic to the bereaved pet owners.

Only a small percentage of pet owners request burial and memorials at pet cemeteries. Many caretakers take their deceased pets home for private burial on personal property and others choose to have their pets cremated individually, requesting that the cremains be returned to them. (This service generally goes through the hospital's chosen crematorium.) The vast majority of pet owners request cremation by the hospital's contracted facility.

When your hospital refers clients to facilities for cremation or burial, those facilities become an extension of your hospital. Evaluate any facility that you recommend to clients for after-life services. Make sure that they are professional, thoughtful, and respectful. The stressed client is amenable to trusting the doctor's choice for a good and reputable cremation or burial service for the pet's body once the client makes the decision.

Cecilia's Case (Respect the Client's Spiritual Belief System)

One more important aspect about Cecilia, our Golden Retriever with hemangiosarcoma, involved her after-life care. Corbin wrote:

"Dr. V,

I am glad that you agree about post-euthanasia/follow-up care. I never gave that a second thought until now and how that is such a powerful bridge to one's grieving process. Another issue is the handling of the body.

While the life force may have left the body, should we not honor the body with dignity and respect—especially if that is part of one’s spiritual belief system? We would never just throw a human body on the ground of some cold warehouse wrapped in a garbage bag (yes, that is where I found Cecilia’s body—100 miles away from the clinic—and I know this is common practice). Why do we not extend the same dignity and respect for the body of our companion animals that we do humans? . . .

Seeing Cecilia’s body stuffed in a trash bag laying on the ground like a heaping pile of garbage with the “Pet Memorial” staff just staring at me with these blank looks was more than I could take. Ever hear of a gurney or a table to transport her into my car or something a bit more dignified? My girl was better than that, and I am glad that I heard her call for me to pick up her body and take it to a place that would treat it with dignity and respect. It was quite odd how all that happened . . . Through this experience, I see so many areas that need to be addressed if we are to truly honor the human-animal bond. I know my thoughts and ideas may not be readily embraced by all veterinarians but those are the ones that need to hear it the most! Thanks for your encouragement.

J.”

It is part of everyday practice for the attending veterinarian to gently and compassionately advise and make arrangements for the final disposition of the deceased pet’s body. Make it a policy to greet the family when they come to pick up their pet’s remains from your hospital. This is an opportunity to give the grieving caregivers a hug and see how they are getting along. Take this moment to encourage caregivers to write about their pet and send an e-mail tribute to friends and family if they have not already done so.

Also, suggest a memorial service. Caretakers may find that holding a memorial service for their pet provides great emotional support. In the manner of a wake, invite friends and family to gather together in honor of the pet. The caretaker may want to prepare a eulogy to present at the service. The following eulogy, written for 14-year-old Bullet by his caretaker, Laurie Kaplan, might help your clients in writing their own eulogy. Bullet survived more than four years with lymphoma and two years with dilated cardiomyopathy before passing from renal failure. Kaplan is also the author of the book *Help Your Dog Fight Cancer*, which she wrote to help others with cancer dogs through the journey (JanGen Press 2005).

Bullet’s Eulogy

Thank you all for coming today to share some memories of Bullet, to help me celebrate his life and to say a loving farewell.

Bullet and I walked these trails thousands of times in the 12 years, 2 months and 1 day that he was with me. I calculated that we crossed these very stepping stones more than 2,000 times. I can almost see him now, prancing regally, wearing that wonderful husky smile and lifting each paw high with every step . . . moving from stone to stone with the pure, natural grace that can be seen only in a wild creature completely unaware of and unimpressed by his own beauty.

Rarely did anyone pass by us without stopping to admire Bullet. But he also had a great inner strength, a strength and temerity that enabled him to survive lymphoma. That same indomitable spirit enabled him to survive a heart disease expected to kill him within 6 months. That was 2 years ago.

But there’s one thing that Bullet was NOT—he was not an easy dog. (I have a funny feeling we might hear a story or two today reflecting that.) But to me, his willfulness, his wildness and his “growliness” were all just part of his charm.

Bullet stole my heart in a split second in September 1992 and Bullet will always have my heart. He is my heartdog, the love of my life and the dog of my dreams. Thank you all for coming today. Thank you for listening. It means a great deal to me that Bullet's favorite people—and mine—are here to share this moment. Now Ru is going to say a prayer and then whoever wishes to will share a special memory about Bullet.

Invite your clients to come back into the cycle of life in the bond with a fresh set of paw prints by their side. "Doctor's advice" for caregivers should be, "Don't remain petless for long, and stay in touch."

Compassion and Compassion Fatigue

There is no doubt that many veterinarians experience burnout from the pressures that euthanasia, a very sad part of daily practice, places upon them. It is easy to get attached to clients and pets in geriatric cancer care. The loss is felt by the nursing staff, receptionists, and everyone else involved in the case. It is especially hard to lose our long-term geriatric oncology patients and their loving caregivers.

Practicing oncology plays tug-of-war with our emotions. One minute we are struggling to save a pet's life, and the next minute we are asked to euthanize that same pet. One minute, we are responsible for the medical care and management of the patient, and the next minute we are acting as a mortician. The veterinarian must jump back and forth from one exam room obligation to the next. One exam room may be filled with grief while the next client has a new pup or kitten.

These extremes in professional task performance represent the rich dichotomy in our practice lives. Every chance we get to hold puppies and kittens allows us to bear witness to new beginnings. Every time we are there to help a client celebrate the adoption of a homeless pet, it brings us back from an ending to a new beginning. Sometimes, I bring grieving clients into the homeless ward at our clinic and place a kitten or a puppy in their arms to cheer them up. If a client is clearly not ready to take a new pet into his or her heart, suggest that the client foster a pet from the local shelter.

Suggest to your newly grieving clients that they join a volunteer club or an animal shelter to help socialize kittens and care for homeless animals. Our oncology team finds that feeding kittens in the homeless ward gives us cheer when our losses are piling up. Be sure to find pleasurable outlets for your staff during the tough times, to avoid compassion fatigue.

Compassion means: "Suffer together, deep sympathy." Unfortunately, the dictionary includes the word "pity" as a synonym for compassion. Fatigue: "Exhaustion or weariness, to tire out." Weariness: "Worn out, without patience or zeal." Exhaust: "To use up, to empty completely to drain." Burnout generally applies to job frustration or weariness. The moral and emotional stress surrounding euthanasia can be enormous. In fact, this stress is the single largest source of job dissatisfaction for companion animal veterinarians (Rollin 2003). Most veterinarians feel some or all of these emotions on a daily basis.

In his book *Compassion: Our Last Great Hope* (1996), Dr. Leo Bustad tells us what compassion is not. "It is not pity, which is feeling sorry for someone. With pity, there is condescension and separateness; one does not celebrate with a person one pities. Compassion is suffering with, having empathy with, or feeling for. It includes joy as well as grief. It is the feeling of togetherness. . . . Compassion is not only feeling or sentiment, but also actively helping to relieve pain and suffering in others."

Compassion fatigue is internal emotional depletion. It is different from burnout, which comes from organizational bureaucracy or policies and procedures. Compassion fatigue comes from caring and feeling responsible for patients and sharing the burdens and sorrows of their caregivers. The physical symptoms of compassion fatigue are varied. They are similar to regular burnout: GI symptoms, headaches, sweating, blurred vision, along with frustration, anxiety, and depression, to name a few. If you feel these symptoms, be sure to recognize that it is natural and understandable. Give yourself a break, change your routine, be kind to yourself and exercise. Hug some kittens and puppies. Pamper yourself and get your spirit re-energized. Don't let your internal emotional resources become depleted. Never quit caring about each and every human-animal bond you encounter and the unique people who entrust us with their companion animals. Our highly attached clients need and expect us to keep caring (Mitchener 2005).

Compassion vs. Cure without Care

Bustad quoted Matthew Fox: "Compassion is the world's richest energy source." I feel that veterinarians are the best people and healers on the planet. We are the energy source for great compassion and for honoring the human-animal bond. When people ask how you can go on, tell them your spirit is like a candle, no less bright for lighting another candle.

Bustad lamented the exile of compassion from medicine and the mechanization of medicine and the hazards of "cure without care." He wrote, "Cure without care makes us preoccupied with quick fixes and makes us impatient, and also unwilling to share one another's burdens, unable to experience compassion. Care is more important than cure. In fact, cure without care may be, in the long run, more harmful than helpful." Bustad wrote that compassionate people have a keener awareness of the interdependence of all living things: "We feel a kinship with animals and are stewards of the earth and all within it."

Post-Euthanasia Follow-Up

When a long-term geriatric cancer patient dies, a little part of your practice goes with them. Your staff will miss seeing the pet and the family. Send one or two sympathy cards with staff notes and signatures. Ask the pet owner to visit and bring pictures of the deceased pet. Put the owner's e-mail address on your hospital list of dog or cat lovers so you can contact them with pet-related issues, news, and pictures. Let clients know that you believe that they should remain in a human-animal bond because it will benefit their life and, of course, the life of another pet. Encourage them to get back into the love cycle again by adopting a homeless pet.

Let them know that you would be honored if they considered adopting one of your own rescue pets. Ask them to call when they feel the time is right for them to adopt. We say, "It would be hard to imagine you walking around this planet without a set of paw prints at your side." Offer a genuine invitation for your pet-loss clients to come back and visit the hospital at their old appointment times or during lunchtime with cookies and pictures.

Give the family a phone call anywhere from one day to several weeks after the pet has passed to ask how things are going. This is often the toughest call to make because now we are not talking

medicine or a protocol. You can start by asking a question, “How is your heart? I know you must be missing Bullet very much. These days of pet loss are difficult and we all want you to know that we are thinking of you.” Talking about a deceased pet often helps the grieving family. If the caregiver is having trouble, you can offer emotional support or referral to a pet-loss counselor or a pet-loss hotline like the one at the University of California, Davis, run by students trained to handle pet-loss issues.

A very helpful piece of advice that you can offer grieving caregivers is to set aside special times for tears and feelings of grief. Instruct clients to limit their sad feelings, perhaps to 30 minutes a day, preferably in the morning or the evening. This encourages caregivers to continue working through the grieving process while helping them face their workaday world with more clarity. If the client needs pet-loss counseling, make sure to initiate a referral or contact a pet-loss hotline.

The family may also draw closure by conducting a memorial service or donating to animal charities (Butler et al. 1991). If clients ask for your direction, you can suggest that they donate to your alma mater’s cancer center, the Veterinary Cancer Society, the Morris Animal Foundation, Animal Cancer Foundation, AVMF, AAHA Helping Pets Fund, or the Magic Bullet Fund, which helps pay for cancer treatments for dogs. Tell clients that you and your staff miss them and then encourage them to make the full cycle back into the wonderful world of the human-animal bond with another loveable pet as soon as they feel up to it.

Sending an After-Life Gift

Sending flowers or a potted plant or making a memory gift to a favorite charity honors the bond that the family shared with their deceased geriatric pet. A gift symbolizes your care about the family’s emotional pain and loss (Butler et al. 1991). As an after-life gift, we send the family a six-inch bronze memorial paw print with an engraved plaque that reads, “In Loving Memory of Mitzie.” We contact our engraver by phone with the pet’s name and instructions to create the plaque and send it to our office. We attach the plaque onto the base and ship it a few days after the sympathy card. When the family receives the gift, their emotions may be settling down but their hearts are still heavy. We have received very touching letters of gratitude for sending this symbolic remembrance that so solidly honors the relationship that we shared with their deceased geriatric pet.

A Poem by Sir Walter Scott

Sir Walter Scott wrote an insightful short poem that honors the human-animal bond. It helps caregivers when they are dealing with pet loss. The poem is featured in *Angel Pawprints*, by Laurel Hunt (1998). With one changed word (dog to pet), this poem expands to include cats and other species of pets:

I have sometimes thought of the final cause of dogs [pets] having such short lives, and I am quite satisfied it is in compassion to the human race; for if we suffer so much in loving a dog [pet] after an acquaintance of ten or twelve years, what would it be if they were to live double that time?

Sir Walter Scott

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Appendix 1: Specific Tumor Protocols

SKIN CANCER
Mast Cell Cancer

Dx	Sx	RTx	CTx
- FNA all tumors prior to Sx to rule out MCT. - Recently diagnosed MCT is generally confined to the skin in dogs (dermoepidermal); therefore, aspirates of spleen, liver, and bone marrow are generally negative in dogs. - Buffy coat smears are considered useless in early canine disease. - For more prognostic information, order the "MCT Panel." It stains for KIT, Ki-67, PCNA, Agnors, and IDT mutation analysis. It is available from Michigan State University and the Animal Medical Center laboratories. - It is acceptable to proceed with CTx when indicated without complete staging.	- If narrow or dirty margins at first Sx, a second Sx is indicated. - Follow the soft tissue sarcoma protocol for wide and deep excision of all grade II and higher grade cases. At least 2 cm lateral margins and one deep tissue plane below the mass is desired. Prefer more aggressive margins (3 cm) for grade III tumors. - Sx for stage I–II mast cell tumors with histologic grade I and II (excluding scrotal, muzzle, and distal extremities) that yielded 2 cm lateral clean margins and clean deep margins of one fascial plane provided >90% cure rates (Fulcher et al., JAVMA 228 (2):210–215). - PREMEDICATE DOGS WITH BENADRYL BEFORE SURGERY.	- RTx or CTx provides >90% cure rate when used for stage I–II mast cell tumors with histologic grade I and II. - RTx and/or CTx recommended for patients with high grade II and grade III MCT with narrow or dirty margins and unresectable lesions. Evaluation of local nodes, spleen, liver, and bone marrow is recommended for staging if elected.	- Pepcid® (famotidine) at 10 mg/20# SI for dogs and ½ of a 10 mg tablet per cat PO on an empty stomach. OR Tagamet® (cimetidine) at 5–10 mg/kg PO TID. Must use when residual tumor is suspected. - Prednisone 2 mg/# daily for 4–7 days, then 1 mg/# daily for 10 days, then 1 mg/# every other day for 2 wks, then 0.5 mg/# q 48 hrs. for 6 months, then taper. - Leukeran® (chlorambucil) 0.2 mg/kg or 6 mg/m² (dogs) q 48 hrs. for dogs and 2 mg q48–72 hours for cats PO. - Grade III cases or resistant cases: Lomustine at 40–90 mg/m² in dogs q 21 days and cats q 30–42 days. Must check CBC and platelets before each dose of lomustine. - If no recurrence in 7 months, begin taper. Expect recurrence within 6–7 months in high-grade II–III tumors. Unresectable grade III disease/metastases have poor survival (less than 6 months) without treatment. Some treated cases may respond or stabilize.

SKIN CANCER (continued)
Solar-Induced Squamous Cell Carcinoma

Sx	RTx	CTx
• Initial carcinoma in situ lesions and eyelid lesions may be controlled with cryosurgery. • Excisional biopsy with clean margins is often curative: nosectomy, pinnectomy, resection of bulky lesions, and so forth. • Sx is used for reconstruction and grafting after curative Sx, such as eyelids.	• Used as primary treatment to spare structures such as nasal planum and eyes. Not used for pinnae lesions. • Strontium 90 probe is helpful in focal superficial lesions such as Bowen's disease. • Remind clients to use sunscreen and/or shelter the pet from the sun between 10:00 A.M. and 2:00 P.M.	• Use imiquimod (Aldara[®]) topical ointment for in situ lesions. • Check updates on using 1–2% capsaicin cream for in situ lesions. • Systemic CTx is rarely used. May try carboplatin and mitoxantrone (as RTx enhancer) for cats. • Also use oral Xeloda[®] (dogs only—toxic in cats). • Retinoids may be helpful in some cases.

Cutaneous Hemangiosarcoma

Sx	RTx	CTx
• Initial macular lesions may be controlled with cryosurgery. • Excisional biopsy with clean margins is often curative for resection of larger, blood-filled lesions.	No information. Lesions are often too numerous for external beam approach. • Strontium 90 probe may be helpful. • Remind client to use sunscreen and/or shelter pet from sun between 10:00 A.M. and 2:00 P.M.	Not used when tumor is in superficial stages. • Adriamycin or VAC protocol or carboplatin may help cases with metastatic disease.

MAMMARY CANCER

Sx	RTx	CTx
Sx is the first modality of treatment. - In dogs, perform simple, regional, or unilateral mastectomy or acquire deep and wide margins equal to tumor diameter. - In cats, remove the involved mammary chain first and follow with excisional biopsy of the remaining mammary chain in 3–4 wks.	RTx of any type is seldom used for mammary tumors in canine and feline patients. It may increase tumor-free intervals and reduce local recurrence in difficult cases.	CTx is indicated for solid, inflammatory, metastatic, and high-grade tumors. Use the protocols suggested for carcinomas as in chapter 6. - Mitoxantrone at 5–6 mg/m² is preferred over Adriamycin at 30 mg/m² in dogs and 1 mg/kg in cats/small dogs. - Carboplatin at 300 mg/m² in dogs and 180 mg/m² in cats. - Gemzar® at 200–800 mg/m² with dose escalation. - Xeloda (dogs only) at 250 mg/50# BID x 10 days q 21 days. Tamoxifen has not been successful. Check on availability of novel and vaccine therapies.

SOFT TISSUE SARCOMAS

Sx	RTx	CTx
- Excisional biopsy should have at least 2 cm (optimally 3 cm) margins around the mass and at least one or two fascial planes on all deep margins. - If margins are dirty, expect recurrence and early death. - CT or MRI scan needed for all ambiguous and/or fixed masses prior to Sx.	- Used as first line of therapy for inoperable masses. - Used as palliation. - Used prior to Sx to shrink tumors to increase tumor-free interval. - Used intraoperatively to increase tumor-free interval. - Used following Sx delivered to a wide field to sterilize tumor beds, especially if resection was inadequate or residual disease remains.	- Carboplatin and/or Adriamycin are helpful at doses discussed above. - Piroxicam and other anti-angiogenesis agents may be helpful. - Ifosfamide with mesna-diuresis may be helpful. - Check updates for data on small molecule and/or novel therapies.

CUTANEOUS LYMPHOMA (MYCOSIS FUNGOIDES, MF)			
Sx	RTx	CTx	
Sx is rarely helpful other than for diagnostic purposes.	RTx may be helpful in solitary lesions and for palliation. Half body irradiation may theoretically help but is unproven.	CTx is the primary treatment for MF. - Dogs: Prednisone 0.5–1 mg/# on days oil is given (see * below) and lomustine 40–90 mg/m² divided over 4–7 days. Repeat every 21–30 days if CBC allows. Monitor patients for oral and mucocutaneous lesions. - Cats: Prednisone at 5 mg BID and lomustine at 10 mg (divided over 4 days) every 4–6 wks. if CBC allows. - Dietary oil is helpful in the management of MF. - Dogs: 3 ml/kg of Hollywood safflower oil, fed on 3 consecutive days per wk. - Cats: The oil from 3–4 oil of evening primrose capsules, twice daily.	

HEAD AND NECK TUMORS

	Sx	RTx	CTx ± Immunotherapy (ITx)
Oral Cancer in the Canine Most common types: FSA (mandible) and malignant melanoma (of maxilla or lip)	Mandibulectomy or maxillectomy with clean margins of at least 2 cm is the first choice therapy for oral tumors.	RTx to the primary tumor bed and draining neck nodes is indicated. Intralesional CTx and intraoperative RTx may provide additional local tumor control.	CTx with carboplatin 300 mg/m ² q 21–30 days for one year. Chest x-rays are recommended q 4–6 months. Carboplatin at 300 mg/m ² in dogs every 3 wks. yielded 68% objective response in malignant melanomas at UCD according to Dr. Carlos Rodriguez by personal communication (VCS <i>Proceedings</i> , Oct. 1992, p. 59). Malignant melanoma is highly metastatic to local nodes and lungs. Follow Sx and RTx with systemic treatment. Use CTx (carboplatin or liposome encapsulated CTx), Itx, or novel therapy. DNA vaccines and/or gene therapy are promising. The Wisconsin DNA vaccine is an option. The AMC xenogenic Tyrosinase vaccine is USDA approved and may become widely available as an option.
Feline Mandibular SCC	Sx mandibulectomy and esophageal feeding tube.	RTx follow-up to include primary site and neck nodes.	CTx with mitoxantrone as a radiation sensitizer. It is wise to prepare the client to expect a poor prognosis. However, cats with rostral lesions may have long-term survival.
Feline Lingual SCC	Sx for an esophageal feeding tube to offset starvation and wasting. No consistent treatment has extended life.	Poor response.	CTx is palliative only. Use carboplatin and/or mitoxantrone IV in rotation. Use piroxicam at 1 mg PO q 48 hrs. or Metacam® 1–2 drops q 24–48 hrs. for pain control to improve quality of life and possibly exert an anticancer effect. Use pain patches and nalbuphine injections. Dilute 0.1 ml nalbuphine to 1 cc in a tuberculin syringe. Clients may give s.q. injections of 0.1–2 ml q 6–8 hrs. PRN for pain at home.
Feline Maxillary SCC	Sx with aggressive maxillectomy may help some cases but recurrence is common.	RTx with palliative protocols using mitoxantrone enhancement may occasionally yield excellent but temporary results. Monthly palliative booster treatments may extend survival times in some cases.	CTx may yield some stable or partial clinical responses with a rotation of carboplatin/Adriamycin or carboplatin/mitoxantrone every 2–4 wks. Monitor leukopenia, BUN, and creatine. • Mitoxantrone at 5–6 mg/m² is preferred over Adriamycin. • Carboplatin at 180 mg/m² IV q 21d • Gemzar at 200–800 mg/m² with dose escalation. • Check on availability of novel and vaccine therapies.

(continued)

HEAD AND NECK TUMORS (continued)

	Sx	RTx	CTx ± Immunotherapy (ITx)
Palliative Radiation Therapy for Advanced or Disseminated Head/Neck Cancer		RTx palliation helps cats with nasal planum, facial or oral squamous cell carcinoma. It is given as a short course of 3–4 high dose fractions. The goal is to achieve relief from ulceration and pain in a rapid, effective way.	CTx enhancement and/or adjunct IL chemotherapy given prior to RTx may improve tumor control for oral-facial tumors (melanoma, SCC, FSA), nasal tumors, tonsilar SCC, OSA, etc. High dose 800–1,000 cGy fractions are delivered on days 0, 7, 21, and 42. Some patients do well with a monthly follow-up using IL chemotherapy and a palliative high dose RTx fraction. Published data using palliative radiation alone shows 74% of dogs experience pain relief and 25% benefit with extended quality life (VMTH, Guelph, <i>JVIM</i> 8, 1994).
Nasal Passage Tumors in Dogs No treatment yields 5–7 month survival time.	Sx is used for diagnostic purposes following proper imaging. Rhinotomy alone may reduce survival time. Post RTx, Sx to remove residual disease is helpful in some cases.	RTx with orthovoltage after rhinotomy yielded 40–45% 1-year survival. Optimal treatment foregoes rhinotomy in preference to cobalt or linear accelerator RTx. This yields 45–50% survival at 1 year.	If RTx is declined, recommend palliation and a Pawspace program. Treat the symptoms, provide comfort to improve the quality of life with pain control medication, CTx, and immunonutrition. This may slow down the process and offer the family a chance for a peaceful farewell with their pet. • Use carboplatin for CSA and OSA. Other cell types, use mitoxantrone, carboplatin, gemzar, or Adriamycin in rotation q 21 days to evaluate for best response. CTx may reduce stridor and nasal discharge. Piroxicam at 10 mg/60# daily may alleviate pain and exert an anticancer effect. • For respiratory carcinoma or SCC, use Gemzar at 200–800 mg/m² IV with dose escalation. On day 10, start Xeloda at 250 mg/50# BID PO for 10 consecutive days. (Do not use Xeloda in cats). Repeat Gemzar 10–12 days after finishing Xeloda. Use piroxicam at 10 mg/60# PO daily for dogs with this protocol.

(continued)

HEAD AND NECK TUMORS (continued)

	Sx	RTx	CTx ± Immunotherapy (ITx)
Nasal Passage Tumors in Cats Most common types: Nasal Respiratory CA, SCC, LSA	Sx is not beneficial.	RTx is indicated for respiratory carcinoma and nasal lymphoma that are presumed to be solitary.	CTx is an excellent option for management of nasal passage tumors in cats. Adriamycin-based protocols are best since lymphoma is often considered a systemic disease by many oncologists. Rotate mitoxantrone, carboplatin, gemzar, and Adriamycin for carcinomas at doses described for use in cats in chapter 6. Look for the best response and then continue the therapy every 21–30 days. Use piroxicam at 1 mg q 48 hrs. or meloxicam at 1–2 drops per day for pain control and anticancer effect of NSAIDs.
Brain Tumors Treat symptomatically to control circling, wandering, disorientation, seizures, headache pain, etc.	• Sx is helpful for selected peripheral tumors if MRI or CT scan confirm accessibility. • Meningiomas are most amenable, especially in cats. • Consultation with a neurologist, surgeon, and radiation oncologist is advised for specialized biopsy procedures.	RTx is helpful for some cases (pituitary macroadenoma, astrocytoma, meningioma) yielding excellent remissions lasting 1 year plus.	CTx palliation is indicated. CTx may be palliative for most carcinoma cases. CTx may produce dramatic responses in granulomatous lymphoma and lymphoma. • For dogs, use lomustine at 40–80 mg/m² PO q 21 days divided over 4–5 days and safflower oil at 3 ml/kg on 3 consecutive days per wk. • For cats, give 3–4 oil of evening primrose capsules (538 mg) q 12 hrs. and lomustine and prednisone. Give one 10 mg lomustine capsule (divided over 4 days) PO for a 7- to 12-pound cat q 4–6 wks. Monitor platelet and white blood cell counts. Patients benefit with prednisone at 0.5–1 mg/kg PO q 12–24 hrs. for relief of CNS edema and inflammation. Dexamethasone injections may be helpful to alleviate CNS symptoms initially and as follow-up therapy if symptoms reappear.

CHEST TUMORS			
	Sx	RTx	CTx
Primary Chest Cavity Tumors	Lobectomy is helpful if the mass is removed intact and if local nodes are negative. Survival for thymoma may be good if entirely removed. Bronchogenic carcinoma patients may survive 1 year following lobectomy if lymph nodes are negative. Resection of localized esophageal and tracheal tumors may be helpful.	RTx is useful to reduce anterior mediastinal lymphoma.	CTx is palliative in most cases other than LSA.
Chest Cavity Secondary Tumors (metastases)	Metastasectomy may be helpful in a subgroup of selected cases where tumors are limited and amenable to excision.	RTx is not used.	CTx is used palliatively and occasionally achieves a remission. CTx is individualized for each case. - Use carboplatin dose for its wide range of action against carcinomas and sarcomas and its low toxicity. - May use Adriamycin, mitoxantrone, Gemzar, and xeloda for carcinoma. - Agents such as verapamil or valproic acid may enhance response.

ABDOMINAL TUMORS

	Sx	CTx
HSA, Splenic Tumors	Sx is used for diagnostics, debulking, and resection of abdominal tumors following appropriate imaging. Splenectomy is commonly performed due to hemoabdomen from bleeding hemangiosarcoma. • Surviving patients generally face metastasis and death within 6–8 wks. Inform client of the prognosis prior to electing surgery. • It is appropriate to stabilize the patient with supportive care and a belly wrap to allow resorption of blood. Some families decline surgery yet are reluctant to euthanize. They appreciate the chance for extra time with their pet in Pawspice care. • Occasionally, cats develop splenomegaly due to mast cell cancer. They respond well to splenectomy and CTx.	Follow protocols for sarcoma or carcinoma as in chapter 6. • CTx using piroxicam and xeloda. For carcinoma, xeloda is used at 250 mg PO BID per 50# (dogs only)—TOXIC in cats) for 10 days and repeat every 21–30 days for 1 year. CBC before each new course of xeloda. • Cytoxan® 50 mg/m² q 48 hrs. PO x 8 wks. can be added to piroxicam and xeloda as above. Watch for Cytoxan-induced cystitis. Give Cytoxan with extra fluids (broth) 20–30 mins. before morning urination. Use leukeran as a substitute for Cytoxan after 8 wks. of high dose oral therapy at 2 mg/m² every other day. • Metronomic therapy for abdominal organ carcinoma is an option: – Xeloda at 250 mg PO daily/50# dog or 5 mg/#/day. *Do not use xeloda in cats. Check the CBC before each round of xeloda. – Cytoxan at 25 mg/m² q 48 hrs. PO with fluids (broth) before urination. – Piroxicam 10 mg/60# PO or 0.3 mg/kg daily in dogs and 1 mg q 48 hrs. in cats. • Check for updates on the use of novel therapy and HDAC inhibitors (valproic acid, SAHA, and others) for antitumor effect and CTx enhancement.
Mast Cell		
Carcinomas		

ABDOMINAL TUMORS (continued)

CTx			
Bladder Cancer	CTx with piroxicam provides anti-inflammatory and anticancer benefits.		
	• Use piroxicam at 0.3 mg/kg daily or 10 mg/60# daily PO in dogs. For cats use 1 mg/cat PO q 48 hrs. Use pepcid or tagamet to avoid gastric ulcers. • CTx with mitoxantrone 5 mg/m² escalating up to 6.5 mg/m² IV q 21–30 days. Use with piroxicam as above. Benefit is seen in 50% and some go into complete remission.		
		RTx	CTx
Prostate Tumors	Sx (prostatectomy) can benefit selected dogs when neoplastic tissue is confined within the capsule with minimal to no urethral involvement. Imaging technology and exploratory surgery can determine operability.	RTx should be a carefully considered option. Responders may survive up to 1 year.	Protocols used for TCC are appropriate with the addition of xeloda for dogs. The carcinoma protocols described above may be helpful in cases resistant to mitoxantrone/piroxicam/xeloda.
		• Brachytherapy is more finely targeted than external beam.	

ABDOMINAL TUMORS (continued)

	Sx	RTx	CTx
Hepatic Tumors	- Sx may benefit dogs with massive hepatocellular carcinomas localized to the left liver lobe. Lobectomy improves survival over medical management. - Choledochal senting.	Liver-directed therapy incorporating multimodality therapy may be useful.	- CTx may be helpful using gemzar, and/or (in rotation) carboplatin. - Use xeloda PO IN DOGS ONLY. - Supportive care with appropriate supplements and nutrition may also be helpful.
Intestinal Tumors	Sx resection with wide margins is the treatment of choice. - Presurgical imaging and FNA or biopsy for diagnosis of abdominal tumors will assist the surgeon in planning and post-operative recovery. - Sx for cytoreduction can be very helpful for patients with hormone-producing tumors such as gastrinomas, insulinomas, adrenal tumors, and metastatic anal sac tumors associated with hypercalcemia (dogs). - Sx plans that include second look celiotomy may improve management of residual disease and recurrent abdominal masses.	- RTx to the sublumbar (iliac) nodes for metastatic anal sac carcinoma may be beneficial. - Liver-directed therapy incorporating multimodality therapy may be useful.	- CTx using drugs such as gemzar, carboplatin, mitoxantrone, and Adriamycin combined with small molecule therapy is indicated for treating pancreatic, adrenal, and renal carcinomas. - Use xeloda PO (dogs only, do not use in cats). - Supportive care with appropriate supplements and nutrition may also be helpful.

LYMPHOMA

CTx with Adriamycin-based protocols yields the longest survival data observed in dogs (14 months). Consider a permanent maintenance protocol well into the second year. One-third of responding patients may survive 2 + yrs.

Protocol

Use modified Wisconsin protocol (see Table A.1) or Table 6.2.

Maintenance

• Start maintenance protocol with a 2-week interval for dogs and 10-day interval for cats and all dogs that presented with a high tumor burden or organomegaly. Rotate Oncovin[®], Cytoxan, Oncovin, leukeran, Oncovin, Cytoxan, Oncovin, leukeran, etc., for 2 yrs. Theoretically, the last tumor cell cannot be killed using low-toxicity CTx that is preferred in geriatric veterinary oncology.

This is the rationale for permanent maintenance CTx.

- Use leukeran at 1.4 mg/kg divided PO for 1 day only or 20 mg/m² PO for 1 day only on the rotation schedule.
- If oral Cytoxan causes GI signs or hemorrhagic cystitis, leukeran is used in its place.
- To increase visit intervals:
 - Use leukeran and then Cytoxan in a 10- to 14-day rotation between Oncovin treatments.
 - Give Oncovin IV.
 - 2 wks. later give leukeran PO.
 - 2 wks. after that give Cytoxan PO with 20 mg/m² prednisone in the morning before first urination along with extra broth (fluids).
 - The recheck visit and CBC for vincristine follows in 2 wks.
- Each drug is rotated at 2-week intervals. To taper this routine further, intervals may be increased to 2½- to 3-week intervals. Other effective PO drugs such as lomustine, melphalan, procarbazine may be rotated into the schedule to extend the interval between recheck visits; however, CBCs should be routinely monitored.

BONE CANCER
Osteosarcoma

Sx	RTx	CTx
Sx generally involves amputation, limb sparing, rib resection, etc. Poor prognosis if located in vertebrae.	• May be used for palliation in non-amputated cases. • May be used intraoperatively with high megadoses to kill osteoclasts.	CTx addresses the high potential for metastasis. • For dogs, use carboplatin 300 mg/m² IV or in combination with Adriamycin (use precautions from the modified lymphoma protocol above) q 21–30 days and piroxicam 3 mg/kg PO daily. CTx is generally not needed in cats with OSA due to low rate of metastasis. • Consider novel therapies as they become available including the use of HDAC inhibitors such as valproic acid, SAHA, and others to enhance CTx effect.

Multiple Myeloma

CTx
• CTx with leukeran 4–6 mg/m² q 48 hrs. or Alkeran[®] (melphalan) 2 mg/m² q 48 hrs. • Use prednisone 40 mg/m² for 7 days then 30 mg/m² for 7 days then 20 mg/m² q 48 hrs. for 18 mos. as needed. • If hypercalcemia is present, patients must receive saline diuresis. If fever or sepsis is present, use antibiotics and treat symptomatically. • Monitor serum and urine proteins for a 50% reduction over 30–60 days.

MISCELLANEOUS TUMORS
Histiocytosis

	Sx	RTx	CTx
Histiocytic Tumors	Sx used for diagnosis. This is a perplexing group of tumors and often hard to pin down. • Request tumor cell markers to identify cell of origin such as dendritic cell origin (monocyte/macrophage/Langerhans cell lineages), T-cell, B-cell, or mesenchymal origin. • Wide and deep complete excision should be attempted if the mass is localized. • Splenectomy is very helpful in grade I and II disease, while grade III disease is very aggressive with metastases to lungs, lymph nodes, omentum, and organs.	Rarely used but may be beneficial to control regional recurrence of localized tumors.	• May produce some responses with steroids and combination chemotherapy. • Cyclosporine and leflunomide are helpful as potent inhibitors of T-cell activation. • Ifosfamide may have a role in treatment for this disease.

Table A.1. Dr. Villalobos's Modified Madison/Wisconsin Protocol for Lymphoma for Large/Giant Geriatric Dogs, Including Split Dose Administration of Adriamycin

Day #	Drug	Canine Dosage	Feline Dosage
Day 1	Oncovin®	0.7 mg/m ² IV	0.25 mg/kg (0.5 mg/m ²) IV
	L-Asparaginase® (use pretreatment)	10,000 iu IM	400 iu/kg or 2,000 iu SQ
	Prednisone crushed in food in the A.M.	30 mg/m ² daily x 7 days, all in A.M.	5 mg BID PO (forever)
Day 8	Cytosan® (with extra water/ broth intake 20 mins. before urination)	100 mg/m ² PO	25 mg tablet PO
Day 9	Cytosan® (with extra water/ broth intake 20 mins. before urination)	100 mg/m ² PO	25 mg tablet PO
	Prednisone	20 mg/m ² daily x 7 days	Continue 5 mg BID
Day 15	Adriamycin® (with pre- treatment) 15-minute infusion for dogs	Small or frail dogs: <20# 1 mg/kg IV Med/large dogs: 30 mg/m ² IV once Large/giant dogs: 20 mg/m ² IV	1 mg/kg IV over 5–7 mins. (pretreat with 0.1 ml dexamethasone)
	Prednisone	10 mg/m ² daily x 7 days (dogs), then discontinue	Continue 5 mg BID PO
Day 19, 20, 21, or 22	Adriamycin	Repeat day 15 for large/ giant dogs on split dose protocol	No treatment
Day 22	Oncovin®	0.7 mg/m ²	0.025 mg/kg (0.5 kg/m ²) IV
Day 29	Cytosan® (with extra water/ broth intake 20 mins. before urination)	100 mg/m ² PO	25 mg tablet PO
Day 30	Cytosan® (with extra water/ broth intake 20 mins. before urination)	100 mg/m ² PO	25 mg tablet PO
Day 36	Adriamycin	Repeat day 15	1 mg/kg IV as above
Day 40, 41, 42, or 43	Adriamycin	Repeat day 15 for large/ giant dogs on split dose protocol	No tx
Day 50	Oncovin®	0.7 mg/m ² IV q 21–30 days with the maintenance protocol	0.25 mg/kg (0.5 mg/m ²) IV

Appendix 2: Handouts for Clients

Guidelines for Feeding and Supplements

Enhancing your pet's immune system and nutritional status during the battle against cancer is an important aspect of our total health care approach. You may be given supplements from our immunonutrition protocol that are in the form of powders, liquids, capsules, and tablets. Administering supplements, especially to cats and geriatric pets, may prove to be challenging and perhaps at times very frustrating. Some pets have no qualms about eating anything placed in front of them. Then there are those pets that are simply not going to accept some or any of the supplements. On occasion, some pets develop loose stool, diarrhea, or nausea from a particular item. You should suspect that a pet feels nausea if he/she looks at food but will not eat. Nausea may result from chemotherapy but it may also be induced by a distasteful supplement. If giving a particular supplement causes stress and mistrust, it will defeat the healthy positive goal of the immunonutrition protocol. You need to develop a technique for administering at least the most important supplements successfully.

If your pet refuses to eat food containing the supplements, then we suggest another approach. We don't want to cause food aversion and mistrust. Try to determine which item has the offending taste, and then omit that one while serving the others with regular feedings. See if your pet will accept at least one or two items in the meal. The most important suggestion is to remove the offending taste from your pet's regular food. You can mix the unwanted supplements into a delicious treat and make feeding the supplements a more pleasant experience and something that your pet looks forward to. You may need to explore different methods before you discover a successful technique.

Here are a few suggestions from clients who have experienced the trial and error of immunonutrition administration with not-so-willing pets:

- Hotdog method: Some dogs will readily accept most supplement pills or capsules stuffed into a hotdog.
- Broth method: Some pets are eager to lap up anything placed in a broth or gravy. Empty capsules, crush pills, and add powders to a beef or chicken broth or gravy mixture. This mixture may be given orally with a syringe or turkey baster.
- Meatball method: Some pets will eagerly eat anything disguised into a meatball type of treat. Suggested items include lunchmeat (turkey or roast beef) and liverwurst. Flatten them onto your counter then pour powders, capsules, and pills into the middle of the selected meat. Roll up the chosen meat until you have the supplements hidden deeply inside.
- Peanut butter or cream cheese method: Some pets accept pills, capsules, and powders disguised in a ball of peanut butter or cream cheese.
- Syringe method: Some pets prove to be more of a challenge and may need to have all supplements mixed into a liquid or paste and then syringed orally with coaxing. Be sure to maintain an upbeat, encouraging attitude during the feedings. Your pet may become accustomed to and tolerant of the ritual with repetition.

Feeding

As your pet undergoes cancer therapy, you might find that the normal diet has less appeal. This can be expected. When people or pets feel sick, the normal diet may not seem appetizing. It may be necessary to offer your pet different, more appealing foods as treatment progresses. Following are

some suggested food items to try if your pet develops an aversion to the regular diet. Also included are diets for good health, diets for gastrointestinal discomfort, and healthy snack suggestions.

- **Regular diets:** For overall healthy cancer patients, we suggest feeding a low-carbohydrate diet. This minimizes sugar, which cancer cells easily utilize. The idea is to feed the patient and starve the cancer. This theory is the basis for feeding cancer patients the Hill's prescription n/d[®] diet. For regular store-bought foods we suggest feeding a high-quality canned food diet such as Pinnacle and Wellness diets.

There is also the option of preparing a homemade diet. You can put the ingredients together and cook once a week and freeze in portions for future feedings. Avoid high-glycemic foods such as fruit and vegetables like carrots, corn, rice, and potatoes. Instructions for such a diet can be found in the book *Help Your Dog Fight Cancer*, by Laurie Kaplan.

- **Gastrointestinal diets:** For pets that experience vomiting, diarrhea, or nausea a temporary bland diet is recommended. Some pets need to stay on special diets such as Hill's i/d[®] continuously. Suggested foods include boiled hamburger, chicken, or turkey, with boiled barley, canned pumpkin, and cottage cheese. Proportions should be equal. Feed the same amount as you would feed canned food. Add vitamins and calcium to home-cooked diets being fed continuously.
- **Snacks:** Try to keep your pet on the low-carbohydrate diet. This includes selecting snacks. Suggested snacks include frozen fish fillets (not breaded), turkey and other lunchmeat slices, meatballs, and cooked liver strips prepared and kept in the freezer.

These are only suggestions for enhancing the well-being and nutritional status of pets with cancer. If your pet accepts a suggested food or treat over a less optimal one, then follow our suggestions. But if your pet adores carrots and declines other suggested items, then give the carrots. The main point is to provide quality of life including fun at feeding and treat time.

Exercise

With some specific exceptions, most pets being treated for cancer should be allowed to perform all the activities of enjoyment especially when it comes to exercise. However, it is important to be attentive. If your dog wants to go for a walk, jog, or hike then go for it. However, if your pet seems reluctant, more sluggish, or less enthusiastic on a particular day, then you should skip that day's exercise or modify it to accommodate your pet's level of energy. If unexpected lethargy persists, be sure to take the temperature to rule out fever, and see your veterinarian as soon as possible.

Most importantly give your pet as much time as you can for love and enjoyment. Most pets being treated for cancer are actually giving their family, caregivers, and friends an extended and happy farewell. The majority of our clients are amazed and comment that their pet cancer patient feels healthier and more energetic on immunonutrition. Together, as a team, we are striving to achieve the best quality of life for the rest of your pet's life.

CHEMOTHERAPY DISCHARGE INSTRUCTIONS FOR HOME CARE

Care facility name: _____

Contact Information: _____

Client name: _____ Patient name: _____

Date: _____

Chemotherapy agent administered: _____ Route: _____

A chemotherapy agent was administered to your pet today. If complications develop, please notify our office, your local veterinarian, or your local emergency hospital. Your pet may need medical care to treat or offset a serious adverse event. Below are some answers to common questions regarding chemotherapy, home care, and decision making.

NORMAL AND ABNORMAL SIGNS

IV Administration

1. If the injection site or injection leg becomes swollen or red, this is abnormal and should be reported immediately to our office or to your local doctor.
2. Nausea and/or vomiting usually occur within the first 72 hours after treatment. This problem is to be expected from some chemotherapy treatments. If your pet is vomiting or has nausea, administer the Reglan[®] sent home in your “Chemo Care Package.” Offer your pet only small amounts of water at a time. Do not offer your pet large amounts of water or food if vomiting. If there is excessive vomiting (more than four episodes in 24 hours), see your family veterinarian or take your pet to an emergency clinic for injectable anti-vomiting medications and assistance.
3. Diarrhea may result following some chemotherapy agents. It may occur within the first 72 hours and contain a small amount of mucous or blood. Do not panic if there are two or three loose movements a day with control. But if your pet has over three episodes of loose stool in a 24-hour period with little or no control, dehydration may result. Use the Azulfidine[®] tablets that are part of your “Chemo Care Package” at the first sign. Start your pet on a bland diet of chicken or boiled hamburger, cottage cheese, and boiled white rice. Continue this diet for 3 days after the diarrhea is resolved. If diarrhea persists beyond 48 hours with no improvement, be sure to call us or see your family veterinarian for help.
4. A body temperature above 102.5 degrees or below 99.5 degrees is considered abnormal. Do not give any fever-reducing medications without first talking to your veterinarian. Temperatures above 102.5 degrees may indicate infection. Take your pet to your local or emergency veterinarian for an evaluation for sepsis.
5. Your pet may experience some lethargy for the first 72 hours. If lethargy persists beyond 24 hours, take the temperature. See your local doctor if you detect a fever.

After Intralesional Administration of Chemotherapy

1. After an intralesional injection of chemotherapy, the injection site may be mildly swollen or red as an expected side effect. If ulcerated, provide wound care.

2. If your pet is licking occasionally at the injection site this can be normal. If your pet is licking excessively at the injection site, this can cause irritation or infection. An E-collar or bandage should be placed to protect the lesion from self-trauma.
3. Nausea, vomiting, and diarrhea are rarely seen with intralesional injections.
4. A body temperature above 102.5 degrees or below 99.5 degrees is considered abnormal. Do not give any fever-reducing medications without first talking to your veterinarian. Temperatures above 102.5 degrees with lethargy should prompt a visit to your local or emergency veterinarian for a complete blood count (CBC).

After Subcutaneous Administration of Chemotherapy

1. The injection site should not become swollen or red or painful. If you detect one of these adverse effects, it should be reported to our office, and see your local doctor.
2. If your pet is licking at the injection site, there may be a problem with local reaction or an abscess. If your pet is licking excessively at the injection site, this may cause irritation or infection. Use a bandage or E-collar to provide protection.
3. Nausea, vomiting, diarrhea, and fever are rare following subcutaneous injections. If your pet becomes ill, do contact us and follow the precautions recommended.
4. A body temperature above 102.5 degrees or below 99.5 degrees is considered abnormal. Do not give any fever-reducing medications without first talking to your veterinarian. Temperatures above 102.5 degrees should be reported to your local or emergency veterinarian and prompt a visit to evaluate for sepsis.
5. Your pet may experience some mild lethargy for the first 72 hours. If the lethargy is profound or persists beyond 72 hours, be sure to see your veterinarian for help.

EMERGENCY SIGNS

1. If your pet's gums are pale, light gray, or bluish in color.
2. If your pet is having difficulty breathing or is wheezing or gasping for air.
3. If the rectal temperature is 99.5 degrees or below or 103.5 degrees or above.
(Normal temperature ranges between 100.5 and 102.5 for dogs and cats.)
4. If your pet is vomiting excessively (more than four times in 24 hours).
5. If your pet has liquid stool with poor control of eliminations for more than twice daily, dehydration may develop.
6. If your pet has seizures or is profoundly listless for several hours or refuses to eat or drink for more than 24 hours.

**IF YOU HAVE CONCERNS OR IF YOUR PET IS EXPERIENCING AN
EMERGENCY, CALL YOUR LOCAL VETERINARIAN OR
LOCAL EMERGENCY HOSPITAL IMMEDIATELY!**

Cancer Pain Management and Your Pet

Cancer pain is the most distressful aspect of managing pets with cancer. Your pet's cancer pain needs to be properly controlled so that he or she truly enjoys a good quality of life. The suggestions in this handout are only guidelines. You need to be alert and empathetic to be able to understand when your pet is in pain. Your veterinarian definitely needs your input regarding how your pet feels. The problem with trying to interpret pain in animals is that too much pain goes unnoticed and underappreciated. The solution is for us to agree that we should anticipate that certain conditions cause pain and to treat for that pain regardless of our personal opinion. Since pain of any sort is immunosuppressive and counterproductive to quality of life and survival, this approach results in healthier and happier cancer patients.

Cancer causes pain in many ways. Dogs with bone cancer have throbbing pain. They show their pain by limping; however, because the nature of dogs is to remain cheerful, many pet owners don't understand the magnitude of their dog's bone pain.

For bone cancer dogs not receiving amputation, the pain may very difficult to manage. Aredia® (pamidronate) may have some benefit. It is given as a 1–2 mg/kg IV drip with saline monthly over 1 hour. It is costly and won't work every time. But it has enough effect in humans to justify clinical trials in dogs and continued use by some veterinary oncologists. The other option for pain control for bone pain and other ulcerative or bulky tumors is palliative radiation therapy. Ask your doctor about this.

Cancer pain may be caused by inflammation and infection at the tumor site. This is commonly found in nail bed tumors and oral cancer. Oral tumors are traumatized by teeth and infected with gingivitis organisms. Cancer pain and inflammation may be what initially alerts you to the problem.

Tumors that put pressure on nerves or invade and obstruct organs or tubes such as the intestines, ureters, and urethra (urine outflow from the kidneys and bladder) cause visceral discomfort, nausea, vomiting, constipation, diarrhea, ataxia, lethargy, and pain. You can well imagine that pets with brain tumors have headaches. Their behavior changes motor control and seizures must cause fear, anxiety, and pain. But we, as caregivers, can only guess at the magnitude of their feelings and emotions.

Animals have a strong survival instinct that masks pain very well. This trait exists even in our most domesticated house pets. Pets with chronic, steady pain still follow family members (their pack) from room to room despite intense, chronic pain from abdominal tumors.

We need to eliminate, minimize, and control pain for our cancer patients. We need to set up plans that include the control of cancer pain for pets, especially if they are to receive procedures or any type of surgery

Your veterinarian may prescribe a single drug for pain control. A single drug may be effective; however, it is important to assess if your pet needs more than one drug to achieve good pain control. Many times your cancer pet will need more than one type of drug to completely resolve the pain. In fact, there may times when several drugs are needed. Each drug would be selected to act upon various pain pathways so that the combination will properly alleviate the pain. Your doctor is aware of the graduated scale for pain control that is recommended from the World Health Organization.

Various pain scales are used to measure factors such as heart rate, vocalization, restlessness, cramping, crying, hunching, thrashing, and agitation. Studies have shown that no pain scale can assess pain accurately for animals. Unfortunately, we have a huge deficit in recognition of pain, especially in pets recovering from surgery.

The Duragesic® pain patch may be prescribed for your pet. It releases the opioid fentanyl through the skin into the circulatory system over a 3-day period. The time release and effect of pain patches

vary from animal to animal and dogs vs. cats. Studies have shown that it may take up to 24 hours for full analgesic effect in dogs, whereas 70% of cats may experience full effect by 6–8 hours. So if the patch is being used for surgery, the timing of placement is important or the pet will need supplemental injections for pain control. We may recommend a follow-up pain patch 72 hours from the initial patch. Doses vary, but 1 mgc per pound seems to be effective for most pets. For smaller cats, we expose half of the 25 mgc pain patch membrane for the first 3 days and expose the other half for the second 3 days. Leave the pain patch on until suture removal so that staff may remove the patch painlessly and dispose of it properly. Earlier removal of the patch seems to hurt and may cause an ulcer at the membrane contact site.

Post-surgical pain control is important and should be monitored overnight by caring nurses who are trained to assess pain. If the nurse looks for increased panting and heart rate, crying, restlessness, and, in cats, crouching and holding the head down, he or she will find it. At times, you may be the nurse! Ask your doctor to consider all these details.

Researchers at Johns Hopkins found that opioid receptors are upregulated in inflamed tissues and they will respond for up to 48 hours if the tissue is given intraoperative morphine at low doses. Epidural blocks and local nerve blocks eliminate pain. Local infusion of lidocaine or bupivacaine or other long-acting local anesthetics along nerves and onto the surgery site prevents anticipated post-surgical suffering.

All post-op cancer patients need pain control for home care. The most commonly used medications for mild pain are nonsteroidal anti-inflammatory drugs (NSAIDs) such as carprofen, ketoprofen, or acetaminophen (dogs only). Your doctor may send home tablets of butorphanol or codeine or tramadol or a combination NSAID-opioid medication to be given at specified intervals. Some doctors recommend for an appropriate dose of a buffered aspirin for dogs. *DO NOT USE ASPIRIN OR ACETAMINOPHEN IN CATS.*

If your pet has anxiety during visits to the hospital or at home, there are medications that can relieve it such as valium, anti-anxiety drugs, and other gentle sedatives. Anxiety is a form of emotional pain and should be treated as such.

For most cancer patients, one of the first choices for cancer pain is the NSAID piroxicam. It has been shown to have some anticancer value in bone, bladder, and skin cancer and in some sarcomas. Thalidomide, the notorious NSAID, also has anticancer properties but is not widely available. Avoid the using steroids with NSAIDs because ulceration of the stomach and intestines is a predictable adverse effect. Pepcid® or another agent may be needed for protection of the intestinal mucosa in the event of ulceration.

Cancer patients who are in an end of life care program such as Pawspice generally need special routes of delivery for pain control. The steady use of a pain patch every 3 days can be very helpful. Using generic nalbuphine, an injectable opioid-like drug, every 6–8 hours is very helpful for resistant pain. It is an inexpensive option to the pain patch. Nalbuphine is great for pets that won't accept oral medications or are intolerant of the pain patches. It can be given orally as well as by injection. The typical dose would be 0.2–0.5 mg/kg given SQ as needed two or three times daily for dogs. The dose for cats is 0.1–0.3 mg/kg three to four times daily. The drug may be sent home for SQ use without the typical narcotics precautions. It has less sedation effects than other similar compounds.

Good pain management is good medicine. It allows pet caregivers to fully enjoy the life-enriching bond that is shared with their pet. We want to be satisfied knowing that our pet cancer patient is having a happy, comfortable, and good quality of life.

Quality of Life Scale (The HHHHHMM Scale)

Pet caregivers can use a quality of life scale to determine the success of Pawspice care. Using a scale of 1 to 10, patients can be scored.

- H: 0–10 HURT:** Adequate pain control, including breathing ability, is first and foremost on the scale. Is the pet's pain successfully managed? Is oxygen necessary?
- H: 0–10 HUNGER:** Is the pet eating enough? Does hand feeding help? Does the patient require a feeding tube?
- H: 0–10 HYDRATION:** Is the patient dehydrated? For patients not drinking enough, use subcutaneous fluids once or twice daily to supplement fluid intake.
- H: 0–10 HYGIENE:** The patient should be kept brushed and cleaned, particularly after elimination, avoid pressure sores, and keep all wounds clean.
- H: 0–10 HAPPINESS:** Does the pet express joy and interest? Is he responsive to things around him (family, toys, etc)? Is the pet depressed, lonely, anxious, bored, or afraid? Can the pet's bed be close to the family activities and not be isolated?
- M: 0–10 MOBILITY:** Can the patient get up without assistance? Does the pet need human or mechanical help (e.g., a cart)? Does he feel like going for a walk? Is he having seizures or stumbling? (Some caregivers feel euthanasia is preferable to amputation, yet an animal who has limited mobility but is still alert and responsive can have a good quality of life as long as his caregivers are committed to helping him.)
- M: 0–10 MORE GOOD DAYS THAN BAD:** When there are too many bad days in a row, quality of life is too compromised. When a healthy human-animal bond is no longer possible, the caretaker must be made aware the end is near. The decision needs to be made if the pet is suffering. If death comes peacefully and painlessly, that is okay.

Over 5 is acceptable in each category. A total of 35 points or greater is acceptable for a good Pawspice.

Adapted from Villalobos, A.E., Quality of life scale helps make final call, *VPN*, September 2004.

Appendix 3: Cartoon Maps

DIAGNOSIS

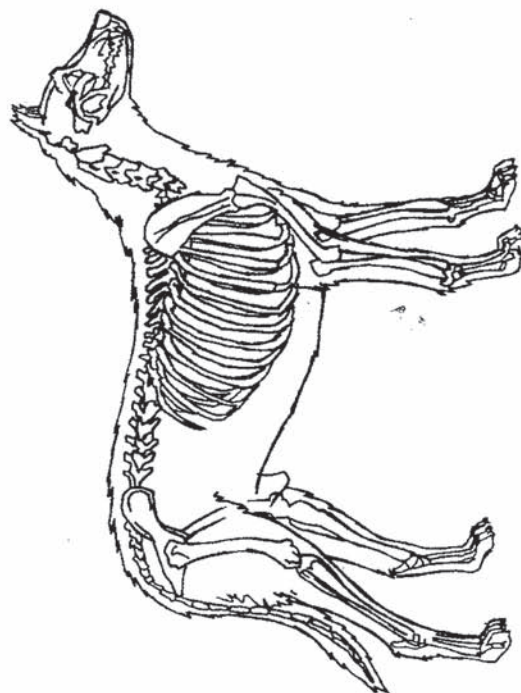
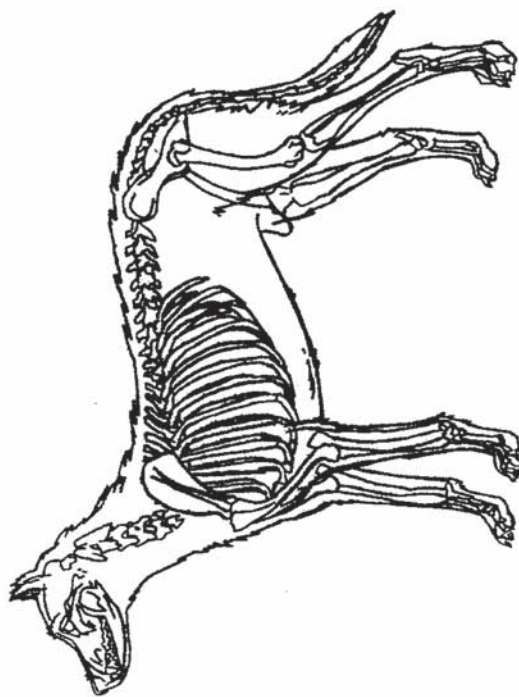
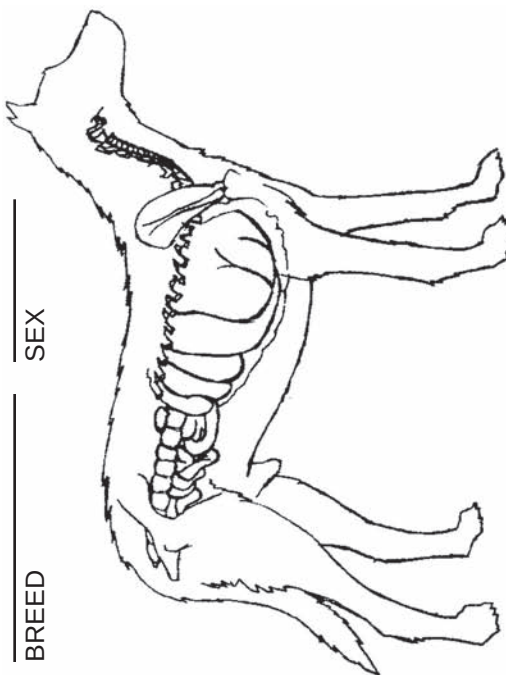
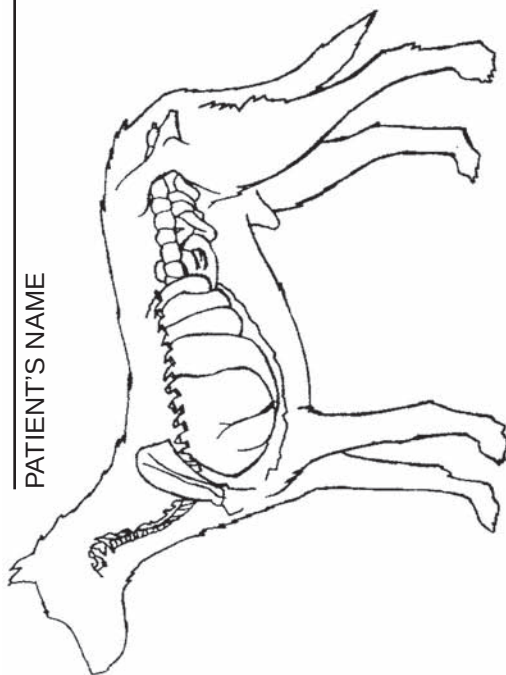
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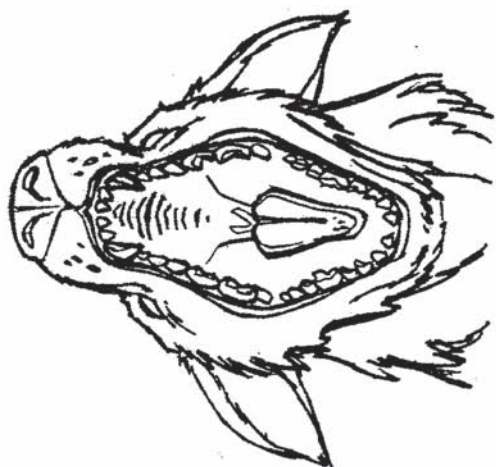
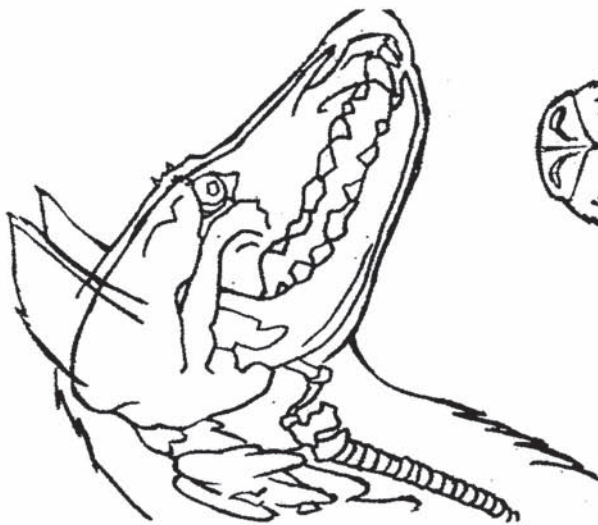
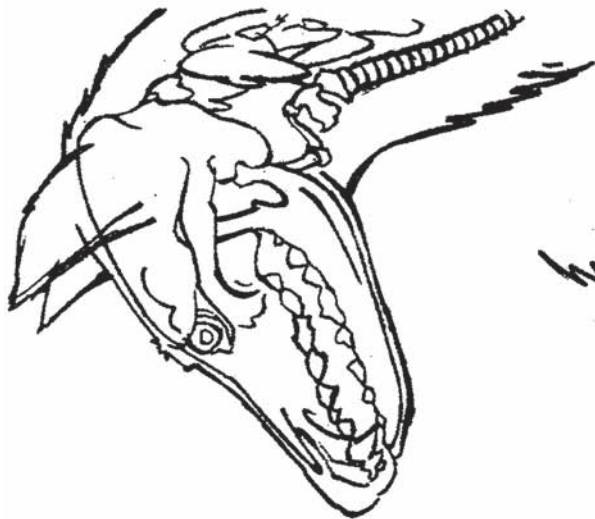
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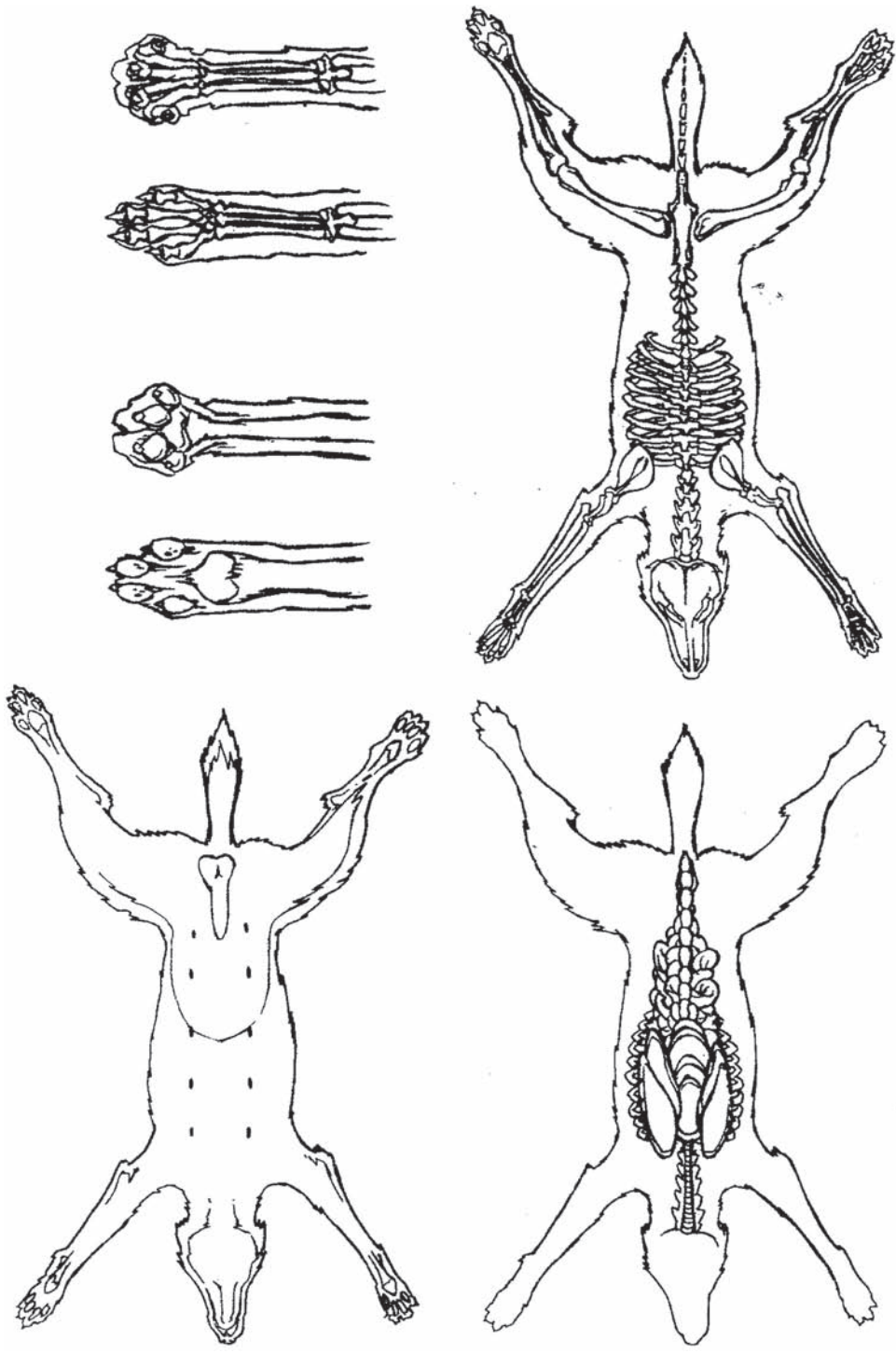
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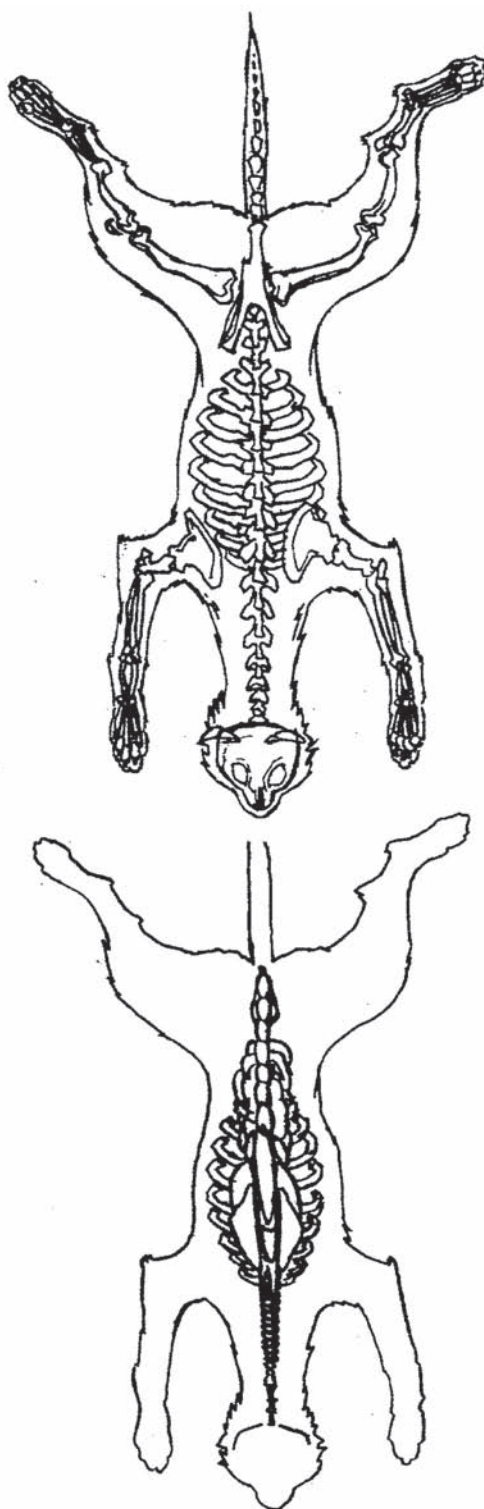
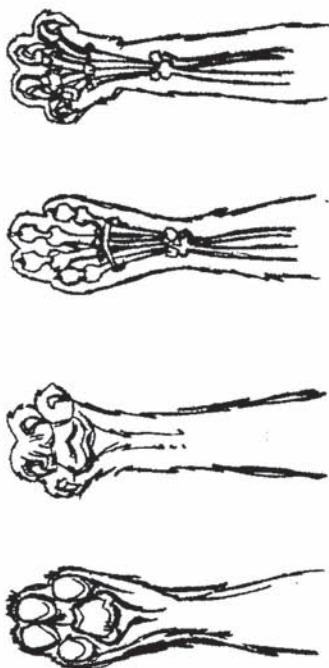
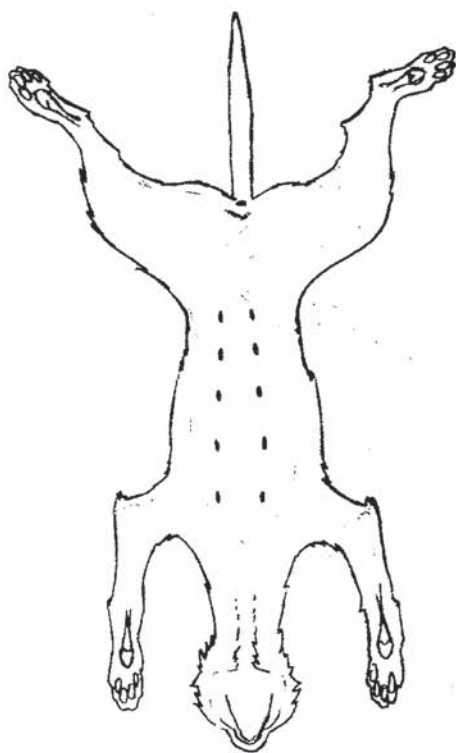
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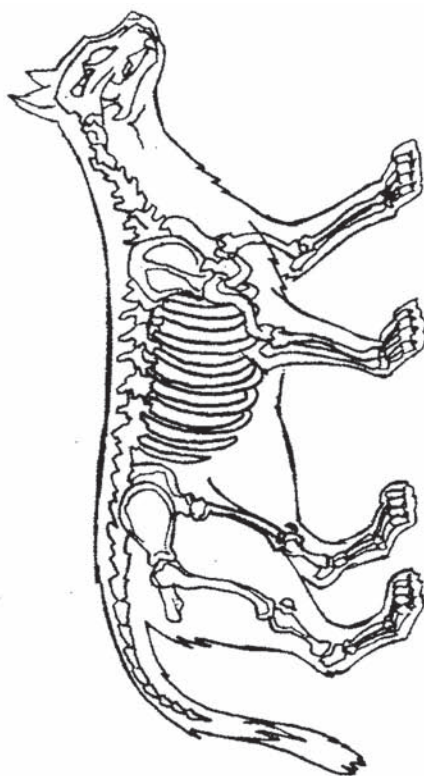
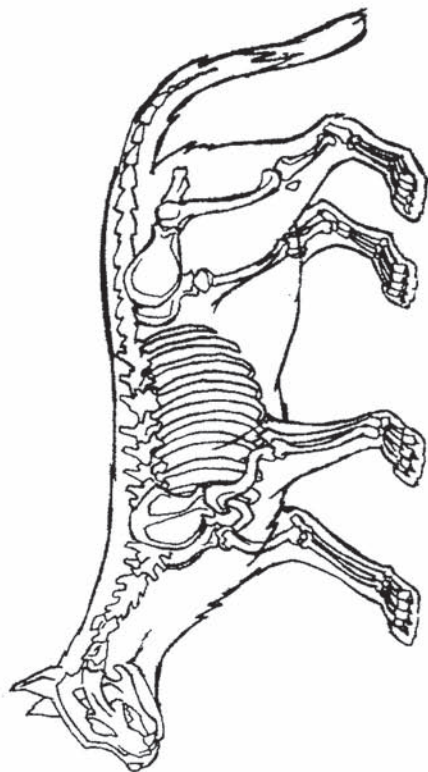
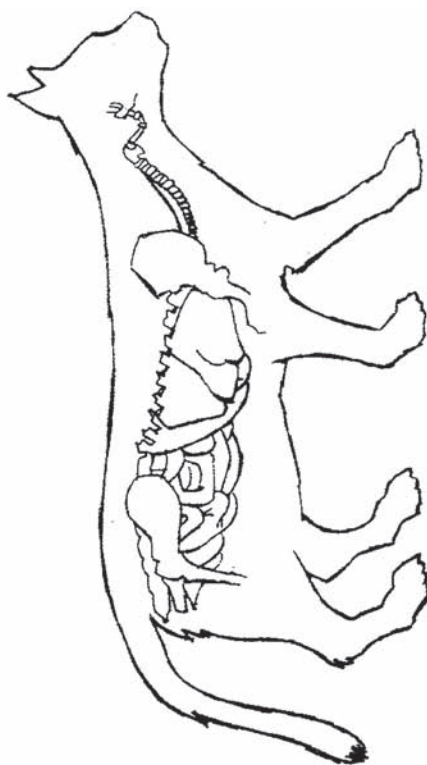
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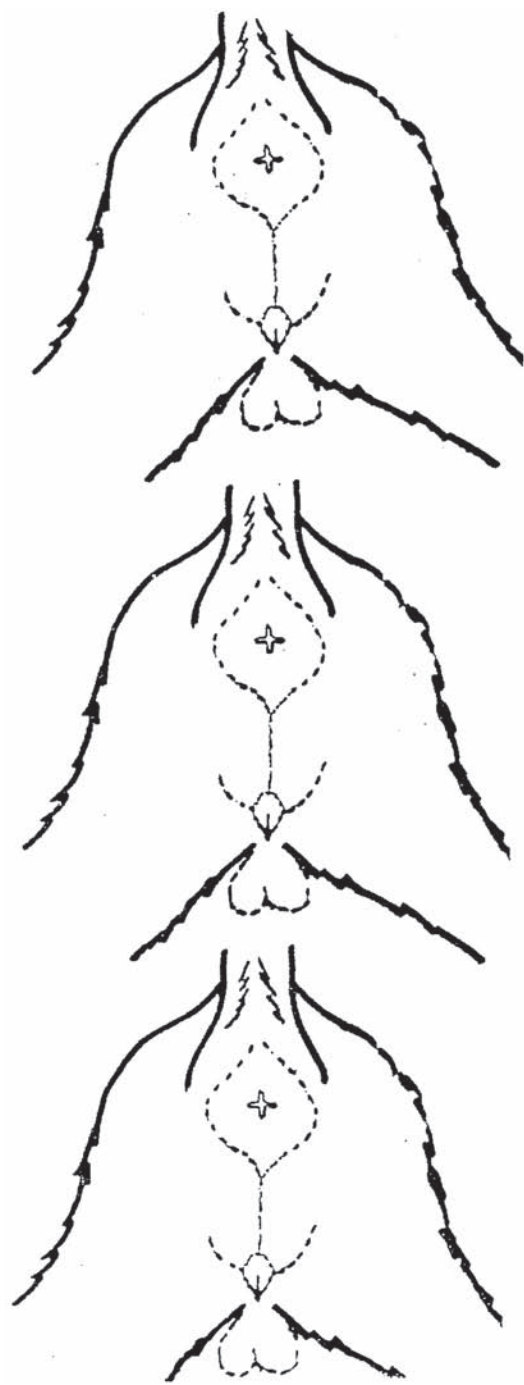
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