

Pain Management in Cancer Care

The Kindest Care

Ralph Harvey, DVM, MS, ACVAA
University of Tennessee
College of Veterinary Medicine





Objectives:

- Appreciate the psycho-social implications of cancer as a diagnosis
- Recognize that different types of pain may combine during one disease
- Understand the sources and significance of pains in cancer and in cancer therapies
- Apply previous knowledge to case examples
- Develop typical therapeutic plans for control of cancer pains

Cancer Pain Fundamentals

- Understand the disease and extent
- Recognize the cause and importance of each pain
- Consider diverse management options
- Staged pain management approach
- Titrate, adjust and balance care to maintain the most appropriate control

Pain in Cancer

- Cancer is often a painful disease
- 30% of all human cancer patients report pain (60-90% with advanced cancer)
- 70-90% can achieve "good" pain control
- pain is often more feared than death
- extension of these same concerns by owners to their pet's cancer

Specific Concerns

- Acute cancer related pain -
 - surgical oncology, radiation therapy
- "Chronic" pain -
 - pain of metastasis, treatment related pain
 - palliative care and terminal cancer pain
- "Pain in dying" -
 - aspects of suffering and the psychology of cancer

Clinical Assessment

- History - comprehensive
- Examine sites of pain and dysfunction thoroughly
 - (may need analgesics!)
- Use appropriate diagnostic tools
 - (Radiography, Ultrasound, CT, MRI, Nuclear Scintigraphy)

Clinical Assessment

- Evaluate extent of disease - extent of pain
- Treat the pain early and aggressively to fully gain control early
- Watch for the development of tolerance and side effects - Then deal with these...
Problems can be managed, without resorting to pain for the patient!

"Acute" cancer pain

- Associated with tumor involvement
 - compression, erosion, nerve compromise
 - paraneoplastic syndromes
- Surgery or other procedures cause pain
- Importance of early operative pain management -
 - Often the first opportunity that we have
 - Preemptive analgesia prevents pain syndromes

Analgesia in Cancer Surgery

- Pre-emptive, balanced and adequate analgesia
- Value of local anesthetics in surgical oncology
- Mandibular alveolar block -
lower lip and gum



Analgesia in Cancer Surgery

- Pre-emptive, balanced and adequate analgesia
- Value of local anesthetics in surgical oncology
lidocaine + bupivacaine
rapid onset + long duration
- Injection of nerve sheath prior to transection in this forelimb amputation –
(So easy, so cheap, so very effective!)



Sources of Cancer-associated Pain:

- Therapeutic interventions can cause pain -
 - Acute post-operative pain
 - ┆ →→→ potential for maladaptive neuropathic pain!
 - Tissue sloughing
 - Pancreatitis
 - Chemotherapeutic neuropathies
 - Gastric ulceration
 - Radiation burns

“Chronic” cancer pain

- More difficult to diagnose and to treat
- Longer duration, less well defined onset
- Increase with tumor progression
- Subsides during periods of tumor regression
- Associated with a “negative quality of life”
Often characterized by behavior changes:
anxiety, depression, anorexia, sleep disturbances, suffering...
“She’s just not been herself.”
“Mal-Adaptive” “Neuropathic” Chronic Pain

Types of pain in cancer:

- Somatic Pain
- Visceral Pain
- Neuropathic Pain
- Inflammatory Pain



Somatic Pain in Cancer

- More acute and specific in nature
- Nociceptor activation: sharp, aching, throbbing or pressure-like
- Metastatic bone pain, postsurgical pain, musculoskeletal pain

Visceral Pain in Cancer

- Less well localized pain
- Nociceptors of thoracic, abdominal or pelvic viscera yield referred pain
- Diffuse gnawing or cramping, aching or throbbing

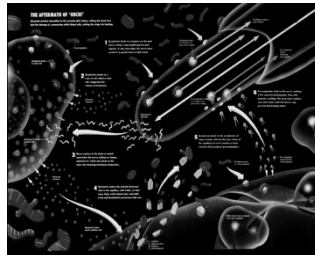
Neuropathic Cancer Pain

- Central or peripheral nerve involvement
- Infiltration or compression of nerves
 - nerve root, brachial plexus or lumbosacral nerve sheath tumors
 - nerve damage by surgery, radiation therapy, phantom limb syndrome
- Corticosteroids, decompression, neurolysis

Inflammatory Mediators

"Allogenic" mediators:

- Histamine, serotonin, bradykinins, leukotrienes, prostaglandins
- These are the forces of darkness!
- These mediators of death, disease and debilitation!



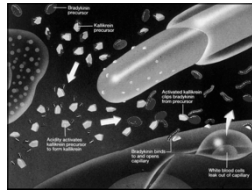
Paraneoplastic Syndrome

- Loretta and Susie
 - 11 yr old Plott Hounds
- Guess which of these pups has the renal adenocarcinoma?
- Symptomatic and supportive therapy



Inflammatory Cancer Pain

- Treatment of paraneoplastic syndromes
- NSAID's
- +/- Corticosteroids
- Antioxidants?
- Anti-inflammatory diets?
- Supportive therapies



Primary Therapy

- Tumor removal or reduction
- Surgery, Radiation therapy, Chemotherapy
- Treat paraneoplastic syndromes, infections
- Prognosis, costs, quality of life are focal issues determining willingness to treat

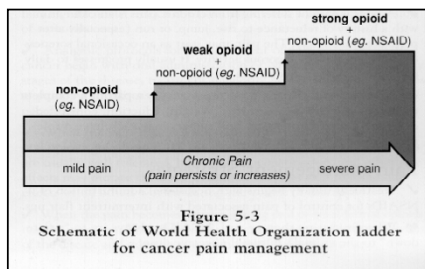
Curative / Palliative

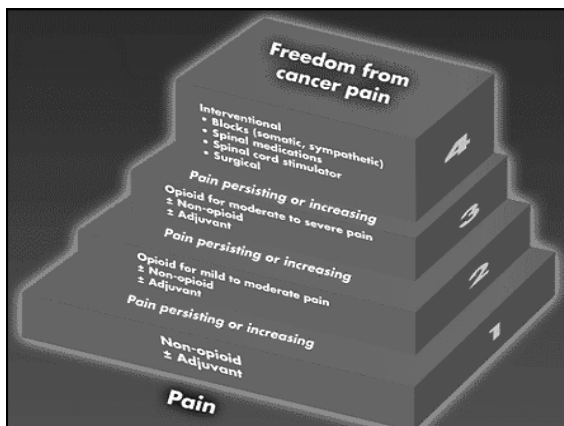
- Tumor removal / Reduction
- Definitive therapy / Supportive care
- Amputation / Limb sparing surgery
- Perioperative analgesic therapy
- Combined strategies:
 - surgical excision, radiation therapy, chemotherapy, immunotherapy

WHO Treatment Strategy for Cancer Pain

- Relies on intensity and severity rather than the mechanism or etiology
- Individualized and titrated management
- Escalation of analgesic strategies
- Three (or four) levels of intervention
 - mild, moderate, severe, (refractory)

WHO Analgesia Ladder





Step one - Mild Pain

- NSAIDs
 - ▮ carprofen (Rimadyl), deracoxib (Deramaxx), meloxicam (Metacam), firocoxib (Previcox), Robenacoxib (Onsior), etc.
 - ▮ many individual options for dogs and cats
 - ▮ Piroxicam (Feldene) anti-angiogenesis action may be shared with some other NSAIDs
 - ▮ +/- adjuvants (some are GI protective)
 - ▮ misoprostol, H₂ blockers, H⁺ blockers
 - ▮ Gabapentin (Neurontin), Amantadine, Tramadol (Ultram)
 - ▮ acetaminophen (dogs only!) (no anti-inflammatory action)

Step two - Moderate Pain

- NSAID's plus mild opioids, many options
- Add low dose weak or partial agonist opioids
 - ▮ acetaminophen plus codeine, aspirin plus codeine
 - 30 or 60 mg codeine plus 300 mg aspirin or acetaminophen (dogs only)
 - ▮ Partial agonists (buprenorphine)
 - ▮ Agonists/Antagonists (butorphanol) poor analgesia
 - ▮ Tramadol (Ultram tablets)
- +/- adjuvants: as above (NSAID's plus mild opioids) and...
 - ▮ antiemetics, antihistamines, corticosteroids, stool softeners, mood elevators, tranquilizers
 - ▮ These and others as needed - Always individualize therapy

Step three - Severe Pain

- Stronger opioid, perhaps added to NSAID
- morphine may be the best choice
 - ▮ sustained release oral formulations
 - ▮ 0.5 to 3.0 mg/kg, BID, variable bioavailability
 - ▮ tablets, syrups, suppositories
- fentanyl transdermal
 - ▮ transdermal patches (Duragesic) – extralabel use
 - ▮ transdermal liquid (Recuvyra) – extralabel use
- +/- adjuvants as needed
 - ▮ NMDA antagonist (Amantadine)
 - ▮ alpha-2 agonists
 - ▮ GABA-pentin (Neurontin)

Fentanyl (Duragesic) patches

- Strictly "off-label"
- Can be very useful for providing a consistent (basal) level of strong opioid analgesia
- Alternative to sustained release oral morphine
- Precautions important



Unwanted drug effects

- anticipate, monitor and manage
- monitor for toxicities - CBC, chemistries
- sedation frequently occurs early in pain therapy
 - wait for a few days for tolerance, reduce dose
- constipation
 - stool softeners, bulk laxatives
- GI toxicity of NSAID's
 - monitor for loss of appetite, etc.
 - change drugs, protect with misoprostol, etc.

Step four - Refractory Pain

- terminal pain patients
- alternative routes of delivery
 - neuroaxial, continuous infusions
- interventions
 - blocks, neural stimulations (TENS), neurolysis
- euthanasia
 - Of course an option to relieve pain and suffering!

Palliative Care

■ WHO definition:

- The active total care of patients whose disease is not responsive to curative treatment
- Control of pain, of other symptoms, and of psychological, social and spiritual problems, is paramount
- The goal of palliative care is achievement of the best quality of life for patients and their families

Palliative Care Includes Planning for Death

- Progression of disease may lead to:
 - unmanageable pain
 - unmanageable drug-effects
- Toxicities from therapy
- Concurrent diseases
- Euthanasia is a good and kind part of cancer care.



Terminal care - "hospice care"

- Can be the most appreciated part of our interaction with the owners and animals.
- When the time comes...euthanasia relieves pain and suffering.



Maintain Quality of Life!

- Function
- Activity
- Appetite
- Involvement
- Maintain the Human/Animal Bond



Case study: Lacey

- 7 y.o. Golden Retriever 24 kg
- Oral Mass
 - Mandibular Fibrosarcoma
 - very poor prognosis



<http://upsideiddogs.com/wp-content/uploads/2009/05/tom-the-golden-retriever>

Staged Balanced Analgesia:

- | | |
|--|---|
| <ul style="list-style-type: none"> ■ Procedural: <ul style="list-style-type: none"> ■ Pure Agonist Hydromorphone Mandibular Nerve Block ■ PostOp: <ul style="list-style-type: none"> ■ Morphine / Buprenorphine ■ Discharge: <ul style="list-style-type: none"> ■ Meloxicam Liquid Tramadol Acetaminophen + Codeine #3 ■ Q12h | <ul style="list-style-type: none"> ■ Adjunctive: <ul style="list-style-type: none"> ■ Gabapentin 50 mg q 12h Diphenhydramine 25 mg BID Famotidine ■ Acupuncture |
|--|---|



<http://upsideiddogs.com/wp-content/uploads/2009/05/tom-the-golden-retriever>

Staged Balanced Analgesia:

- Owners keeping a "Pain Diary" of activity and quality of life
- Call-backs to client by technician or veterinarian -
 - Adjunctive analgesics added as needed:
 - Gabapentin 50 mg q 12h
 - Diphenhydramine 25 mg BID
 - Famotidine
 - Acupuncture
- Palliation – 4 months with quality!
- Appreciative client



Case study: Telstar

- 8 year old male
- Rottweiler
(and a very nice one too!)
- Lamé, with swelling of distal left forelimb
Owner first noticed in late April...



Case study: Telstar

- Osteoblastic/osteolytic mass in distal ulna
 - Radiograph & Biopsy on April 27
 - Refer on May 8
- Biopsy confirmed osteosarcoma
- Otherwise in good health
 - Hx rear lameness, intolerance of carprofen



Telstar

- Limb-sparing ulnectomy
 - resection of mid-body of left ulna & styloid
 - May 9
- Operative analgesia:
 - morphine (preop and postop)
 - brachial plexus block
- Sent home on antibiotics and carprofen (now tolerated) 100mg q12h
- Scheduled for chemotherapy (cisplatin) and rechecks...



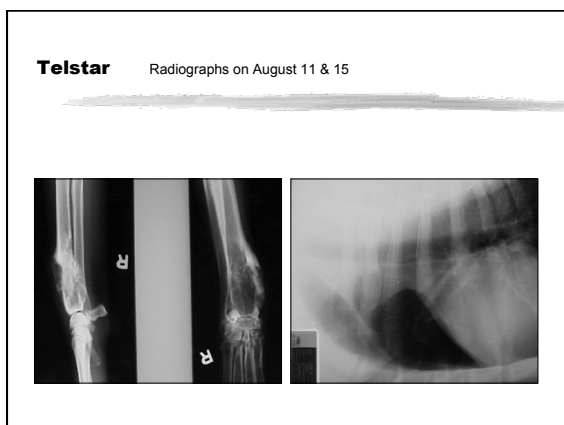
Telstar

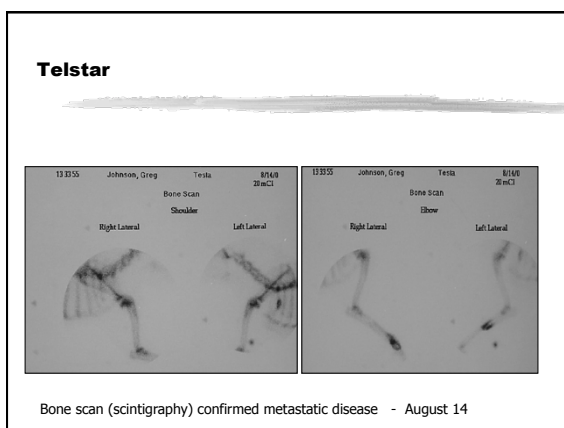
- Left forelimb functionally sound (August 11)
- Radiologists suspect some forces of darkness are at work...
- But not a problem as far as Telstar is concerned
- Pain management rated "good" by owners with the NSAID alone and no adverse effects noted



Telstar

- Radiography at rechecks and chemotherapy sessions ultimately revealed bony lesions involving right forelimb and ribcage
- Bone scan (scintigraphy) confirmed metastatic disease
- Pain management still rated as "good" by owners with no adverse effects





Options specific for OSA

- Palliative RT
 - Extremely effective
- Bisphosphonates
 - Inhibit bone resorption
 - Pamidronate, Zoledronate
- Samarium
 - Radiopharmaceutical
 - Samarium153 lexidronam

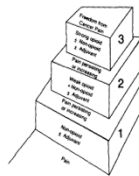
Local Anesthetics

- Continuous infusion via soaker catheter



Telstar

- Disseminated OSA
- No further chemotherapy
- Continue analgesics
- Last visit to UTCVM
 - └ August 15
- Periodic consultations with referring DVM for management of Telstar's cancer pain



Telstar

- Now four months post ulnectomy (September)
- Lameness, lethargy now reported
- Carprofen is no longer providing adequate analgesia
- Morphine sustained release tablets added
 - └ 30 mg q12h added to the carprofen
 - └ (Sedation was noted at the initial 60 mg dose)
 - └ (Evidence for bioavailability in this dog)
- Excellent results, active and happy dog

Telstar

- Morphine SR 30 mg q12h
- Carprofen 100 mg q12h
- Consistent pain relief - reported as "very comfortable" for an additional 3 months after the addition of oral morphine-SR
- Effective pain control returned Telstar to his role in the human-animal bond as a fully functional pet

Telstar

- January 13 - nine months after diagnosis
- Presented for acute deterioration (two days) weakness and lethargy, pale mucous membranes, development of increased swelling/edema
- Owner elects euthanasia
- Termination of the human-animal bond by euthanasia calls for the utmost sensitivity and skill
 - That topic deserves another discussion!

Contemporary Alternative Options We Can Employ:

NSAID's + Codeine, Tramadol, Gabapentin, Pamidronate, Palliative RT

Cancer Pain Fundamentals

- Understand the disease and extent
- Recognize the cause and importance of each pain that is recognized
- Consider diverse management options
- Staged pain management approach
- Titrate, adjust and balance care in order to maintain the best quality of life

Obstacles to Appropriate Cancer Pain Management:

- Clients
 - Fear
 - Denial
 - Lack of knowledge
 - Non-compliance
 - Financial limits
- Veterinarians
 - Lack of knowledge
 - Inability to assess pain
 - Lack of communication with owner and staff
 - Limits on referral options – location and resources
- How do we address these obstacles? ➡



Keys to Success:

- Empower the owner
- Involve your staff
- Keep your knowledge current



Pain Management in Cancer Care

The Kindest Care

Ralph Harvey, DVM, MS, ACVAA
University of Tennessee
College of Veterinary Medicine