Presents:

VETERINARY ONCOLOGY
Care Beyond a Cure:
Extraordinary Advances in Cancer Care

With:

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THE COMMANDMENTS - SECRETS TO IMPROVING QUALITY OF LIFE FOR THE CANCER PATIENT

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Cancer is a word that frightens us all. It creates within us images of pain, discomfort, baldness, nausea, vomiting, cachexia and anorexia. These fears and feelings fill the minds of clients and the entire veterinary health care team of hospitals world wide, yet few patients that are responsibly treated ever experience these adverse effects. In fact, experienced health care teams work hard to ensure that their cancer patients have few if any side effects of cancer therapies. This is done by instituting proactive programs to prevent problems before they ever happen. Similarly, if these unfortunate adverse effects ever happen, then the client should know that their pet will be aggressively and efficiently treated to limit these problems to enhance and improve quality of life. In addition, future treatments will be altered to prevent future occurrences of the same side effect. The development of proactive strategies to prevent and to treat pain, discomfort, nausea, vomiting, anorexia, weight loss and starvation are not only the right thing to do for the patient, but it is also vital to do to meet the fears and apprehensions of the people who bring these animals to us.

The discussion below reviews the generalities associated with the three commandments of cancer care: Do not let them hurt, do not let them vomit (or have diarrhea), and do not let them starve.1-4 It is also recognized that there are many other fears and apprehensions that fill the hearts and minds of each caregiver. One of the most commonly mentioned is hairloss that fortunately does not commonly occur, except in dogs with constantly growing haircoats such as with poodles and schnauzers. Cats can lose their whiskers.

Meeting the fears and concerns of each client head on with frank, open discussions prior to the start of the process of caring for the cancer patient is absolutely vital to optimize meeting the medical needs of the patient and the non medical needs of each client. It is often said that the more time the team invests at the very beginning to make the client as knowlegable about the disease and the treatment as the rest of the members of their pet’s health care team, the less time, frustration and disappointment will be experienced subsequently. The net outcome is that the patient and client are cared for with compassion. The following are the commandments:

**DO NOT LET THEM HURT!**

Providing an active, preemptive, and ongoing pain management/prevention program for the dog with cancer is absolutely imperative. This reassures the caregiver that quality of life is optimal. Management should begin with comfort care and then, when needed, include oral medications (morphine, codeine, piroxicam (Feldene), carprofen, or others), transdermal delivery systems (fentanyl patches), acupuncture or more advanced analgesic delivery systems (eg: constant rate intravenous infusion, epidural catheters, intrathoracic pleural analgesia). The most important principle is that our caregivers know in advance that the veterinary health care team will not tolerate any pain. We work together to recognize, prevent, and manage it.

**DO NOT LET THEM VOMIT OR HAVE DIARRHEA!**

This commandment strikes at the preconceived and unfounded fear that dogs on chemotherapy often experience significant amounts of nausea and diarrhea. This simply is not true. With recent advances in cancer care, nausea, vomiting and diarrhea no longer are commonly associated with chemotherapy.

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Moreover, the introduction of a large number of antiemetics and antidiarrheals in clinical practice is very important to control these problems, should they occur. Dispensing oral medication such as metoclopramide to the caregiver each and every time a potentially nauseating drug is administered empowers the caregiver to prevent this symptom at home. In addition, we must be prepared to stop nausea and vomiting should it occur, ensuring that medications and supportive care are immediately available. Having access to drugs such as Cerenia, ondansetron hydrochloride and dolasetron mesylate, although costly, will provide this level of assurance for all members of the team. Some believe that tylosin, metronidazol and imodium can reduce the risk of small and large bowel diarrhea and often dispense these drugs to their cancer patients to prevent problems. Enhancing fiber content can be of great value at enhancing bowel health.

**DO NOT LET THEM STARVE!**

Appetite is equated with quality of life and rightly so. Dogs and cats that eat will and that are of normal body weight are more likely to thrive and have less toxicity during surgery, chemotherapy or radiation therapy. Placement of an estophagostomy tube is often the most important advance in therapy. Feeding a diet that is low in carbohydrates, moderate amounts of proteins and increased levels of n-3 polyunsaturated long chain fatty acids can be quite helpful.

**Action Steps for Commandments:**

- Make your veterinary technician/nursing team in charge of pain management.
- Make client aware that discomfort, nausea or anorexia is not normal and that early intervention is recommended.
- Make frequent follow up calls to ensure the patient is doing well.

**Quantitating Quality of Life**

Employing the commandments to meet the needs of the patient and the client is one very important step towards the holy grail of cancer therapy: enhancing quality of life.\(^5\)\(^-\)\(^7\) Despite the importance of ultimate goal, very little has been written about the subject. Each and every veterinarian takes a personal and professional oath to alleviate the pain and suffering of animals, yet few published papers directly define and quantitate this most important and essential of all objectives. Contributing factors of quality of life for all animals are subjective but are often comprised of a high level and enjoyment of relationships, mental stimulation, health, food consumption, stress, and control over their environment.\(^5\)\(^-\)\(^7\)

Quality of life is defined by each and every person for themselves and for their pets. Therefore, the veterinary health care team must understand how this is defined by each client for their pet. The team must concurrently dispel the myths and misperceptions associated with cancer therapy to ensure these myths and misperceptions do not cause the client to make inappropriate decisions about cancer and cancer therapy for their pets. When most veterinarians, clients and other members of the veterinary health care team initially describe cancer, chemotherapy, radiation therapy, and cancer surgery, they often do so with words such as pain, vomiting, diarrhea, starvation and the lack of hope. In one study, dogs with lymphoma which were treated with multidrug chemotherapy were interviewed to assess the quality of their pet's life during treatment.\(^7\) Sixty-eight per cent of the owners considered their dog's quality of life to be the same as before the lymphoma occurred, and the remaining 32 per cent felt that their pet's quality of life on chemotherapy treatment was acceptable but poorer than before the lymphoma occurred. Almost all (92%) of clients had no regrets about treating their dog with chemotherapy.

Converting the myriad of subjective parameters into objective, numerical data for subsequent analysis and comparison has been difficult in human and veterinary medicine. Several investigators have tried to enumerate parameters of toxicity and performance.\(^8\) More recent efforts, especially those in enumerating parameters associated with discomfort have employed a scale of zero to 100. The individual is asked to rate the parameter on a scale and then to compare subsequent assessment to the initial finding. These subjective...
assessments are then scored and recorded.

There is little doubt that all therapies should be linked to its impact on the patient and client’s quality of life. This parameter is considered by many at least if not more important than duration of remission and quality of life.

REFERENCES
CLINICAL BRIEFING: NAUSEA AND VOMITING

Emetic Potential

- Nausea and vomiting in association with the administration of chemotherapy is much less common in dogs than people. Cisplatin is an exception. (Do not give cisplatin to cats!)
- Small dogs are at greater risk of vomiting than larger dogs when given cisplatin.
- Emesis primarily originates from the CTZ and the emetic center.
- Acute vomiting occurs shortly after the administration of chemotherapy.
- Delayed vomiting may occur days to weeks after treatment.

Prevention

- Whenever possible, anticipate nausea and vomiting by pretreating with antiemetics, especially in patients with a history of nausea and those receiving highly emetogenic chemotherapy.
- In general, metoclopramide or a serotonin antagonist should be dispensed to each client for home care.
- It may be good practice to have clients not feed patients before they are to receive chemotherapy.

Self-Limiting Vomiting

- **Therapy:** Treat with metoclopramide or oral serotonin antagonist.
- Correct underlying cause.
- Do not feed by mouth until vomiting ceases for 12–24 hours.
- Initiate small amounts of water, then bland low-fat diet.
- Monitor hydration and electrolytes.

Life-Threatening Vomiting

- **Therapy:** Follow same protocol as for self-limiting vomiting except administer IV fluids (maintenance needs + hydration deficits + losses) and correct electrolyte and pH abnormalities (e.g., serum potassium).
- In addition, give antiemetics (e.g., metoclopramide) parenterally.
- Concurrently administer serotonin antagonists such as ondansetron or dolasetron.

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### Selected Antiemetics for use in DOGS

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Product</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Reglan®</td>
<td>1-2 mg/kg constant-rate infusion IV over 24 hr</td>
</tr>
<tr>
<td>Maropitant</td>
<td>Cerenia®</td>
<td>2 mg/kg PO or IM</td>
</tr>
<tr>
<td>Ondansetron</td>
<td>Zofran®</td>
<td>0.1-0.5 mg/kg IV, PO 15 min before chemotherapy then daily to bid</td>
</tr>
<tr>
<td>Dolasetron</td>
<td>Anzemet®</td>
<td>0.1-0.3 mg/kg IV, PO 15 min before chemotherapy then daily to bid</td>
</tr>
<tr>
<td>Butorphanol</td>
<td>Torbugesic®</td>
<td>0.4 mg/kg IM q8h</td>
</tr>
<tr>
<td><strong>Less effective</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>Thorazine®</td>
<td>0.5 mg/kg IM, SC, rectal suppository q6-8h</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>Compazine®</td>
<td>0.1-0.5 mg/kg IM, SC q6-8h 1.0 mg/kg rectally q8h</td>
</tr>
<tr>
<td><strong>Prochlorperazine-</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isopropamide</td>
<td>Darbazine®</td>
<td>0.5-0.8 mg/kg IM, SC q12h</td>
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<tr>
<td>Yohimbine</td>
<td>Yobine®</td>
<td>0.25-0.5 mg/kg SC, IM bid</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>Benadryl®</td>
<td>2.0-4.0 mg/kg PO q8h</td>
</tr>
<tr>
<td>Dimenhydrinate</td>
<td>Dramamine®</td>
<td>8 mg/kg PO q8h</td>
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<tr>
<td>Trimethobenzamide</td>
<td>Tigan®</td>
<td>3 mg/kg IM q8h</td>
</tr>
<tr>
<td>Domperidone</td>
<td>Motilium®</td>
<td>0.1-0.3 mg/kg IM, IV bid</td>
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<tr>
<td><strong>Investigational</strong></td>
<td></td>
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<tr>
<td>Haloperidol</td>
<td>Haldol®</td>
<td>110 µg/kg q 4 days (investigational)</td>
</tr>
<tr>
<td>Pimozide</td>
<td>Orap®</td>
<td>100 µg/kg q 6 days (investigational)</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td></td>
<td>1-3 mg IV (investigational)</td>
</tr>
</tbody>
</table>

### Selected Antiemetics for use in CATS

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Product</th>
<th>Dosage for Cats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpromazine</td>
<td>Thorazine®</td>
<td>0.5 mg/kg q 6-8 hours IM, SQ</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>Compazine®</td>
<td>0.1-0.5 mg/kg q 6-8 hours IM, SQ</td>
</tr>
<tr>
<td>Maropitant</td>
<td>Cerenia®</td>
<td>2 mg/kg PO or IM</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>Benadryl®</td>
<td>2.0-4.0 mg/kg q 8 hours PO</td>
</tr>
<tr>
<td>Butorphanol</td>
<td>Torbugesic®</td>
<td>0.1-0.4 mg/kg q 1-4 hr, IM, IV, SQ</td>
</tr>
<tr>
<td>Dimenhydrinate</td>
<td>Dramamine®</td>
<td>8 mg/kg q 8 hours PO</td>
</tr>
</tbody>
</table>
Prochlorperazine.......................... Darbazine®.......................... 0.5–0.8 mg/kg q 12 hours IM, SQ
Metoclopramide.......................... Reglan®............................ 11.2 mg/kg constant rate infusion IV over 24 hours
                                or 0.6 mg/kg PO q6 hours
Ondansetron.............................. Zofran®.............................. 0.1–0.3 mg/kg IV 15 minutes before and 12 hours
                                after chemotherapy or PO q12 hours
Dolasetron.............................. Anzemet®........................... 0.6–3 mg/kg IV q 24 hours
Dexamethasone........................... Many available ..................... 1–3 mg IV

CLINICAL BRIEFING: PAIN

General Concepts of Pain Management
• Assess each patient for discomfort.
• Believe the client’s perception about quality of life.
• Choose optimal analgesics.
• Deliver the drugs in the most appropriate fashion.
• Empower clients to directly participate in patient care.
• Use analgesics preventively for maximum benefit.
• Compassionate care, gentle handling, and a comfortable environment should be accompanied by local and systemic analgesics to anticipate discomfort and to treat ongoing pain.

Mild Pain
• Eliminate underlying cause.
• Use nonopioids, including NSAIDs, with or without acupuncture and local anesthetic agents, as indicated.
• Constantly reassess the patient’s need for analgesia.

Moderate Pain
• Eliminate underlying cause.
• Use nonopioids, including NSAIDs and opiate analgesics with or without acupuncture and local anesthetics, as indicated.
• If needed, consider α2-adrenergic agonists and anxiolytics; changing the route of administration (e.g., oral to IV, SC, or IM) may be beneficial.
• Constantly reassess the patient’s need for analgesia.

Severe Pain
• Eliminate underlying cause.
• Nonopioids, including NSAIDs, with increasing dosages of opiate analgesics, should be combined as needed with local analgesia (local, regional, intracavitary, or epidural analgesia), acupuncture, and/or sustained-release patches.
• Also can combine above with:
  - Constant-rate infusion of fentanyl
  - Microdose ketamine
  - Palliative procedures (e.g., radiation therapy, surgery)
• Maximize blood levels of analgesics with systemic administration.
## Select Analgesics for Dogs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (mg/kg)</th>
<th>Route</th>
<th>Interval (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioid Agonists</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>0.5–2 mg/kg</td>
<td>PO, IM, SC</td>
<td>2–4</td>
</tr>
<tr>
<td>Morphine, sustained-release</td>
<td>2–5 mg/kg</td>
<td>PO</td>
<td>1–4</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>0.05–0.4 mg/kg</td>
<td>IV, SC, IM</td>
<td>2–4</td>
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<td>Hydromorphone</td>
<td>0.05–0.2 mg/kg</td>
<td>IV, SC, IM</td>
<td>2–6</td>
</tr>
<tr>
<td>Methadone</td>
<td>1–1.5 mg/kg</td>
<td>IV, SC, IM</td>
<td>once</td>
</tr>
<tr>
<td>Meperidine</td>
<td>3–5 mg/kg</td>
<td>SC, IM</td>
<td>1–2</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>2–5 μg/kg</td>
<td>IV bolus prior to CRI*</td>
<td>Duration of infusion</td>
</tr>
<tr>
<td>-Postoperative</td>
<td>2–5 μg/kg/hr</td>
<td>CRI</td>
<td>Duration of infusion</td>
</tr>
<tr>
<td>-Operative</td>
<td>10–45 μg/kg/hr</td>
<td>CRI</td>
<td>Duration of infusion</td>
</tr>
<tr>
<td>(2–3 mg/kg/hr) patch</td>
<td>Dermal application</td>
<td>Replace every 3–5 days</td>
<td></td>
</tr>
<tr>
<td>Sufentanil</td>
<td>5 μg/kg</td>
<td>IV bolus prior to CRI</td>
<td>2–6</td>
</tr>
<tr>
<td>-Postoperative</td>
<td>0.1 μg/kg/hr</td>
<td>CRI</td>
<td>Duration of infusion</td>
</tr>
<tr>
<td>Remifentanil</td>
<td>4–10 μg/kg</td>
<td>IV bolus prior to CRI</td>
<td>2–6</td>
</tr>
<tr>
<td>-Postoperative</td>
<td>4–10 μg/kg/hr</td>
<td>CRI</td>
<td>Duration of infusion</td>
</tr>
<tr>
<td>-Operative</td>
<td>20–60 μg/kg/hr</td>
<td>CRI</td>
<td>Duration of infusion</td>
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<td><strong>Opioid Agonist-Antagonist</strong></td>
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<tr>
<td>Buprenorphine</td>
<td>0.005–0.02 mg/kg</td>
<td>IV, IM, SC</td>
<td>8–12</td>
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<tr>
<td>Butorphanol</td>
<td>0.1–0.4 mg/kg</td>
<td>IV, IM, SC</td>
<td>1–4</td>
</tr>
<tr>
<td></td>
<td>0.5–2 mg/kg</td>
<td>PO</td>
<td>6–8</td>
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<tr>
<td>Nalbuphine</td>
<td>0.5–1 mg/kg</td>
<td>IV, IM, SC</td>
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<td>Pentazocine</td>
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<td>IV, IM, SC</td>
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<td><strong>NSAIDs</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>1–2 mg/kg</td>
<td>IV, IM, SC</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>1 mg/kg</td>
<td>PO</td>
<td>24</td>
</tr>
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<td>Piroxicam</td>
<td>0.3 mg/kg</td>
<td>PO</td>
<td>24–48</td>
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<td>Meloxicam</td>
<td>0.1–0.2 mg/kg</td>
<td>IV, IM, SC</td>
<td>24</td>
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<tr>
<td>Meloxicam</td>
<td>0.1 mg/kg</td>
<td>PO</td>
<td>24</td>
</tr>
<tr>
<td>Carprofen</td>
<td>2.2 mg/kg</td>
<td>PO</td>
<td>12</td>
</tr>
<tr>
<td>Etodolac</td>
<td>1–15 mg/kg</td>
<td>PO</td>
<td>12</td>
</tr>
<tr>
<td>Deracoxib</td>
<td>1–2 mg/kg</td>
<td>PO</td>
<td>24</td>
</tr>
<tr>
<td>Tolfenamic acid</td>
<td>4 mg/kg</td>
<td>PO</td>
<td>SC q24h × 3 days, 4 days off</td>
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<td><strong>Alpha-2 Agonists</strong></td>
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<tr>
<td>Medetomidine</td>
<td>5–10 μg/kg</td>
<td>IM, SC</td>
<td>Once</td>
</tr>
<tr>
<td></td>
<td>1–4 μg/kg</td>
<td>IV</td>
<td>Once</td>
</tr>
<tr>
<td>Romifidine</td>
<td>10–20 μg/kg</td>
<td>IM, SC</td>
<td>Once</td>
</tr>
<tr>
<td>Xylazine</td>
<td>0.2–0.5 mg/kg</td>
<td>PO</td>
<td>12</td>
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<td><strong>Local Anesthetics</strong></td>
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<tr>
<td>Lidocaine</td>
<td>1.5</td>
<td></td>
<td>Intrapleural prior to bupivacaine</td>
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<tr>
<td>Bupivacaine</td>
<td>1–2 mg/4.5 kg</td>
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<td>Local nerve blocks</td>
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<td></td>
<td>Intrapleural administration prn</td>
</tr>
<tr>
<td>Mepivacaine</td>
<td>1</td>
<td>SQ</td>
<td>1.5–2.5 hr</td>
</tr>
<tr>
<td>Ropivacaine</td>
<td>1</td>
<td>SQ</td>
<td>1.5–2.5 hr</td>
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</table>
Other Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amantidine</td>
<td>3–5 mg/kg</td>
<td>PO</td>
<td>24 hr</td>
</tr>
<tr>
<td>Acetaminophen (paracetamol)</td>
<td>5–10 mg/kg</td>
<td>PO</td>
<td>12 hr</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>1–4 mg/kg</td>
<td>PO</td>
<td>24 hr</td>
</tr>
<tr>
<td>Glucosamine Chondroitin</td>
<td>13–15 mg/kg</td>
<td>PO</td>
<td>24 hr</td>
</tr>
<tr>
<td>Ketamine</td>
<td>0.5–1 μg/kg</td>
<td>IM</td>
<td>30 min</td>
</tr>
<tr>
<td>Tramadol</td>
<td>2–4 mg/kg</td>
<td>IV</td>
<td>PRN every 3–6 weeks with diuresis</td>
</tr>
</tbody>
</table>

*CRI = constant rate infusion.

Treatment of Moderate Pain Associated with Invasive Procedures in the Dog

**Indication:** Simple, minimally painful, short-term procedure (e.g., needle-core biopsy of tumor, small incisional biopsy)

- Preemptive analgesia: Oxymorphone (0.05–0.1 mg/kg SC), acepromazine (0.02–0.04 mg/kg SC), and atropine (0.04 mg/kg SC).
- Anesthesia (as indicated): Propofol or thiopental induction followed by inhalant anesthesia.
- Postoperative analgesia: Ketoprofen 2.2 mg/kg SC.

**Indication:** Simple, moderately painful, short-term procedure (e.g., nasal biopsy or bone biopsy in a dog with normal organ and cardiovascular function)

- Preemptive analgesia: Oxymorphone (0.05–0.1 mg/kg SC) and atropine (0.02–0.04 mg/kg SC).
- Anesthesia (as indicated): Propofol or thiopental induction followed by inhalant anesthesia. Xylazine 0.1 mg/kg IV administered just prior to biopsy to enhance analgesia.
- Postoperative analgesia: Ketoprofen 2.2 mg/kg SC.

**Indication:** Relatively short, simple procedure (e.g., thoracoscopy, laparoscopy, abdominal exploratory, skin biopsy)

- Preemptive analgesia: Morphine (1 mg/kg SC), acepromazine (0.02 mg/kg SC), and atropine (0.04 mg/kg SC) with oral NSAID pre- and postoperative (ensure adequate hydration and renal function)
- Anesthesia (as indicated): Propofol or thiopental induction followed by inhalant anesthesia.
- Postoperative analgesia (one of the following):
  - Morphine 0.5 to 1 mg/kg S) prn q4h 6h
  - Nalbuphine 1 mg/kg SC prn q4h 6h
  - Ketoprofen 2 mg/kg SC
  - Carprofen 4 mg/kg SC
- Home analgesia (one of the following):
  - Morphine 0.5 mg/kg PO tid-qid
  - Transdermal fentanyl (2·3 mg/kg/hr); may be administered with or without one of the following: Ketoprofen 1 mg/kg PO, piroxicam 0.3 mg/kg, PO q24-48h, meloxicam 0.1 mg/kg PO q24h, carprofen 2.2 mg/kg PO q12h, etodolac 10·15 mg/kg PO q12h
Treatment of Severe Pain Associated with Invasive Procedures in the Dog

Indication: Procedure thought to cause moderate to severe discomfort (e.g., maxillectomy, hemipelvectomy, chest wall resection)
- Preemptive analgesia: Morphine (1 mg/kg SC), acepromazine (0.02 mg/kg SC) and with nerve block, if appropriate to local area. Ketamine microdose constant-rate infusion at 10 μg/kg/min after an IV bolus of ketamine (0.5 mg/kg) can reduce the need for analgesics postoperatively.
- Anesthesia (as indicated): Propofol or thiopental induction followed by inhalant anesthesia.
- Postoperative analgesia: Fentanyl bolus (2 mg/kg IV) followed by fentanyl infusion 3–5 μg/kg/hr IV constant-rate infusion by syringe pump or IV pump; bupivacaine nerve block and acupuncture.
- Home analgesia (one of the following):
  - Morphine 0.5 mg/kg PO tid-qid
  - Transdermal fentanyl (2–3 mg/kg/hr); may be administered with or without one of the following: Ketoprofen 1 mg/kg PO, piroxicam 0.3 mg/kg, PO q24-48h, meloxicam 0.1 mg/kg PO q24h, deracoxib 3–4 mg orally daily for 7 days then 1–2 mg/kg long-term, carprofen (2.2 mg/kg PO q12h), etodolac (10–15 mg/kg PO q12h)

Indication: Procedure thought to cause severe discomfort (e.g., mandibulectomy, laminectomy in combination with hemipelvectomy)
- Preemptive analgesia: Hydromorphone (2 mg/kg SC), and atropine (0.04 mg/kg SC) with nerve block, if appropriate, to local area (infraorbital block for maxillectomy, for example)
- Anesthesia (as indicated): Propofol or thiopental induction followed by inhalant anesthesia
- Postoperative analgesia: Fentanyl bolus (0.2 mg/kg SC) followed by fentanyl infusion 3–5 μg/kg/hr IV constant-rate infusion by syringe pump or IV pump; bupivacaine nerve block
- Home analgesia (one of the following):
  - Morphine 0.5 mg/kg PO tid-qid
  - Transdermal fentanyl (2–3 mg/kg/hr); may be administered with or without one of the following
    - Ketoprofen 1 mg/kg PO, piroxicam 0.3 mg/kg, PO q24–48h, meloxicam 0.1 mg/kg PO q24h, carprofen 2.2 mg/kg PO q12h, deracoxib 3–4 mg orally daily for 7 days then 1–2 mg/kg long-term, etodolac (10–15 mg/kg PO q12h)

Indication: Procedure thought to cause severe discomfort (e.g., such as rear-limb amputation, hemipelvectomy)
- Preemptive analgesia: Morphine (1 mg/kg SC) and atropine (0.04 mg/kg SC) with bupivacaine epidural
- Anesthesia (as indicated): Propofol or thiopental induction followed by inhalant anesthesia
- Postoperative analgesia: Fentanyl bolus (0.2 mg/kg SC) followed by fentanyl infusion 3–5 μg/kg/hr IV constant-rate infusion by syringe pump or IV pump; bupivacaine nerve block
- Home analgesia: Sustained-release morphine (0.5 mg/kg PO tid) with or without one of the following:
  - Ketoprofen 1 mg/kg PO
  - Piroxicam 0.3 mg/kg PO q24–48h
  - Meloxicam 0.1 mg/kg PO q24h
  - Carprofen 2.2 mg/kg PO q12h
  - Deracoxib 3–4 mg orally daily for 7 days then 1–2 mg/kg long-term
  - Etodolac 10–15 mg/kg PO q12h
Select analgesics in Cats\textsuperscript{2-5}  

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (mg/kg)</th>
<th>Route</th>
<th>Dose Interval (hr)</th>
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<tr>
<td><strong>Opioid Agonists</strong></td>
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<tr>
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<td>IM, SQ</td>
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<td>Fentanyl</td>
<td>0.0002-0.05</td>
<td>IV, Bolus prior to CRI</td>
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<tr>
<td></td>
<td>0.001-0.004</td>
<td>CRI</td>
<td>duration of infusion</td>
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<td></td>
<td>2.5 mg patch</td>
<td>Dermal Application</td>
<td>q 3-5 days</td>
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<td>Ketoprofen</td>
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<td>IV, IM, SQ</td>
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<td>Carprofen</td>
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<td>Medetomidine</td>
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<td>Lidocaine</td>
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<td>intrapleural prior to</td>
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<td></td>
<td>Bupivacaine</td>
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</tr>
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<td>1-2/4.5kg</td>
<td>Local blocks, intrapleural</td>
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<td><strong>ANXIETY TREATMENT</strong></td>
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<tr>
<td>Xylazine</td>
<td>0.05-0.2</td>
<td>IV or IM</td>
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<tr>
<td>Ketamine</td>
<td>0.5-1.0</td>
<td>IM</td>
<td>30 minutes</td>
</tr>
</tbody>
</table>

Example protocols for sedation, anesthesia and analgesia in stable, uncomplicated cats.*
TOP 10 ADVANCES IN ONCOLOGY FOR 2010

Gregory K. Ogilvie, DVM, Diplomate ACVIM (Specialties of Internal Medicine, Oncology), Diplomate ECVIM-CA (Oncology)

Cancer Prevention

Family veterinarians throughout California are incorporating cancer prevention and screening programs. The identification and management of risk factors for preventing cancer such as breed selection and modification of environmental factors that are known to cause cancer is vital to reduce cancer in the pet population.

#1: Lifetime weight management is associated with decreased risk of developing cancer and other diseases such as diabetes mellitus and osteoarthritis (J Am Vet Med Assoc 220; 1315-1320, 2002). Supplementation with eicosapentaenoic and docosahexaenoic acid may reduce the risk of cancer.

#2: It is important to eliminate exposure to environmental carcinogens such as pesticides, coal or kerosene heaters, herbicides such as 2, 4-dichlorophenoxyacetic acid, passive tobacco smoke, asbestos, radiation, and strong electromagnetic field exposure. These steps may be particularly important for clients of susceptible breeds (e.g., a Scottish terrier and herbicide exposure, Environ Res 32(2):305-313, 1983).

Commandments

Perhaps the greatest barrier to enhanced cure and control of cancer is that the caregiver and the veterinary health care team often have preconceived notions about cancer and its treatment. There are three commandments of cancer care that must be dealt with for patient and client comfort. They are:

• Do not let them hurt. Providing an active, preemptive, and ongoing pain management/prevention program for the dog with cancer is absolutely imperative. This reassures the caregiver that quality of life is optimal.

• Do not let them vomit or have diarrhea. Dispensing oral medication such as metoclopramide or more recently, the novel NK-1 receptor antagonist, maropitant (Cerenia) to the caregiver each and every time a potentially nauseating drug is administered, empowers the caregiver to prevent and treat this symptom at home. Tylosin, metronidazol and imodium can reduce the risk of small and large bowel diarrhea and often dispense these drugs to their cancer patients to prevent problems.

• Do not let them starve. Nursing care (e.g., warming food, providing aromatic foods and comfortable environments), medicinal appetite stimulants such as cyproheptadine megestrol acetate and mirtazapine, and, when needed, assisted feeding techniques such as esophagostomy, tube placement should be employed when needed.

#3: Maropitant citrate (Cerenia) is a novel, effective NK1 receptor antagonist that is approved for the treatment of vomiting in the dog and is available as an injectable and oral product.

Recent Advances in Cancer Care: Something New, Something Old

California Veterinarians are entering an amazing new era of veterinary cancer care where molecular therapeutics are being approved for and released to the profession to control and cure cancer. The number of new treatments is expected to increase the ability to conquer this horrible disease while maintaining and improving quality of life. While the new molecular therapeutics are exciting, so are the new uses of old drugs to treat, control and cure cancer.

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#4: The Merial xenogeneic DNA vaccine for the treatment of oral malignant melanoma is an effective therapy that is at the forefront of a new wave of molecular therapeutics (Clin Cancer Res 9(4):1284-1290, 2003).

#5: Doxorubicin is the most effective agent for the treatment of lymphoma and it has efficacy for the treatment of hemangiosarcoma, soft tissue sarcomas and osteosarcoma.

#6: CCNU is effective for the treatment of lymphoma, histiocytic sarcoma, mycosis fungoides, and mast cell tumors.

#7: Piroxicam +/− Mitoxantrone (Clin Cancer Res. 2003 Feb;9(2):906-11) has been shown to be very effective for the treatment of transitional cell carcinoma and squamous cell carcinoma in the dog. Prevocox also appears to have anticancer effects against transitional cell carcinoma in dogs (VCS Proceedings, 2007).


#9: Vinblastine is a relatively safe and effective therapy for mast cell tumors in the dog.

Compassion Fatigue
When we care for our patients with compassionate care, we must do so by expressing empathy. The act of extending empathy as we care for our patients and their clients can lead to compassion fatigue. When any member of the veterinary health care team finds themselves giving more without allowing themselves to be replenished emotionally, it is only a matter of time before there will be a shortage of compassion. Simply put, compassionate fatigue results when there is a depletion of emotional resources from within as we care and provide compassion for others.

#10: Recognizing and treating compassion fatigue is essential to enhance professional, personal and financial success.

References Available Upon Request
Canine lymphoma is rewarding to treat as long as a few secrets or rules are known. The following are a few important prognostic variables for canine lymphoma.

- **Clinical Stage:** IV + V worse than I-III; dogs with clinical signs worse than if asymptomatic.
- **Hypercalcemia:** worse when associated with an anterior mediastinal mass.
- **Sex:** female dogs better than male dogs. **Body size** small dogs better than large dogs
- **Pretreatment corticosteroids:** worse.
- **High grade:** higher response rate and longer duration of remission.

When considering treatment, one must remember that the more complex the protocol, the longer the first remission, higher the cost and toxicity. The following is a general overview of canine lymphoma.

**Background**

Malignant lymphoma (lymphosarcoma) is a lymphoproliferative tumor of solid lymphoid tissues with possible marrow metastasis and a leukemic phase. In dogs, it accounts for 5-7% of all tumors seen and occurs at an incidence rate of 24 cases per 100,000 dogs. It occurs most commonly between 5 and 12 years of age. Boxers, Cocker Spaniels, Fox Terriers, German Shepherds, Scottish Terriers and Golden Retrievers are at an increased risk when compared with other breeds. Etiology for the canine is unknown. In the cat, 90% of the cases are FeLV related and it occurs at an incidence rate of 41.6 cases per 100,000 cats. This accounts for one third of all feline neoplasms and is two and one-half times the rate of lymphoid neoplasia in man. There is a slight male > female predominance in cats.

**Diagnosis**

Once clinical findings compatible with a diagnosis of malignant lymphoma have been found, aspiration and cytology of accessible lesions should be completed. Malignant lymphoma is characterized by the replacement of normal lymph nodes by a uniform population of pleomorphic and bizarre lymphocytes. After a tentative diagnosis of malignant lymphoma has been supported through rapid cytologic methods, confirmation of the diagnosis may be conducted by biopsy. A tissue core may be obtained by Tru-Cut biopsy or, preferably, a node may be excised for final confirmation.

If a dog or cat is to undergo therapy, clinical staging is mandatory. Clinical staging determines the extent of disease in the living animal. Once a baseline of data has been obtained, the clinical oncologist will be able to know which parameters should be monitored in order to reach complete remission. Clinical staging should include radiography of the thorax and abdomen, a complete blood count and platelet count, a bone marrow aspirate and core, an ophthalmic exam, measurement of representative enlarged lymph nodes and a biochemistry panel with special emphasis on calcium and protein levels. Abnormal findings beyond lymphadenopathy are rare; however marrow infiltrate with subsequent release of cells into the peripheral blood is occasionally seen. Hypercalcemia associated with a parathyroid-hormone-like substance is observed in some dogs with malignant lymphoma. This is most often encountered in dogs with anterior mediastinal lymphoma and bone marrow involvement.

**Prognostic Factors**

Prognostic factors are difficult to confirm due to the variation from study to study. Most treatment reports indicate that hypercalcemia and poor performance status are predictive of short remission and survival times. Animals with advanced clinical stages (World Health Organization Stage IV and V), or at least those with malignant cells in their bone marrows, are also considered to have a poorer prognosis than those animals with less advanced clinical stages (WHO Stage I-III). Some reports suggest that treatment with
glucocorticoids prior to therapy with more aggressive chemotherapeutic agents cause a poorer response to therapy than seen in dogs which have not been treated with glucocorticoids, but this finding has not been consistently observed.

**Therapy**

Treatment for malignant lymphoma must be systemic in nature since it is a multi-system disease. Chemotherapy is most frequently utilized; however, some immunotherapy has been effective. Untreated, dogs affected with malignant lymphoma live an average of only six weeks once a diagnosis has been made. With chemotherapy, dogs can survive for 6-10 months with an excellent quality of life. Dosage of chemotherapeutic agents for the cat is the same as for the dog except when Adriamycin is used. While dogs may receive Adriamycin every 21 days at a dosage of 30 mg/m2, cats appear to be more sensitive to the drug and many of them can only tolerate a dosage of 20 mg/m2 given every 21 days. Anorexia and renal failure have been reported as significant side effects in cats.

Malignant lymphoma is one of the most responsive forms of cancer presented to the practitioner. With appropriate chemotherapy protocols, nearly 90% of animals placed on therapy should reach complete remission. Of those that reach remission, approximately 80-90% will maintain a reasonable (>6 mos) timeframe of excellent quality life. Cost is not inexpensive; however, it is within reasonable financial reach of many clients, thus allowing therapy to be possible.

Although marginally effective, prednisone is inexpensive and often used in combination with other drugs to treat lymphoma. With prednisone therapy, the average pet lives 2 months. One-third of the dogs and cats treated with prednisone will go into complete remission, one-third will go into partial remission, and one-third will not respond at all.

Adriamycin is one of the most effective single agent treatments for lymphoma in dogs. Of the dogs treated with Adriamycin, 81% developed a complete and partial remission. The duration of remission is approximately 9 months. Dogs treated with Adriamycin and then switched to COP (cyclophosphamide, oncovin, prednisone) had a higher second remission rate compared to those started on COP and then switched to Adriamycin.

The COP protocol is effective for inducing a remission in 75% of dogs with lymphoma. A median duration of remission of 6 months is commonly seen. Approximately twenty percent of the dogs treated with the COP regimen are in remission at 1 year. In one study, 79% of cats with lymphoma treated with COP achieved a complete remission whereas only 29 percent of cats treated for lymphoblastic leukemia achieved a complete remission. Cats with lymphoma treated with COP had a shorter remission time (64% achieved a complete remission, median remission 5 months) but proportionately more long-term, survivors than dogs. Cats with renal lymphoma tend to have recurrence of tumor in the brain, therefore cytosine arabinoside is frequently recommended as an additional therapy.

The addition of Adriamycin to the COP regiment resulted in longer remission time (7 months vs 6 months). A complete remission was attained in eighty-four percent of dogs treated with COPA. An additional 7% achieved a partial remission. Twenty-two percent of dogs treated with the COPA protocol were in remission at one year.

Garrett et al (JVIM 16: 704-709, 2002) compared a maintenance-free chemotherapy protocol based on CHOP to a similar protocol with a maintenance phase for the treatment of canine lymphoma. Fifty-three dogs with multicentric lymphoma were treated with a 6-month modified version of the University of Wisconsin (UW)-Madison chemotherapy protocol. Disease-free interval (DFI) and survival were compared to a historical control group of 55 dogs treated with a similar protocol with a prolonged maintenance phase. Remission rate for the study dogs was 94.2%. The remission and survival between the 2 groups did not differ significantly. Thus, we and others believe the 6-month chemotherapy protocol based on CHOP with no maintenance phase provides is equal to a similar protocol with a prolonged maintenance phase.
**WISCONSIN PROTOCOL - SHORT**

**LYMPHOMA PROTOCOL TREATMENT**

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<thead>
<tr>
<th>Week</th>
<th>Treatment</th>
<th>DATE</th>
<th>DOSE</th>
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</thead>
<tbody>
<tr>
<td>1</td>
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<tr>
<td></td>
<td>Asparaginase, 400 U/kg SQ</td>
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<tr>
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<td>Prednisone, 2 mg/kg PO s.i.d.</td>
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<tr>
<td>2</td>
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<tr>
<td></td>
<td>Prednisone, 1.5 mg/kg PO s.i.d.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Vincristine, 0.5-0.7 mg/m² IV</td>
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<tr>
<td></td>
<td>Prednisone, 1.0 mg/kg PO s.i.d.</td>
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<tr>
<td>4</td>
<td>Adriamycin, 30 mg/m² IV</td>
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<tr>
<td></td>
<td>Prednisone, 0.5 mg/kg PO s.i.d.</td>
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<td>Vincristine, 0.5-0.7 mg/m² IV</td>
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<td>Vincristine, 0.5-0.7 mg/m² IV</td>
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<td>9</td>
<td>Adriamycin, 30 mg/m² IV</td>
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<td>25</td>
<td>Adriamycin, 30 mg/m² IV</td>
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Another protocol involves administering Adriamycin at 30 mg/m² body surface area q3 weeks for 5 treatments as long as the dog stays in remission. One day after the first Adriamycin therapy, l-asparaginase is administered IM weekly for 3 treatments (10,000 Units/m²). When the patient comes out of remission, then COP therapy is started as mentioned above. The duration of remission 1 plus remission 2 is similar to the COPA protocol noted above with less toxicity and less cost to the client.

Rassnick and colleagues (J Vet Intern Med 16[5]:576-580 2002) evaluated the efficacy and toxicity of the MOPP chemotherapy protocol (mechlorethamine, vincristine, procarbazine, and prednisone) as a rescue regimen in dogs with lymphoma. In that study, one hundred seventeen dogs that had resistance to previously administered chemotherapy were evaluated. Thirty-one percent had a complete response (CR) to MOPP for a median of 63 days. Five dogs developed septicemia, and 2 died as a result. MOPP was an effective treatment for dogs with resistant lymphoma but caution should be employed to monitor for septicemia.

References available upon request
CANINE MAST CELL TUMOR: HOT NEW DIAGNOSTICS AND TREATMENT

Gregory K. Ogilvie, DVM, Diplomate ACVIM (Specialties of Internal Medicine, Oncology), Diplomate ECVIM-CA (Oncology)

Very few tumors present in such a wide variety of clinical signs: they are indeed the great impostors! They can look like anything and behave differently depending on the histologic type, location and the extent of the disease. The following is a brief discussion about these tumors. Some highlights are as follows:

• Mast cell tumor granules do not stain well with Diff Quick type stains unless they are "soaked" in the alcohol for several minutes prior to staining.
• Some important prognostic indicators include duration of presence, location and histologic type in the dog.
• Mast cell tumors tend to metastasize to nodes, liver spleen and bone marrow...rarely to lungs.
• Radiation therapy is extremely effective for controlling local disease.
• Prednisone and vincristine when used as single agents induce a remission (partial or complete) in about 23% of the tumors.

Diagnostics
Diagnostic workup of mast cells usually includes a number of procedures. These include a complete blood cell count (CBC), serum chemistry profile, and urinalysis. In addition, fine needle aspiration of the lesion, regional lymph nodes and examination of buffy coats or bone marrow helps to determine the extent of tumor involvement. A CBC is valuable in assessing animals with mast cell tumors because those animal patients with systemic mastocytosis occasionally have peripheral eosinophilia and basophilia in addition to circulating mast cells. Mastocytosis is a more common clinical phenomenon in the cat than in the dog. The CBC may also give evidence of gastrointestinal bleeding or gastrointestinal perforation. In general, mastocytosis associated with primary cutaneous tumors is more easily detected by examination of the buffy coat or bone marrow than by examination of peripheral blood. Care must be exercised in interpreting buffy coats since mastocytosis has been reported in a variety of acute inflammatory diseases of the dog including parvovirus infections. Peripheral mast cell counts may be high in cats with mastocytosis and have accounted for up to 25% of the total white cell count. Buffy coat smears of blood samples may be examined microscopically for the presence of mast cells but bone marrow smears appear to be more sensitive and are not associated with as many false positives. Bone marrow evaluations should be performed in animals with mast cell tumors. Recent studies have demonstrated that normal dogs have less than 1 mast cell per 1,000 cells in the bone marrow. Veterinary investigators suggest mast cells in greater concentrations than 10/1,000 cells is abnormal. Any animal patient with mast cell tumors should be carefully examined for lymphadenopathy in areas draining the primary tumor. Enlarged lymph nodes should be examined for the presence of mast cells as evidence of tumor spread. Such findings have important implications with regard to therapeutic strategies.

Therapy
Surgical considerations include wide surgical margins with at least 3cm of normal looking skin around the tumor should be removed when possible. The 3cm recommendation is a guideline and might not be feasible when the tumor is located on the face, lower limbs or in the inguinal region. It should be remembered that most mast cells extend laterally to adjacent tissue rather than deep into underlying muscles. All excised

tumor should be examined histologically for the completeness of excision. Extension of the tumor beyond the surgical borders should prompt either wider excision or radiation therapy of the tumor bed. Approximately 50% of the mast cell tumors recur at the surgical site traditionally. Histologic grade is an important factor in predicting recurrence at the surgical site. Those that are undifferentiated tend to have a higher recurrence rate. Cats with mast cell tumors with splenic involvement often will benefit from splenectomy. Survival times of 10 weeks to 30 months have been reported following splenectomy, even in patients with evidence of sytemic mastocytosis.

Seguin et al (J Am Vet Med Assoc 218[7]:1120-1123 2001) evaluated 60 mast cell tumors that were surgically excised with cleanmarings in 55 dogs were included. Median follow-up time was 540 days. Three mast cell tumors recurred locally; median time to local recurrence was 62 days. Six dogs developed another mast cell tumor at a different cutaneous location; median time to a different location was 240 days. Three dogs developed metastases; median time to metastasis was 158 days. The authors concluded that additional local treatment may not be required after complete excision of grade-II mast cell tumors and that most dogs do not require systemic treatment.

Glucocorticoid therapy frequently results in partial or occasionally complete remissions in canine mast cell tumors. However, cats appear to be less responsive to glucocorticoid treatment. The effect of glucocorticoids is to reduce markedly the number of mast cells in the mast cell tumor. The exact mechanism by which glucocorticoids exert their cytotoxic effects on mast cell tumors is unknown although it may be similar to the effects of glucocorticoids on lymphocytes. The susceptibility of mast cell tumors might depend on the presence of intracytoplasmic glucocorticoid receptor sites. Glucocorticoid receptor sites have recently been found in the cytoplasm of canine mast cell tumors. Although sex steroid receptors for progesterone and estrogen have been recently described in dogs with canine mast cell tumors, the role of sex steroids in the treatment of canine mast cell tumors has yet to be investigated. The type of glucocorticoids administered appears to be unimportant but it has been suggested that intralesional corticosteroid may be more effective than systemic therapy for local disease. Fewer Cushingoid side effects have been seen with short-acting glucocorticoids such as prednisone or prednisolone when used in the dog. The usual dose of prednisone is .5 mg/kg orally administered once daily and that of triamcinolone is 1 mg for every cm diameter of tumor intralesionally, administered every two weeks. Remission times are usually 10 to 20 weeks. Dogs that are tumor free after six months however have a low incidence of recurrence and therefore therapy is usually discontinued at this time. Tumor resistance may be caused by the emergence of mast cells with fewer or ineffective glucocorticoid receptors. Survival data based on histologic grade correlates with various chemotherapeutic regimens has not been reported.

Vinblastine and prednison or CCNU appear to be the most favored drug protocols for the treatment of mast cell tumors. The use of these drugs is always with surgery.

Rassnick and colleagues (J Vet Intern Med 13[6]:601-605 1999) evaluated the efficacy and toxicity of CCNU in 23 dogs with measurable mast cell tumors (MCT). Response could be evaluated in 19 dogs. Eight of the 19 dogs (42%) had a measurable response to CCNU. One dog had a durable complete response for 440 days. Seven dogs had a partial response for a median and mean duration of 77 days and 109 days, respectively (range, 21-254 days). The acute dose-limiting toxicity was neutropenia 7 days after administration of CCNU. Thamm et al (J Vet Intern Med 13[5]:491-497 1999) evaluated 41 dogs with mast cell tumors treated with oral prednisone and vinblastine both in the adjuvant setting and in dogs with gross disease. Adverse effects were noted in 20% of the patients, usually after the 1st dosage. Median survival time (MST) for the entire patient population was not reached with a median follow-up of 573 days; however, the MST for dogs with grade 111 MCT was 331 days, with 45% of dogs alive at 1 and 2 years. Ancillary drug therapy is important with canine mast cells. Animals with mastocytosis or palpable mast cell disease should receive H2 antagonists. Cimetidine (Tagamet) reduced gastric acid reduction by competitive inhibition of the action of histamine on H2 receptors of the gastric parietal cells. Ranitidine (Zantac, Glasco? Inc, Fort Lauderdale, FL), a newer H2 antagonist that requires less frequent ad-
administration, is in some clinics. The objective of the therapy is to prevent gastrointestinal ulceration associated with elevated levels of histamine and to treat ulcers already present. Some new evidence indicates that cimetidine may also alter the immune response to this tumor as well as activation of certain alkylating agents. Dogs and cats with evidence of gastrointestinal ulceration and bleeding might also benefit from sucralfate (Karafate, Marion Labs Inc, Kansas City, MO) therapy. Sucralfate reacts with stomach acid to form a highly condensed viscous adherent paste-like substance that binds to the surface of both gastric and duodenal ulcer sites. The barrier formed at the ulcer site protects the ulcer from potential ulcerogenic properties of pepsin, acid and bile allowing the ulcer to heal. Because sucralfate interferes with absorption of cimetidine, these two drugs should be given at least two hours apart. The usual dosage of sucralfate is 1 gm given orally. H₁ antagonists such as benadryl should be used along with cimetidine prior to and following surgical removal of canine mast cell tumors to help prevent the negative effects of local histamine release on fibroplasia wound healing. H₁ antagonists also should be used with cryosurgery or hyperthermia therapy. Another recommended ancillary medication is an antiserotonin agent (cyproheptidine). The use of this drug is controversial since serotonin has only been identified in rat and mouse mast cells and definitive studies in the dog and cat are lacking. The use of drugs that stabilize mast cells (sodium chromoglycate) have been described in the treatment of human patients with mastocytosis but not in animals.

Radiotherapy has been used alone or in combination with other treatment modalities. Most reports indicate remission rates of 48 to 77%. Doses of 3,000 to 4,000 rads were used in these studies. Total radiation therapy is usually fractionated and delivered over a period of three to four weeks. The use of radiotherapy is somewhat expensive and is confined to referral centers. Mast cell tumors in regional lymph nodes and bone marrow appear to be more resistant to the effects of radiotherapy than those confined to the skin. Response of mast cell tumors to radiation therapy may correlate to histologic grade but has not been studied.

References Available Upon Request
INJECTION-SITE AND OTHER SOFT TISSUE SARCOMAS
NEW PROTOCOLS FOR 2010

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Fine needle aspiration of an injection site sarcoma may reveal a spindle cell sarcoma or mesenchymal tumor. The exact histologic diagnosis matters less than the classification as a soft tissue sarcoma. Most oncologists recommend an initial needle or incisional biopsy rather than an attempt at excisional biopsy. This is because an aggressive first surgery or presurgical radiation therapy will provide a better outcome than will treating a recurrence.

Treatment
Surgical excision has been the principal treatment modality for soft tissue sarcomas. Due to the extensive infiltration and invasion of surrounding normal tissue, it is necessary to resect a wide and deep (more than 2 cm) margin of normal tissue in all surgical planes around the palpable tumor. While this is often possible in larger species such as dogs and humans, it is rarely possible in cats, particularly following an initial unsuccessful attempt. Exceptions to this would be tumors on a distal limb or other extremity that can be amputated. For this reason the first attempt at surgical removal should be the definitive one, and wide surgical margins that include bone, muscle, and other structures should be obtained. The aim should be to remove the tissue en bloc without incising tumor tissue itself.

Because aggressive surgeries require specific surgical skills and adequate planning, the preferred approach is an incisional or Tru-cut needle biopsy prior to consulting with an experienced surgeon and/or radiation oncologist. As stated earlier, pretreatment staging should include a CT scan to more clearly define the tumor margins and areas of infiltration.

In a study of 84 cats surgically treated for soft tissue sarcoma, 60 cats (70%) had tumor recurrence an average of 3.5 months later. Tumors recurred as soon as 2.5 weeks and as long as 1.5 years after surgery. Only 34 of the 60 cats had a second surgery; the other 26 were euthanized. Of these 34 cats, 27 (80%) had a second recurrence and 12 of these were euthanized. Of the 84 cats originally treated, only 9 cats became disease free and only 4 of those were disease free longer than 18 months. A similar recurrence rate of over 80% was seen in another study in which the median tumor free period following surgical excision was 4 months. Only 10% of 61 cats were tumor free a year after surgery in another study; these cats had all been treated by wide excision or amputation.

Tumors that involve the limb often recur after an attempted local excision, but the likelihood of long-term control following amputation is high. Similarly, tumors of the pinnae or even nictitans may be removed with complete surgical margins. For more extensive limb tumors that approach the pelvis, a hemipelvectomy may be required; if complete margins cannot be obtained, a rapid recurrence should be expected. Procedures that are less aggressive than amputation, such as scapulectomy, may leave tumor cells and lead to recurrence.

Aggressive surgical excisions in other areas may lead to long-term tumor control even after other methods have failed. However, the first surgery should be considered definitive rather than relying on a second or third surgery for salvage. Wide resection on the chest wall or flank may require rib or body wall removal and the use of propylene mesh. Even with extensive surgery and reconstructive attempts, recurrences may still occur.

Some prognostic factors following surgery were explored in one study of 35 cats. Tumor location did not seem to affect whether a tumor recurred. However, cats that had a surgery with histologically complete margins had a median tumor-free survival of more than 16 months. Surgeries that had “dirty” margins led to tumor recurrence a median of 4 months after surgery, which is consistent with other studies cited above.
and a median survival of only 9 months. In addition, cats that had not been treated with surgery prior to the definitive resection (i.e., this was their first surgery) had a median disease free interval of longer than 16 months. In comparison, cats that had undergone one or more attempts at excision prior to definitive surgery had a median disease free interval of only 5 months and a median survival of 13 months.\textsuperscript{25}

**Radiation Therapy**

Most early studies report very little efficacy for radiation therapy in reducing recurrence rates for soft tissue sarcoma. A combination of minimal surgical excision and low doses of radiation therapy probably contributed to the apparent ineffectiveness.\textsuperscript{35,37} More recent studies suggest that the treatment of choice for this tumor type is aggressive surgery in combination with high doses of pre- or postoperative radiation therapy.

In two studies, cats were treated with brachytherapy using iridium-192 (\textsuperscript{192}Ir) implants after surgery. The dose in one study was 60 Gy\textsuperscript{24} but was not provided in the other.\textsuperscript{31} The recurrence rate in one study was 70\% (11 of 16 cats), with a median survival of 8 months\textsuperscript{24}; in the other group of cats, 50\% of tumors recurred and the median disease free interval was 12.5 months,\textsuperscript{31} which was better than for cats in the same study treated with surgery alone (discussed previously).

Selection of cats with poor prognostic factors may have influenced outcome in another study in which \textsuperscript{192}Ir brachytherapy or cobalt-60 teletherapy resulted in a median disease free interval of only 4.5 months\textsuperscript{25}. Information about radiation doses was not provided.

In a study of 31 cats treated with orthovoltage radiation to a dose of 51 to 60 Gy following incomplete surgical excision, median tumor free interval was 18 months and median survival was 22 months\textsuperscript{38}. Acute toxicities were mild, but systemic toxicities led to the euthanasia of 6 cats, 2 due to pneumonitis and 4 due to renal failure. These toxicities occurred because of radiation of underlying structures when injection site sarcomas of the interscapular area or the flank were treated.

High-dose radiation therapy (57 Gy) was used to treat 25 cats with soft tissue sarcomas. An electron beam was used to deliver the radiation to most cats; this method delivers radiation to superficial tissues while sparing the underlying normal tissue, thereby avoiding toxicity. Median survival for all cats was 700 days\textsuperscript{39}. In this small group of cats, the administration of doxorubicin chemotherapy was not associated with longer survival, but further studies are warranted as other anecdotal experience indicates that chemotherapy may improve survival. Increasing numbers of surgeries prior to radiation was not associated with decreased survival.

Sarcoma recurrence after radiation may be due to improved tumor cell survival along the relatively hypoxic surgical scar. Hypoxia reduces the effectiveness of radiation therapy. One study investigated the efficacy of presurgical radiation therapy to an area surrounding the tumor followed by wide surgical excision\textsuperscript{26}. The tumor recurred in 11 of 33 cats, and 8 of 33 developed metastases (4 also experienced tumor recurrences). The tumor was more likely to recur quickly in cats in which surgical excision was incomplete after radiation therapy. Tumors recurred in the 5 cats with incomplete resection a median of 3.5 months after surgery, while those with complete resection were tumor free a median of 23 months after surgery.\textsuperscript{26} Tumor volume at the time of radiation did not influence recurrence or survival, implying that even large tumors could be treated in this manner. Some cats developed transient pneumonitis, and wound dehiscence occurred and was repaired in 4 of 33 cats. It appears that radiation may act to "sterilize" the margins of a tumor, enabling a more effective surgical excision. Radiation therapy followed by aggressive surgery may be the treatment of choice for feline soft tissue sarcomas.

**Chemotherapy**

There is very little information regarding chemotherapy in the treatment of soft tissue sarcomas in cats. The reportedly low metastatic rate has meant that chemotherapy is rarely used in an adjuvant setting. The higher metastatic rates now reported and the reduction in the rate of local recurrences following the use of
surgery and radiation therapy indicate that chemotherapy may have an increasing role in the management of soft tissue sarcomas in cats.

Drugs that anecdotally appear to have no efficacy are vincristine, methotrexate, and cyclophosphamide.\textsuperscript{19,27,35} Doxorubicin has been used with apparent success to treat cats with local recurrence after surgery,\textsuperscript{40} although other studies indicated no response to treatment.\textsuperscript{35} Mitoxantrone did not influence tumor recurrence in a cat with soft tissue sarcoma.\textsuperscript{33} The use of carboplatin chemotherapy did not seem to improve survival rates in another study,\textsuperscript{25} although some oncologists believe that this drug is helpful. Similarly, studies are currently in progress to investigate the efficacy of ifosfamide,\textsuperscript{4} a drug that is very effective against soft-tissue sarcomas in humans.

In an investigation of a novel approach to treat recurrent sarcomas, IV bleomycin (0.5 mg/kg) was combined with electric stimulation of sarcoma and immunotherapy.\textsuperscript{41} Tumor regression was seen in only one cat, but survival appeared to be prolonged (5 months) compared with untreated cats (0.7 months).

In another study, doxorubicin, mitoxantrone, or carboplatin was administered to seven cats in which sarcoma recurred after surgery and radiation\textsuperscript{26}. The median survival for these cats was 3.5 months, and two cats lived 10 to 22 months after treatment. Doxorubicin and carboplatin need to be further evaluated in the treatment of soft tissue sarcomas in cats, particularly as an adjuvant to surgery and radiation therapy.

\textbf{Immunotherapy}

Acemannan is another nonspecific immunomodulator that has been evaluated in a small number of cats with fibrosarcoma. Cats were injected with 2 mg/kg intralesionally weekly for 6 weeks prior to surgery and megavoltage radiation therapy (60 Gy). The cats then received 1 mg/kg intraperitoneally weekly for 6 weeks and then monthly for 1 year. Of four cats so treated, one had tumor recurrence 8 months after surgery but the other three had no recurrence for 14 to 19 months after surgery\textsuperscript{42}. The true contribution of acemannan to survival in these cats is difficult to evaluate.

Tenogeneic cells (Vero hIL-2) that secrete human recombinant interleukin-2 (hIL-2) were infiltrated around the tumor at the time of surgical resection and implantation of \textsuperscript{192}Ir seeds for brachyradiotherapy.\textsuperscript{24} This infiltration was repeated 5 days later and another five times over the next 2 months. Of 16 cats treated by this protocol, two had local recurrence and three had metastases, with an overall median survival of 16 months. In comparison, 11 of 16 cats that did not receive Vero hIL-2 cells had tumor recurrence and a median survival of 8 months.

References Available Upon Request
UNDERSTANDING COMPASSION FATIGUE

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COST OF CARING: COMPASSION FATIGUE
Providing care from both the heart and science requires the ability to express empathy. However, the empathetic response can lead to compassion fatigue\(^1\)\(^\text{–}^\text{10}\). When we find ourselves giving without adequately replenishing ourselves, it is only a matter of time before we experience a shortage of compassion and a sense of fatigue. Simply put, compassion fatigue occurs when we have depleted our emotional resources as we care for others. Compassion fatigue is not a reflection of our character, professionalism, or skill level but is directly related to our willingness to be emotionally engaged with another being that is hurting. Compassion fatigue has or will strike every member of a caring health care team. The phenomenon is not limited to veterinary professionals but occurs in physicians, nurses, firemen, combat medics, and the like\(^1\)\(^\text{–}^\text{10}\). Compassion fatigue is why many caring, compassionate veterinarians, nurses, receptionists, and other caregivers leave the profession. The desire to leave the profession can happen at any age but seems to occur most often when a person is at the height of their professional career as a veterinary caregiver. Awareness and understanding of this condition is essential in its prevention and treatment and in maintaining the health of the team.

COMPASSION FATIGUE VERSUS BURNOUT
Compassion fatigue is perhaps the greatest threat to the health and happiness of any member of the veterinary health care team. Although compassion fatigue is considered to be a form of burnout,\(^1\) the two conditions are uniquely different; however, they have many of the same clinical signs. The conditions must be distinguished because they have uniquely different causes and paths to recovery.

Compassion fatigue is not predictable; it results when one’s internal emotional resources are depleted.\(^1\) Sometimes a member of the veterinary health care team provides so much care and compassion to clients who are experiencing an emotional moment, such as when a diagnosis of cancer is being discussed, that they find themselves depleted. Compassion fatigue is triggered by one or more emotionally charged events (called critical incidents) at a time when one’s emotional resources are exhausted. Members of the veterinary health care team often experience critical incidents when other people become emotionally distressed. An extreme example is the experiences of those who identified or provided care to people or animals killed or injured in the September 11 World Trade Center disaster or to the search-and-rescue dogs involved in the recovery efforts; more commonplace examples include performing and experiencing euthanasia, helping an owner through the loss of a pet informing a caregiver that his or her pet has cancer providing terminal patient care, and discussing the financial affordability of care.\(^\text{11}^\text{–10}\) Each member of the veterinary health care team must be considered unique, and the way each person deals with critical incidents differs, often based on his or her individual experiences, beliefs, and values. In addition, compassion fatigue may intensify the emotional and physical symptoms in team members who are already experiencing burnout, and burnout can likewise intensify compassion fatigue.

The following feelings or thoughts are sometimes associated with compassion fatigue:\(^\text{11}^\text{–10}\)

- Avoidance of thoughts, feelings, activities, or situations that remind one of a frightening experience.
- Feeling estranged from other members of the veterinary health care team.
- Difficulty falling or staying asleep, especially when reliving memories or experiences in one’s mind.
- Outbursts of anger or irritability with little provocation.
- Flashbacks connected to clients or patients.
• Needing to "work through" a traumatic experience associated with a patient or client to get over the events, feelings or experiences.
• Feeling that there is no one to talk with about highly stressful experiences.
• Experiencing intrusive thoughts of a critical incident, especially difficult patients or clients. Sudden, involuntarily recall of a frightening critical incident while working with a client, patient, or the patient's family.
• Preoccupation with more than one patient, client, and the rest of the family.
• Loss of sleep over a patient, client, and the rest of the family.
• Feeling less concerned about the well-being of patients, clients, and their families.
• Feeling trapped by one's work as a member of the veterinary healthcare team.
• Feeling a sense of hopelessness associated with working with patients, clients, and their families.
• Feeling "on edge" because of one's working with certain patients, clients, and their families.
• Desire to avoid working with some patients, clients, and their families.
• Feeling disliked by clients and their families.
• Feeling weak, tired, or rundown because of one's role as a member of the veterinary healthcare team.
• Feeling depressed because of one's role as a member of the veterinary health care team.
• Feeling unsuccessful at separating work and personal life.
• Feeling little compassion toward coworkers.
• Feeling like one works more for the money than for personal fulfillment.
• Feeling like one is a failure rather than a successful member of the veterinary healthcare team.
• Feeling that one is achieving one's life goals.

Suggest revising list as follows:
• Avoidance of thoughts, feelings, activities, or situations that remind one of a frightening experience.
• Feeling estranged from other members of the veterinary health care team or that there is no one to talk to.
• Difficulty falling or staying asleep, especially when loss of sleep is related to memories or experiences being played over and over in one's mind.
• Outbursts of anger or irritability with little provocation.
• Needing to "work through" a traumatic experience associated with a patient or client to get over the event.
• Being preoccupied with a previous critical incident or with specific patients or their caregivers.
• Loss of concern about the well-being of coworkers, patients, and caregivers.
• Feeling trapped, hopeless, edgy, weak, tired, rundown, or depressed.
• Desire to avoid certain patients and their caregivers.
• Feeling disliked by clients and their families.
• Inability to separate work and personal life.
• Feeling like one works more for the money than for personal fulfillment.
• Feelings of failure.
Burnout is predictable and very common. It is not necessarily associated with the exhaustion of emotion or empathy but rather is a state of mental and/or physical exhaustion caused by excessive and prolonged stress. Two major causes of burnout are bureaucratic atmospheres and overwork. Burnout is not associated with the aforementioned critical incidents, but it is predictably associated with the stress of overwork, repetition, or the bureaucracy of seemingly less-important tasks, such as paying bills, reviewing reports, and endless paperwork without apparent value or worth.

**PREVENTION AND THERAPY**

So how do people provide compassionate care, meet the medical and nonmedical needs of caregivers and patients, and stay true to what brought them to a caring profession without experiencing fatiguing and potentially devastating consequences? First, we must acknowledge that we, as a profession, by the very nature of what we do and who we are, are at risk for compassion fatigue. Simply by acknowledging the condition and accepting that we are vulnerable, we can see the potential hazards, recognize likely inciting situations, and hopefully prevent devastating outcomes. We also must work with all staff members to experience and then celebrate the sense of achievement in the work in which we are involved. On a daily basis, veterinary healthcare teams intervene in the lives of clients and their pets to provide high-quality medical, surgical, and preventive care while offering emotional support and validating the bond that brought those pets and people to our offices. This is compassionate care; to accomplish it well requires a great deal of emotional energy from every team member. In this manner, we provide for the needs of our patients and caregivers. The act of caring is the epitome of success in our profession, regardless of the emotional nature of the situation or the medical outcome. Although compassion fatigue cannot be completely avoided, there are many strategies to help team members mitigate its impact.

**CONCLUSION**

When we employ compassion in caring for our patients, we must do so by expressing empathy, yet the act of empathizing with our clients can lead to compassion fatigue. When any member of the veterinary healthcare team finds themselves giving without allowing themselves to be replenished emotionally, it is only a matter of time before there will be a shortage of compassion. Simply put, compassionate fatigue results when there is a depletion of internal emotional resources as we care and provide compassion for others. This depletion is not a reflection of the character, professionalism, or skill level of the team member. Rather, one’s strength and willingness to be emotionally engaged with another being is affected. All members of the veterinary healthcare team joined the profession to provide care, which comes from both their minds (through medical and surgical skills) and their hearts (by supporting and providing for the emotional needs of caregivers). The success of veterinary care stems from providing this level of compassionate care and supporting the individuals who provide it. By appreciating the reality of compassion fatigue and providing mechanisms to mitigate its effects, a practice can thrive by providing the finest in compassionate care.

**Key Points in Mitigating Compassion Fatigue**

- Educate the entire veterinary healthcare team about compassionate fatigue and its consequences
- Establish weekly debriefing sessions where the entire staff can discuss needs, concerns, and cases that weigh on them
- Establish resources about compassion fatigue, including a library, for team members
- Use relaxation techniques both within the hospital and outside the workplace.
- Take breaks during the day
- Define and preserve a sanctuary or comfort room where team members can be alone to meditate or relax
• Inform all team members about every case and allow them to have adequate closure at the end of any patient’s life

• Whenever possible, work out sabbatical or continuing education opportunities for personal reward and growth

• Teach team members how to set limits and boundaries on interactions with clients and patients, especially when especially susceptible to compassion fatigue

• Employ humor when appropriate

• Find a friend or colleague who understands and appreciates the experience of providing empathy and compassion, and share with that person

• Eat right and exercise

• Get in touch with nature and the outdoors

• Interact with children and animals

REFERENCES


Clients arrive at our clinics and hospitals frightened about the possible loss of their pet’s life to the disease that threatens their pet. Cancer is perhaps their greatest fear. In their minds, the disease is in effect a one-word death sentence. Sadly, many members of the veterinary healthcare team, including some clinicians and nurses, believe that many diseases requiring specialty care is a one-way trip to death. In reality, that is just not true. In short, each and every patient can and should be helped.

Each member of the veterinary healthcare team plays a critical role in providing compassionate care for seriously ill patients. Before compassionate care can begin with specific therapeutics can be initiated, three steps of advanced care need to be undertaken. The first is to dispel the myths that blind us to the possibilities of providing exceptional care for the patient. The second is to build a team to care for the people and the patient with equal focus. After these first steps have been accomplished, the third step—true compassionate care—can begin.

**STEP ONE: DISPEL THE MYTHS**

Regardless of our culture, nationality, or religion, most of us are indoctrinated from an early age that advanced illness and its therapy is horrible. Therefore, clients, nursing staff, and even veterinarians often perceive diseases such as cancer and its therapy as something dark and hopeless. The truth is that most of the fears and misconceptions about advanced illness and its care are wrong or out of proportion. These myths serve as barriers that often preclude early, decisive therapy. The myths envelop the disease in a cloud that obscures true understanding and vision and blocks out all hope. Such surgical procedures as laparoscopy, thoracoscopy, amputation, chest wall resection, hemipelvectomy and maxillectomy are perceived as traumatic to patient, client, and healthcare providers. We imagine chemotherapy protocols as being inevitably linked with horrible side effects. We fear that therapy will be financially devastating and physically debilitating with little benefit for client or patient. In essence, we are often frozen in indecision as we, our team, and our clients wonder, “Is it all worth it?”

The initial steps in providing compassionate care are to first identify and then dispel the misconceptions and myths existing within all team members. This can be achieved by erasing the myths and misconceptions from the heart of each member of the veterinary healthcare team, including client support services representatives, nurses, veterinarians, and other allied team members. We all drag in our own misconceptions, prejudgments, and preconceived notions that can stifle the hope in care. The consequence of not dispelling these myths is that the patient and caregiver are hurt by shortsighted or ineffective care.

Few would ever debate that the goal of most veterinary healthcare teams is to enhance, maintain, or improve quality of life. True, small sacrifices in quality sometimes might have to be made, but these sacrifices must be temporary and made only to gain significant, additional length of life. We must assure our staff members, the caregiver, and ourselves that quality time during therapy is a reality, and we must always work to maintain that quality throughout treatment. It is then that hope begins to supplant the myths and misconceptions.

**STEP TWO: ESTABLISH THE TEAM**

The second step of compassionate care, establishing the team, is a crucial move toward providing care from the heart as well as the science. A dedicated, trained, cohesive, caring veterinary healthcare team is essential to adequately care for patients and their caregivers and to fight the disease. All members of the staff, including client support services, nurses, and other staff, must understand that they play a vital role in caring for patients and the people who bring them to us. Everyone must be united in focus, philosophy, and the ultimate goal of enhancing and improving the quality of life for the patient while supporting each other. Each veterinarian, nurse, and receptionist within a facility must be prepared to accept a role as part of the
team. This team must then reach out beyond the walls of the practice to specialists and consultants such as pathologists, pharmacists, and allied specialists whenever appropriate. Finally, the most vital link to the team is the caregivers themselves. They must be incorporated into this team through education, support, and empowerment to provide ongoing day-to-day care and assessment. Without their input, attention, care, and ongoing assessment, care of the patient cannot be optimal.

In our society, advanced illness, no matter who it affects, is associated with many negative feelings. The presence of these feelings in staff and colleagues often results in a mental roadblock to hope, care, and cure. It is imperative that these feelings are acknowledged by everyone on the veterinary healthcare team. The treatment of advanced disease is not easy. It requires total dedication of all staff involved and often can be emotionally taxing. Preconceived notions about the disease and the toxicity and efficacy of therapy must be acknowledged. It is vital for the team members to openly discuss these matters and to provide realistic information about disease and its therapy. Once the healthcare team overcomes these misconceptions, client education is possible in a comprehensive, team-based manner. As mentioned, all involved must overcome their biases and ingrained feelings about the disease before rationally approaching disease and its cure or patient support and care. Ongoing support, information, and care must be provided to all members of the veterinary healthcare team to prevent burnout and compassion fatigue and to retain individuals who will provide quality, compassionate care on a continuous basis. After the misconceptions have been replaced with realities and options for care, the healthcare team and caregiver can begin to make decisions and provide the necessary care for the patient.

Care of the seriously ill patient requires unique skills, knowledge, drugs, procedures, and philosophies. The healthcare team must dedicate itself to an aggressive continuing education program to maximize care for their canine patients. Veterinary patients usually have a dynamic course to their disease and thus ongoing communication is essential to maximize care for both the patient and the caregiver. Communication during hospitalization should be a daily procedure, but ongoing communication by multiple members of the veterinary healthcare team can greatly improve the patient’s quality of care by providing the veterinarian with ongoing reassessments and progress reports. These and other policies and procedures regarding patient care should be established long in advance and applied in a team approach to maximize seamless care for each patient and build the team.

The caregiver is perhaps the most vital and often most overlooked member of the healthcare team. Once their misconceptions have been dispelled and they are able to make rational, educated decisions regarding patient care, caregivers must know that they are empowered and necessary members of the team. Quality of life assessments, administration of medication, and daily or even hourly patient monitoring can be appropriately accomplished only by the clients and are most effective when clients are empowered and educated and know that they are a vital extension of the healthcare team at home. Emergency preparedness as well as prevention is only possible with an informed, alerted caregiver. Patient care takes a tremendous positive leap forward when 24-hour outpatient care as provided by the caregiver. In addition, including caregivers as members of the healthcare team gives them an active responsibility and restores the bond between them and their beloved pet.

The following are a few examples of ways to form, empower, and enhance the veterinary healthcare team:

- Identify, reward, and promote only the best, most compassionate people.
- Openly celebrate, review, and revise mission statement and goals written by the team.
- Ensure the team participates in all interviews and assists in decisions to hire new applicants.
- Share and celebrate when a team member is recognized by clients or others.
- Meet at least weekly to listen to team members: Value their input, feelings, and thoughts.
- Introduce clients to the team, including nurses and receptionists, during the first visit.
STEP THREE: DELIVERING THE CARE¹⁻⁸

Once the caring team is forged to include at least the veterinarian, veterinary healthcare staff, and caregiver and the misconceptions of diseases are shed, the emotional component of the disease is defeated. Stripped of its emotional cloud, the disease or disorder is attackable, diagnosable, treatable, manageable, and, in many cases, curable. In fact, it is the most curable of all chronic diseases. At this point, the team is prepared for the third step, delivering the care.

Compassionate care is the single most important term in veterinary medicine and is imperative in care as well. The first phase of compassionate care is defining and describing the disease and the health status of the patient through diagnostics and staging. The second phase is providing caring support by responding to the pet’s needs and client’s concerns through the commandments of care. The final phase is providing direct therapy for the underlying disease using the appropriate tools, such as surgery or chemotherapy or radiation therapy. Each step of the process of compassionate care is interdependent on the others.

The average caregiver of a patient with cancer or other serious illness or problem will visit your clinic frequently over the next year, and therefore a bond of trust must be developed between the veterinary healthcare team and the client. This bond must begin with communication, which requires time and an open, honest discussion with all parties involved. Ideally, sufficient time should be set aside during the first visit to discuss the pet’s condition, prognosis, and options for therapy. It is helpful for the client to see your facility and meet any involved staff. During this initial office visit, information should be provided in oral and written form. Preprinted, plain language information sheets are essential and should describe your practice, the patient’s disease, and the treatments that may be used. The client may be encouraged to take notes and, ask questions, or the veterinarian can take notes during the discussion and give them to the client. A summary of all major discussions with the caregiver should be either taped or written so that a copy is available for the record and the client. The members of the veterinary healthcare team should realize that most clients are overwhelmed by emotion and are not able to make a rational decision or even completely absorb or comprehend the information provided to them during the first visit. Therefore, the written or recorded information and a follow-up telephone call or personal conference is of tremendous value. Clients should not be forced to make quick or immediate decisions but should be allowed to think about the options available for their dog. By providing the client with an accurate prognosis, information regarding quality of life and duration of therapy, and treatment choices, you restore a sense of control and power to the client. When discussing the option of euthanasia, information about the philosophy, procedures and aftercare of the animal’s body should be provided in both oral and written forms. The disease by itself can engender many feelings of loss and bereavement even though treatment is a viable option and the patient’s prognosis may not be guarded. However, the emotional and physical impact of pet loss and bereavement should be discussed at some point during the care of the canine cancer patient.

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TOP 10 SECRETS FOR TREATING CATS WITH CANCER

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FELINE CUTANEOUS SQUAMOUS-CELL CARCINOMA

Incidence, Signalment, and Etiology
Squamous-cell carcinomas occur mostly in adult cats especially around the head and neck, and particularly the ears, nose, and eyelids of cats lacking cutaneous pigment. In these locations the tumor is sunlight-induced in the same manner as described for dogs. Siamese cats appear less likely to develop cutaneous squamous-cell carcinoma than other felidae. In a series of 90 cats with nasal planum SCC, 66 cats (73%) had some white skin or hair color. (2)

Clinical Presentation and History
On the face and ears of cats lacking cutaneous pigment, there is a clear clinical progression of these lesions. Initially the area is erythematous and may have a waxy, dark crust that is easily removed. These lesions appear histologically as either actinic keratosis (precancer) or as carcinoma in situ (non-invasive cancer). Ulceration progresses if the lesion is untreated, with subsequent invasion and destruction of surrounding structures by the tumor.

Staging and Diagnosis
Actinically induced cutaneous squamous-cell carcinoma in cats rarely, if ever, metastasizes. In a series of 90 cats with nasal planum SCC, 6 were found to have metastasis to mandibular lymph nodes and 1 to lungs. However, this often occurred late in the course of disease. Regional lymph nodes should be palpated, and fine-needle aspiration or biopsy performed if they are enlarged. Thoracic radiographs are not usually indicated for this tumor in cats. In a study of 90 cats, 17% were found to be in stage T1, 31% as T2, 37% as T3, and 15% as T4.

Prognostic Factors
Tumor proliferative fraction, as measured by immunohistochemical detection of Proliferating Cell Nuclear Antigen (PCNA) was found to be prognostic for control of nasal planum SCC in cats treated by radiotherapy. In addition, tumor stage was found to be prognostic for tumor control. Cats with smaller tumors (T1) had not reached a median survival (i.e., fewer than half of the cats had tumor recurrence) but the average was 53 months while larger tumors (T3) were controlled for a median of 9 months.

Treatment
While the synthetic retinoid 13-cis-retinoic acid has not been shown to reverse pre-neoplastic changes for SCC in cats, newer retinoids such as etretinate have not yet been evaluated in this species. In view of the efficacy of etretinate in dogs, it would seem logical that these newer retinoids may also show efficacy for feline preneoplastic squamous-cell carcinoma.

Resection of the pinna for aural SCC is effective in the majority of cats if adequate resection is achieved. Essentially the entire pinna should be removed. However, these tumors may recur locally, as can SCC of the eyelids and nasal planum.

Actinically induced SCC in the cat is very sensitive to radiation therapy. Precancerous plaques and early lesions may be treated with brachytherapy radiation (e.g., strontium-90) at a single high dose. In a group of 25 cats treated with strontium-90, nearly 90% were free of tumor at one year with an average tumor-free period of 34 months.
Local current-field radiation hyperthermia (50°C for 30 seconds) was very effective in causing tumor regression in superficial SCC of cats. Of 19 cats with SCC, 13 (68%) had complete regression. Tumors that did not extend 2 mm or deeper in tissue responded best. Duration of response was observed for only 2 to 6 months.

For more advanced lesions, external-beam teletherapy produces long remissions. It should be remembered, however, that the cat is still susceptible to acquiring new tumors from sunlight exposure, and its behavior should be appropriately modified. Preferably cats should be protected from sunlight exposure during the middle part of the day. Ninety cats with SCC of the nasal planum were treated with orthovoltage-radiation therapy to a dose of 40 Gray in 4-Gray fractions. The median control of tumors for these cats was 14 months. However, advanced tumor stage (i.e., larger tumors) affected outcome adversely (see above). Fifteen cats whose tumors recurred were re-irradiated successfully.

Cryotherapy has been recommended as a treatment for SCC of the face in cats. In one study, however, this modality was considerably less effective than either surgery or radiation therapy in achieving local tumor control. Eleven of 15 cats had local tumor recurrence within a median of 6 months after cryotherapy. We recently completed a study involving 87 cats with squamous cell carcinomas of the head that were treated with cryotherapy. The median disease free interval was 14 months. Cats that had lesion less than 1 cm in diameter had a much higher probability of having tumors controlled than those with larger tumors. Therefore, we recommend that tumors that are larger than 1 cm in diameter be treated with other procedures other than cryotherapy.

Reminder: Cisplatin can cause severe, fatal pulmonary edema and pleural effusion if administered systemically. Therefore, Photodynamic therapy has been shown to be quite effective in controlling this tumor in cats. In one study, 7 of 11 feline SCCs of the pinna or nasal planum completely resolved using a chloroaluminum sulfonated-phthalocyanine photosensitizer, and 5 of these responses lasted 44 weeks or longer. In another trial using aluminum phthalocyanine tetrasulfonate, long-term (3 to 18 months) responses were seen in 12 of 17 patients. However, toxicities, including 1 fatality, were more prevalent in this study. Paradoxically, cisplatin was used successfully in a unique collagen-matrix intralesional implant system to treat 118 feline squamous-cell carcinomas. In this study, 83% of cats had a > 50% reduction in tumor volume and 64% had complete resolution after 6 treatments. The lack of systemic toxicity seen in these cats was ascribed to the depot nature of the treatments and subsequent slow release of cisplatin. Sterilized sesame oil appears to function as a similar vehicle to collagen matrix, and may be used at a dose of 2 ml of sesame oil to 10 mg cisplatin in 1 ml of saline.

Mitoxantrone chemotherapy rarely brings objective response in feline oral SCC, but could be considered as an option for metastatic skin lesions. When combined with external-beam radiation therapy, mitoxantrone has been shown to control oral SCC for a median of 170 days, which is substantially longer than when either modality is used alone. Three cats with dermal SCC showed partial responses of short duration to bleomycin chemotherapy. Carboplatin is a new cisplatin-like compound that may be of value for treating metastatic squamous cell carcinoma. Alan Theon recently reported that when a carboplatin/sesame seed oil compound was used to treat cats with squamous cell carcinoma, the results were excellent.

**ORAL SQUAMOUS-CELL CARCINOMA IN CATS**

In contrast to the situation in dogs, oral SCC in cats is a highly aggressive disease that responds poorly to surgical treatment or to radiation therapy regardless of its location in the mouth. The longest control and survival rates have been obtained using a combination of radiation therapy and mitoxantrone chemotherapy.

The biggest problem for cats that have oral squamous cell carcinomas is that they do not maintain an adequate plane of nutrition. Appetite stimulants and very aromatic foods should be used whenever possible.
Care should be taken when feeding baby foods because they often contain onion powder that can cause heinz body anemia.

Carboplatin chemotherapy with or without radiation therapy appears to be resulting in good efficacy. The single most important prognostic feature appears to be bone involvement.

HEMANGIOMA-HEMANGIOSARCOMA IN CATS
Incidence, Signalment, and Etiology
Cutaneous hemangiomas and hemangiosarcomas are rare in cats, and occur mainly in older animals. This tumor is similar to squamous-cell carcinoma in that it is actinic, or sunlight-induced. Cutaneous hemangiosarcoma occurs commonly in cats from areas where actinically induced tumors are common\(^{(18)}\) (California, Missouri, Florida), but not in cats from the northeastern United States\(^{(18,19,20)}\)

Clinical Presentation and History
Feline hemangiomas appear as solitary tumors in the dermis and subcutis without any site predilection. In contrast, feline hemangiosarcomas may have a predilection for the head (ear tips, nasal planum) and also have a predilection for non-pigmented skin\(^{(17)}\). They are usually solitary.

Treatment
Surgical excision of cutaneous hemangioma usually has a good prognosis, although local recurrence following surgical excision of cutaneous hemangiosarcoma is frequent. Metastasis appears to be rare. It is therefore appropriate to treat this tumor as a soft-tissue sarcoma in cats, with aggressive initial surgery as the best therapeutic approach.

ROUND (DISCRETE) CELL TUMORS
This group of tumors may equally be called discrete cell tumors, and their appearance on cytologic preparations is that of clumps or individual cells that are round in appearance without obvious attachment to other cells. Round cell tumors include mast cell tumors, histiocytoma, lymphoma, plasmacytoma and transmissible venereal tumor.

MAST-CELL TUMORS
Introduction
Masses composed of mast cells can be either reactive or neoplastic, and this can pose certain problems in nomenclature. Mast-cell tumors are a very common neoplasm of the cat. Mast cells contain dark-staining granules that contain histamine, heparin, and other vasoactive amines. These characteristic granules make recognition of mast-cell tumors on cytology relatively simple. For further information please refer to the Mast Cell Tumor section.

MAST-CELL TUMORS IN CATS
Incidence, Signalment, and Etiology
Mast-cell tumors were the only cutaneous tumor diagnosed in cats younger than one year in one study\(^{(1)}\). In the same study, Siamese cats were three times more likely to develop cutaneous mast-cell tumors. Tumors in Siamese cats are usually subcutaneous and composed of "histiocytic" cells. These tumors may regress without therapy\(^{(24)}\).

Clinical Presentation and History
The most common cutaneous mast cell tumors in cats are single, firm, and circumscribed dermal nodules\(^{(25)}\). Appearance of multiple similar masses is the next most common presentation. These tumors are usually histologically well-differentiated and have a benign clinical course\(^{(2)}\). While most cutaneous MCTs in the cat are benign, in some studies, cutaneous tumors are associated with malignant disease evidenced by visceral involvement\(^{(25,26)}\). Lymphoreticular mast-cell tumors are often seen in cats, with
marked splenomegaly the most common finding. Diffuse cutaneous disease may occur with this form of MCT. Mastocytethemia and bone-marrow involvement are seen in many of these cats, and the presenting signs of vomiting and anorexia are presumably owing to tumor degranulation. Intestinal mast-cell tumors have been described in cats; they are always malignant.

Staging and Diagnosis
The suspicion of MCT in a chronically vomiting cat with marked splenomegaly can be confirmed by fine-needle aspirate of the spleen. Less frequent sites for lymphoreticular mast-cell tumors in cats are the mediastinum (with resultant pleural effusion) and lymph nodes. These cats often have high numbers of circulating mast cells as well as anemia and other cytopenias from bone-marrow infiltration and erythrophagocytosis by malignant cells.

Treatment
The treatment of choice for cutaneous MCT in cats is surgery; for solitary tumors, a good prognosis can usually be given. Some cats may develop multiple well-differentiated tumors, and these cats may be treated with multiple palliative surgeries or corticosteroids (1 mg/kg prednisone daily). For invasive or incompletely excised MCTs, radiation therapy appears to be a successful adjunct to surgery; however, data regarding tumor control and patient survival are not as well established as for dogs.

Mitoxantrone caused a partial response in a feline mast-cell tumor, but the drug has not been further evaluated for the treatment of this disease. (10)

The treatment of choice for lymphoreticular MCTs in cats is splenectomy; long-term survival occurs in many cats receiving no other therapy. Response to splenectomy seems greater than would be explained by simple tumor mass reduction, as hematologic and other organ involvement apparently resolve. It is possible that splenic suppressor-cell activity may be reduced after splenectomy allowing for some control by the cat’s immune system. For this reason the use of postoperative corticosteroids in these cats is controversial. (27,28)

MAMMARY ADENOCARCINOMA

Background
Owners frequently present their cat with mammary mass for a skin condition on the underside. When a cat with a mammary mass is presented, a malignancy must be considered. At least 70-90% of feline mammary tumors are malignant. Mammary tumors are known to be at least the third most frequently occurring tumor in the cat, following hematopoietic neoplasms and skin tumors. The incidence of mammary tumors in the cat is less than half that of dogs. Although there is no proven breed-associated predilection for mammary tumors, some investigators have suggested that domestic short-haired and Siamese cats have higher incidence rates than other cats. Siamese cats may have twice the risk of any other breed of developing mammary tumors.

Mammary neoplasia has been reported to occur in cats from nine months to 23 years of age, with a mean age of occurrence of 10 to 12 years. One study suggests that the disease occurs at an earlier age in Siamese cats and the incidence reaches a plateau at about nine years of age. The majority of affected cats are intact females; however the disease is occasionally seen in spayed females and rarely in male cats. More than 80% of the feline mammary tumors are histologically classified as adenocarcinomas. The frequency of diagnosis of the specific types of adenocarcinomas differs slightly among pathologists, but most agree that tubular, papillary, and solid carcinomas are the most common. The majority of the adenocarcinomas have a combination of tissue types in each tumor. Sarcomas, mucinous carcinomas, duct papillomas, adenosquamous carcinomas and adenomas are rarely seen.

Clinical Presentation and History
Cats with mammary tumors are often presented to the veterinarian five months after they were initially noted. Thus, the tumors are usually in an advanced state of development when they are handled clinically.
The mammary tumor often appears as a locally invasive mass that has metastasized frequently. The neoplasm may adhere to the overlying skin but rarely is adhered to the underlying abdominal wall. The tumor is usually firm and nodular. At least one-quarter of affected patients have ulcerated masses.

The infiltration of lymphatics may be clinically apparent as subcutaneous linear, beaded chains. Swelling due to tumor thrombosis or decreased vascular return can cause discomfort, edema, and a change in the temperature in the pelvic limbs. The involved nipples are red and swollen and may exude a tan or yellow fluid. The tumor can involve any or all mammary glands and is noted equally in the left and right sides. A slightly higher incidence has been noted in the cranial two glands by some investigators. More than half of the affected cats have multiple-gland involvement. These tumors can be associated with chronic mastitis, uterine disease, and other unrelated tumors, as well as anemia, osteoporosis, ascites, and leukocytosis.

**Staging and Diagnosis**

Before any diagnostic or therapeutic steps are taken, the health status of the cat must be fully assessed. A chemical screen, urinalysis, and a complete blood count should be done to identify any presurgical abnormalities. In several studies, more than 80% of the cats with a mammary malignancy had metastases to one or more of the following organs at the time of euthanasia; lymph nodes, lungs, pleura, liver, diaphragm, adrenal glands, and kidneys. Thoracic radiographs in both the right and left lateral and ventrodorsal planes should be made to search for pulmonary, lymph node, and pleural metastases. Mammary tumor pulmonary metastases appear radiographically as interstitial densities. They range from those that are faintly seen, to those that are several centimeters in diameter, to miliary pleural lesions that can produce significant effusion. Sternal lymphadenopathy is occasionally seen. Whenever regional lymph nodes are evaluable, they should be assessed by fine needle aspiration cytology or biopsy. Aging changes in the lungs and pleura as well as inactive inflammatory lesions may stimulate metastatic disease. Treatment should not be withheld because of equivocal radiographic findings.

Because of the high frequency of malignancy, an aggressive approach should be taken to confirm the diagnosis. A preliminary biopsy is not recommended unless it will change the owner’s willingness to treat or the surgical procedure. Tissue for histopathology is taken at the time of mastectomy and should include the regional lymph nodes. If pleural fluid is removed from a cat with a mammary gland lesion, cytology should be done on the fluid to search for malignant cells.

A variety of nonmalignant lesions must be considered in a differential diagnosis of mammary neoplasia. The most common benign growths are classified as cysts, papillary cystic hyperplasia, lobular hyperplasia, and mastitis. Fibroepithelial hyperplasia is a common benign lesion involving one or more glands and is frequently seen one to two weeks following estrus. The gland may be so large that the patient may walk with an abnormal gait and the skin overlying the mass may be discolored, edematous, and painful. Cats with fibroepithelial hyperplasia are often young, intact females. The signs are similar to those seen with most malignant tumors. Because the benign masses closely resemble malignant neoplasms, they are often treated as malignancies.

**Prognostic Factors**

In the last 20 years, little progress has been made in extending the survival time of canine and feline mammary tumor patients. Because stromal invasion is almost always present and metastases are frequently present at the time of surgery, a guarded to poor prognosis should always be given. Sixty-six percent of the cats that have had their tumors surgically excised have a recurrence at the surgical site. Most studies state that the time from tumor detection to the death of the cat is rarely over 12 months. The most significant prognostic factors influencing tumor recurrence and survival for cats with malignant mammary neoplasia are tumor size, the extent of surgery needed to remove the tumors, and histologic grading of the tumors.

MacEwen has shown that tumor size is the most important of these prognostic factors. Following surgery, the median for survival for cats with tumors >3 cm in diameter is 6 months; for cats with tumors 2 to 3 cm in diameter, the median for survival following surgery is 2 years; and for cats with tumors <2 cm in
diameter, the median for survival after surgery is approximately 3 years. Radical surgery, when compared with regional "lumpectomy", has been shown to reduce local tumor recurrence but not to increase the overall time of survival. Cats with well-differentiated tumors with few mitotic figures per high-power field live longer compared with those with tumors that are not as well-differentiated histopathologically. The one-year survival rate was high in cats with a tumor that did not show lymphatic infiltration. There is a good correlation between the grade of malignancy, method of growth, and prognosis. Patients with pulmonary metastatic disease rarely survive longer than two months.

Mammary neoplasms in the cat have been treated in a variety of ways; however, surgery is the most widely used treatment. There have been no reports documenting the efficacy of radiation therapy or commercially available biological response modifiers for the treatment of this disease. The biological response modifier, liposome-encapsulated muramyltripeptide-phosphatidyethanolamine (L-MTP-PE) may not be effective when used in combination with surgery or chemotherapy.

The success of surgery is hindered by the invasive nature of the disease and its tendency for early metastasis. Radical mastectomy (i.e. removal of all glands on the affected side) is the surgical method of choice because it significantly reduces the change of local tumor recurrence. This procedure is frequently utilized regardless of the size of the tumor.

Several surgical principles are observed when performing a mastectomy on feline mammary tumor patients. During or prior to surgery, a bacterial culture and antibiotic sensitivity testing may be indicated because of approximately one-fourth of mammary carcinomas are ulcerated. An en bloc resection is often employed in such a way that the tumor and draining nodes and vessels are removed by wide surgical excision and a partial or complete resection of the underlying tissue is done. If bilateral mastectomy is indicated, the affected glands and their associated lymph nodes are removed and a second surgery is performed 10 to 14 days later, the interim allows the skin to stretch for a complete closure at the second surgery. Early vessel ligation is essential; one study noted that two-thirds of the cases examined had tumor invasion of lymphatics and veins. Gentle handling of all damaged tissue is essential. Copious flushing of the surgery area after the tumor is removed helps eliminate exfoliated neoplastic cells. Although spaying has been shown not to decrease the incidence of recurrence, some believe that it is warranted because of the occasionally seen coexisting ovarian and uterine disease. If the mammary mass is due to a benign condition such as fibroepithelial hyperplasia, spaying often results in regression of the hyperplastic tissue. Regression may take up to five months. This condition often resolves spontaneously within a few weeks of diagnosis; in some cases without performing an oophorectomy.

**Radiation therapy**
Radiation therapy is not used routinely to treat feline mammary tumors. Presently, there are no major claims that radiation dramatically increases the survival rate of feline mammary tumor patients; however it may reduce local recurrence rates.

**Chemotherapy**
Chemotherapy, alone or in combination with surgery, is not as successful for feline mammary tumors as it is for other feline tumors such as lymphoma. Cyclophosphamide has been used alone or in combination with other chemotherapeutic agents and has not consistently helped the feline mammary tumor patient. The combination therapy of doxorubicin and cyclophosphamide has been shown to induce short-term partial and complete responses in 50% of cats with metastatic or nonresectable local disease. This chemotherapeutic protocol has been shown to be toxic in some cats and does not prolong survival. Other drugs that may be used include mitoxantrone and taxol. The role of the later two drugs is still being elucidated; however both have some efficacy in cats with malignant neoplasia. Further studies are necessary to quantify the benefit of adjunctive therapy for mammary neoplasia in cats. Chemotherapy should be used by practitioners that are familiar with the use of these drugs and their side effects.
VACCINE ASSOCIATED SARCOMAS

Recent epidemiologic studies have associated the administration of a number of vaccines and the development of soft tissue sarcomas in the cat. Vaccines have also been associated with hematological or immunological diseases. Perhaps the most disconcerting problem is the vaccine associated malignancy problem. In a recent epidemiologic study, sarcomas were temporally associated with previous injection of various vaccines into specific body locations. Feline leukemia virus, rabies vaccination, and development of fibrosarcomas at the injection site within a year following vaccination were statistically associated. This study demonstrated a 5.5% increased risk of developing sarcomas in response to feline leukemia virus vaccination and a twofold increase in risk of development of sarcomas after rabies vaccination. The actual incidence of the tumor was estimated to be approximately one sarcoma per 10,000 feline-leukemia virus and rabies vaccines administered. No association between sex, breed, and concurrent viral infections in the development of these sarcomas was found. The aluminum adjuvant in many of these vaccines may be associated with development of vaccine-associated sarcomas. However, Kass, et al., demonstrated that certain aluminum-free vaccines may also be associated with development of these soft-tissue sarcomas. Increase in development of soft-tissue sarcomas following one vaccination was 50%, following two vaccinations was 127%, and following three or four vaccines simultaneously administered at the same location was approximately 175%. Therefore, there appears to be a multifactorial association between vaccines and growth of sarcomas. The development of sarcomas in response to vaccines, especially those that contain aluminum as an adjuvant, may suggest an association between foreign bodies and the growth of these neoplasms. This is not a new observation. Indeed, other metals such as arsenic, chromium, and nickel have been shown under an array of conditions to induce sarcoma formation. Histologically, vaccine-associated sarcomas are enveloped in dense, fibrous connective tissue and infiltrated with inflammatory lymphocytes and macrophages. Macrophages often obtain bluish-gray foreign material that electron-probe x-ray microanalysis identifies as aluminum and oxygen. Other tumors develop in apparent association with other foreign bodies. For example, ocular sarcomas have been associated with foreign material in the eye. In addition, osteosarcomas have been associated with metallic implants. Despite the compelling information, no specific etiology has been determined for the development of these sarcomas, only causal association. Additional research must answer the question of etiopathogenesis. Vaccine associated soft-tissue sarcomas are frequently located in such areas of previous vaccination as between the shoulder blades and in the hind leg. A diagnosis is made by fine-needle aspirate cytology or, preferably, incisional biopsy. The clinician should keep in mind that these soft-tissue sarcomas are encased in a pseudocapsule that is actually compressed tumor tissue. In addition, tendrils of tumor extend far beyond the site of palpable tumor.

Radiation is very important for the treatment of cats with vaccine associated sarcomas. This may be given before or after surgery and is given along with chemotherapy in most cases.

Treatment must be aggressive regardless of tumor size. These soft-tissue sarcomas are extremely aggressive and extend far beyond the palpable site. While the most effective treatment is not known, surgery should be employed whenever possible. In each case, extremely wide and deep surgical margins (> 3 cm), including all the soft-tissue structures and, if appropriate, any bony structures in the region of the postvaccinal sarcoma should be obtained. Essentially, the tumor and a large cuff of normal tissue surrounding the mass should be removed en bloc. All lateral and deep margins should be marked and submitted for histopathology after appropriate formalin fixation to determine presence of residual neoplastic disease. In some veterinary oncology centers, presurgical radiation therapy is routine to minimize the amount of viable tumor around the palpable tumor. If recurrence is noted or suspected after surgical removal of the tumor, radiation therapy can be directed widely around the surgery site. In addition, doxorubicin may be effective for controlling local disease for a period of time. In some centers, surgery, radiation therapy, and chemotherapy are used in conjunction to control this tumor. Until more effective treatments are known, the following recommendations may help prevent development of postvaccinal...
sarcomas:

1) Avoid administering multiple vaccines in the same site;
2) Administer vaccines in extremities (Rabies Right; Leukemia Left, FVRCP in the right shoulder) that may allow amputation as an effective treatment;
3) Remove postvaccinal granulomas that persist several months after vaccination; and
4) Continue research on different adjuvants to reduce the development of vaccine-induced sarcomas.

Finally, many have questioned the wisdom of administering vaccines on a yearly basis, especially when using multivalent products.

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SCIENCE BEHIND POLYUNSATURATED FATTY ACID CANCER THERAPY

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Cancer is a major cause of morbidity and mortality in dogs, cats and women worldwide. The ultimate goal for the treatment of malignancies is to eliminate all evidence of cancer resulting in a cure. With high grade malignancies, this is usually accomplished with a combination of surgery, chemotherapy, radiation, and more recently, molecular approaches of cancer therapy. Despite decades of intense effort and billions of dollars of expenditure, cures for high grade cancers have remained elusive. Fortunately, new knowledge about new and older therapeutic agents such as the n-3 polyunsaturated fatty acid (PUFAs), docosahexaenic acid (DHA) and eicosapentaenoic acid (EPA) have resulted in improved quality and quantity of life.

Many referring veterinarians around the world have noted that the medical, surgical and radiation oncologists are treating with n-3 PUFA's such as docosahexaenoic acid to enhance the effect of chemotherapy and radiation therapy as an adjuvant therapy to prevent cancer progression and metastasis. These same caring veterinarians have often asked:

- Should all cancer patients be treated with PUFA's such as DHA?
- Should PUFA's such as DHA and EPA be administered to cancer patients to enhance the efficacy of chemotherapy and radiation therapy?
- Should PUFA's such as DHA and EPA be prescribed to reduce the toxicity of radiation therapy?
- Should antioxidants such as vitamin E be administered to cancer patients receiving DHA or EPA?

PUFAs and Cancer Prevention by Delay
The use of fatty acids such as docosahexaehoic acid is designed to enhance disease free interval, survival and quality of life after surgery by reducing the rate of cancer development or incidence. This concept, known as cancer prevention by delay has recently been recognized and is an important mechanism behind the successes of several therapeutic agents including (Lippman and Hong, 2002):

- Tamoxifen that has been shown to significantly diminish the risk of human breast cancer
- Retinoids and interferon-alpha to reduce the risk head and neck cancer in dogs, cats and people
- Nonsteroidal anti-inflammatory drugs to delay or reduce the development of colorectal cancer in human beings, transitional cell carcinomas in dogs and cats, and squamous cell carcinomas in dogs and possibly cats.

The delay of cancer growth and development, also known as clinical cancer chemoprevention is a valuable clinical tool until permanent or absolute cancer prevention can be achieved. The value of DHA as an agent to delay the occurrence of cancer can only be understood by exploring its value as a cancer chemopreventative, and as an agent to enhance the effect of radiation and chemotherapy.

PUFAs and Cancer: The Evidence
For the last decade, our laboratories in Japan, France, Colorado and now at Angel Care Cancer Center in California has been involved in the search for dietary lipids associated with a delay in cancer relapse. Dietary lipids such as DHA appear to influence the growth of many types of cancer including breast and prostatic cancer (Franceschi et al., 1995; Braga et al., 1997, Fay et al., 1997, Thompson et al., 1996). From a cohort of women treated for localized presentations of breast cancer, the group in France used adipose tissue sampled during surgery as a biomarker of past dietary intake of polyunsaturated fatty acids (Bougnoux et al., 1994). They found elevated n-3 fatty acids, especially DHA to be associated with a higher metastasis-free survival, suggesting that these fatty acids could potentially delay metastasis by...
decreasing tumor growth or development. Furthermore, using a case control approach comparing the fatty acid composition of adipose breast tissue obtained at the time of the surgical removal of either malignant or benign breast tumors, the French group found both alpha linoleic acid and docosahexaenoic acid (DHA) to be positively associated with a decreased risk of having breast cancer (Maillard et al., 2002). They also explored the role of n-3 PUFA on mammary tumor growth using the experimental system of NMU-induced mammary tumors in rats. Because fatty acids are substrates for lipid peroxidation processes, the group in France studied the effects of n-3 fatty acids on tumor growth in interaction with anti- or pro-oxidant compounds. They found that dietary n-3 fatty acids in the form of fish oil that contains docosahexaenoic acid inhibited tumor development. Furthermore, this tumor growth inhibition was most evident in the absence of the antioxidant vitamin E. Inhibition of tumor growth was even greater when the n-3 fatty acids were given in the presence of pro-oxidants (Cognault et al., 2000). Such effects were not found when the lipid diet was low in fatty acids. These data suggested that oxidized n-3 fatty acids have an inhibiting role on tumor growth and emphasize the importance of the interaction of anti- and pro-oxidant compounds with n-3 fatty acids. There is a growing body of data based on our work as well as work does by others that suggests the effect of n-3 fatty acids such as DHA seem to involve several steps of tumor formation. N-3 fatty acids such as DHA and EPA:

i. Inhibit tumor vessel formation (angiogenesis)

ii. Inhibit cell proliferation in several epithelial cell lines.

iii. Enhance the rate of tumor cell death

iv. Induce lipid peroxidation which enhances the efficacy of radiation and chemotherapy induced cancer cell death; this effect is diminished or reduced dramatically with vitamin E.

v. Suppress the expression of cyclooxygenase-2 in tumors therefore decreasing cancer cell proliferation.

vi. Suppression of NF kappa B activation and bcl-2 expression thus allowing apoptosis of cancer cells

**PUFAs and Chemotherapy**

Dietary lipids such as DHA have been suggested to modify the sensitivity of tumors to ROS-generating anticancer drugs which is the reason it is incorporated into the treatment regimen of some patients worldwide. For example, when dogs with lymphoma were treated with doxorubicin chemotherapy and a diet supplemented with n-3 fatty acids in the form of fish oils, that there was a direct correlation between the level of docosahexaenoic acid in the blood and improved disease free interval (Ogilvie et al, 2000). Another study using the same randomized study design was used to assess the efficacy of n-3 fatty acids in combination with doxorubicin chemotherapy to improve the disease free interval in dogs with hemangiosarcoma, a highly metastatic, rapidly fatal malignancy. There was a statistically significant positive correlation between the n-3 fatty acids and disease free interval (Richardson et al, In press). A similar approach was used in rats bearing autochthonous, NMU-induced mammary tumors. We found that dietary supplementation with fish oil or DHA increased the sensitivity of mammary tumors to anthracyclines, compared with dietary supplementation with saturated fatty acids (de Poncheville et al., 2000). Since DHA is the most polyunsaturated of the polyunsaturated fatty acids, lipoperoxydation is suspected to be a likely molecular mechanism implied in the enhancement of the response of the cancer cells to cytotoxic drugs. Addition of vitamin E to diet provided to mammary tumors bearing rats abolished the enhancing effect of DHA on tumor sensitivity to anthracyclines. (de Poncheville et al, 2000). In all studies done to date, there has been no clinically significant toxicity other than transient gastrointestinal distress linked to the dietary change (Ogilvie et al, 2000, McNiel et al, 1999, Swaim et al, 1989). Therefore, based on the safety and efficacy profile of n-3 fatty acids, it seems reasonable to further define the efficacy of n-3 fatty acids, especially docosahexaenoic acid for the treatment of spontaneously occurring cancer in dogs with the intent to provide evidence for its use in randomized human clinical trials.
**PUFAs and Radiation Therapy**

Radiation therapy is currently the most effective treatment for many localized malignancies including those within the nasal cavity. Research is underway at Angel Care Cancer Center to identify methods to maximize efficacy of radiation while minimizing the adverse effects associated with radiation therapy. Among the agents being evaluated to minimize the normal tissue damage are long chain polyunsaturated fatty acids of the n-3 series such as docosahexaenoic acid and eicosapentaenoic acid, which readily are incorporated into cell membranes and ameliorate inflammation and carbohydrate dyshomeostasis. In a study involving 12 dogs with histologically confirmed malignant carcinomas of the nasal cavity were randomized to receive isocaloric amounts of a diet supplemented with menhaden fish oil including DHA (experimental diet) or an otherwise identical diet supplemented with corn oil (control diet). Megavoltage radiation was delivered to all dogs. The data in that study suggested that feeding a diet supplemented with fish oil and arginine is associated with decreased concentrations of inflammatory mediators involved with radiation damage in skin and mucosa, and improved performance scores in dogs with malignant nasal tumors (Hansen et al, In press 2003).

Tumor sensitisation to radiation by polyunsaturated fatty acids has been investigated. Vartak et al. (1997) (1998) studied the in vitro response of a chemically-induced rat malignant astrocytoma cell line to radiation after the cell culture medium was supplemented with gamma-linoleic acid (GLA) or long chain n-3 PUFA (EPA or DHA), and found that n-3 PUFAs enhanced radiation-induced cell cytotoxicity. Colas et al (2003) documented enhanced radiosensitivity of rat autochthonous mammary tumors by dietary docosahexaenoic acid.

Whether dietary n-3 fatty acids can lead to enhanced sensitivity of tumor tissue in the absence of a similar increase in the radiosensitivity of non-tumor tissue remains a critical issue. Several studies have suggested that PUFAs do not sensitize normal tissues to radiation. For example, since ionizing radiation generate ROS, we initiated a study to determine whether dietary DHA might sensitize mammary tumors to irradiation using a model where mammary tumors were induced by N-methylnitrosourea (NMU) in Sprague-Dawley rats. In the study, we showed that dietary DHA sensitized mammary tumors to radiation. The addition of vitamin E inhibited the beneficial effect of DHA, suggesting that this effect might be mediated by oxidative damage to the peroxidizable lipids (Colas et al, 2003).

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