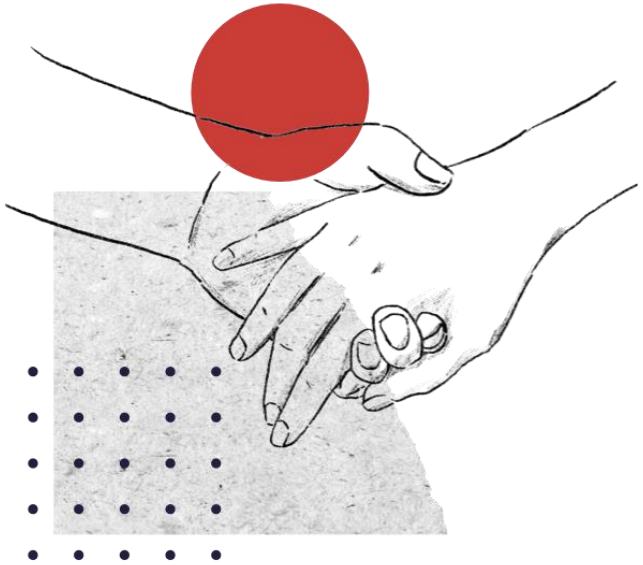

A Practical Approach to Utilizing Adjuvant Analgesics in Adult and Older Populations

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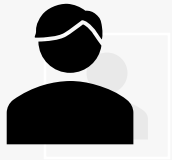
Goals



Understand indications for and side effects of adjuvants for patients with bone pain

Understand indications for and side effects of adjuvants for patients with nerve pain

Learn specific therapies for patients with bone pain from cancer

Adjuvant Analgesics

- Anticonvulsants
- Antidepressants (TCAs, SNRIs)
- alpha-2-adrenergic agonists
- Corticosteroids
- Local anesthetics
- Non-steroidal anti-inflammatory (NSAIDs)
- Topical agents
- gamma aminobutyric acid [GABA] agonists
- N-methyl-D-aspartate [NMDA] receptor antagonists
- Cannabinoids
- Bisphosphonates
- Radiopharmaceuticals

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Dimas

- You are asked to see Dimas, a 70-year-old retired professional golfer with severe right shoulder pain
- He has mild heart failure and Type 2 diabetes.
- His exam is remarkable for 1-2+ pitting leg edema
- His laboratory tests are remarkable for:
  - Cr 2.0, BUN 20, Glucose 160

Which agents/therapies would be safe/effective to treat his bone pain?

- **Acupuncture**
- **Physical Therapy**
- **Yoga**
- **Topical heat or cold patches**
- **Topical diclofenac (Voltaren™) gel**
- **Joint injection**
- **Acetaminophen/paracetamol**

- Ibuprofen
- Naproxen
- Glucocorticoids (e.g dexamethasone)

Dimas

- Dimas improves on your therapy but now complains of **burning and tingling pain in his feet**
- He has mild heart failure and Type 2 diabetes.
- His exam is remarkable for 1-2+ pitting leg edema
- His laboratory tests are remarkable for:
  - Cr 2.0, BUN 20, Glucose 160

Which agents/therapies would be safe/effective to treat his diabetic neuropathy pain?

- **Acupuncture**
- **Desipramine topical cream**
- **Gabapentin 100 hs to start; titrate weekly to 200 mg po bid**
- **Pregabalin 50 mg hs to start; titrate weekly to 75 mg po bid**
- **Duloxetine 30 mg to start; titrate weekly to 60-90 mg**
- **Desipramine 10 mg hs**

- Glucocorticoids (e.g dexamethasone)

What if he develops shingles (Herpes Zoster)?

Which agents/therapies would be safe/effective?

- **Acupuncture**
- **Gabapentin 100 hs to start; titrate weekly to 200 mg po bid**
- **Pregabalin 50 mg hs to start; titrate weekly to 75 mg po bid**
- **Duloxetine 30 mg to start; titrate weekly to 60-90 mg**
- **Lidocaine cream followed by Capsaicin cream as tolerated**
- **Desipramine 10 mg hs**

- Glucocorticoids (e.g dexamethasone)

3 years later…

- Mr Dimas has just been diagnosed with prostate cancer metastatic to his bones
- **In addition to treating his cancer, what can be done for his cancer-related bone pain?**

Which agents/therapies would be safe/effective to treat his cancer-related bone pain?

- Acupuncture
- Physical Therapy
- Yoga
- Topical heat or cold patches
- Topical diclofenac (Voltaren™) gel
- Joint injection
- Acetaminophen/paracetamol

- Ibuprofen
- Naproxen
- Glucocorticoids (e.g dexamethasone)

Treatment of Cancer-related Bone Pain

Bisphosphonates/RANK-L Inhibitors

Radiation therapy

- External beam
- SRS / IMRT

Vertebroplasty / Kyphoplasty

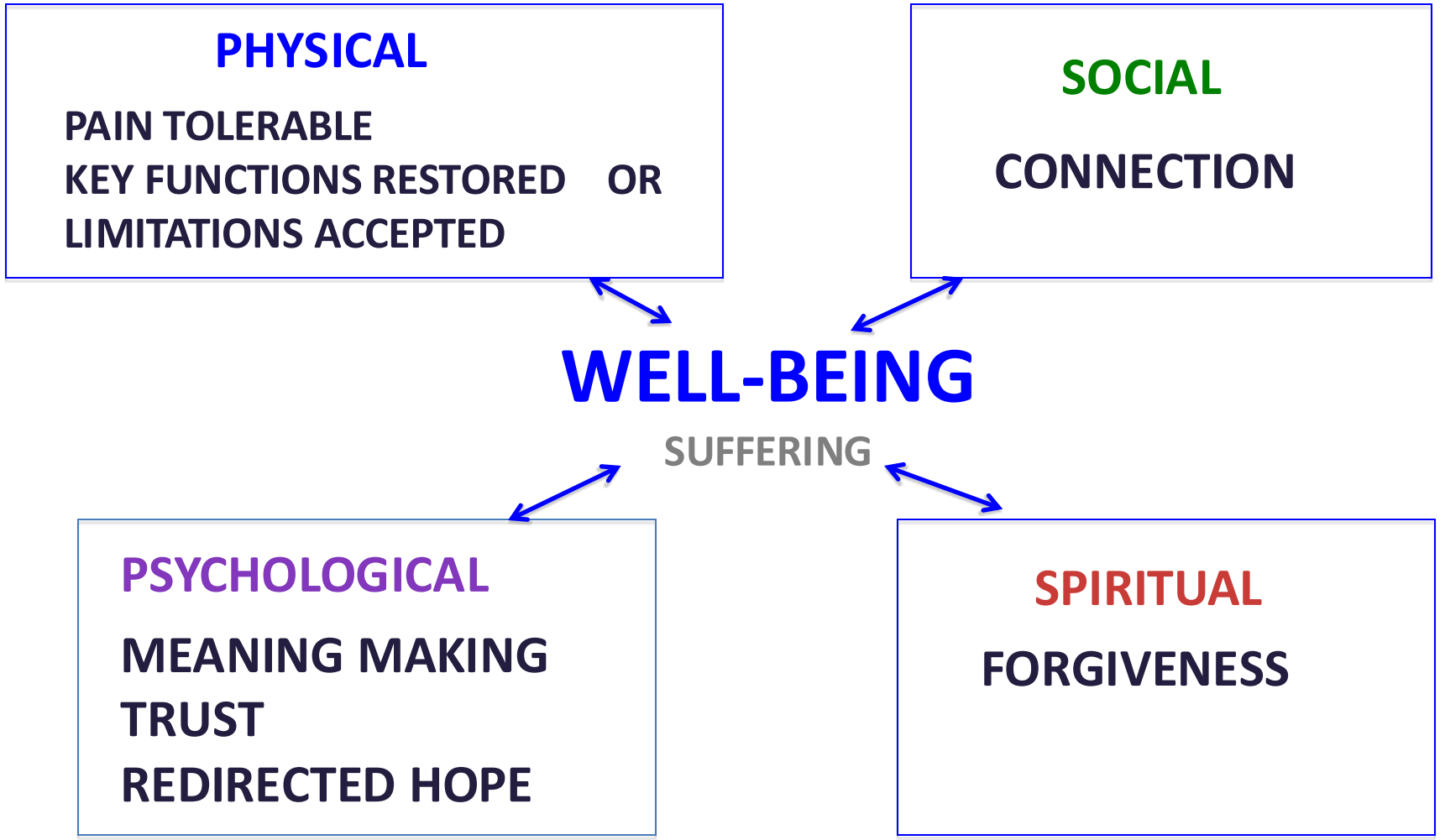
Radionucleotides (consult nuclear med)

- Alpha emitters: alpharadin
- Beta emitters: samarium, strontium, rhenium
- Lutetium-177–PSMA-617

Cryoablation

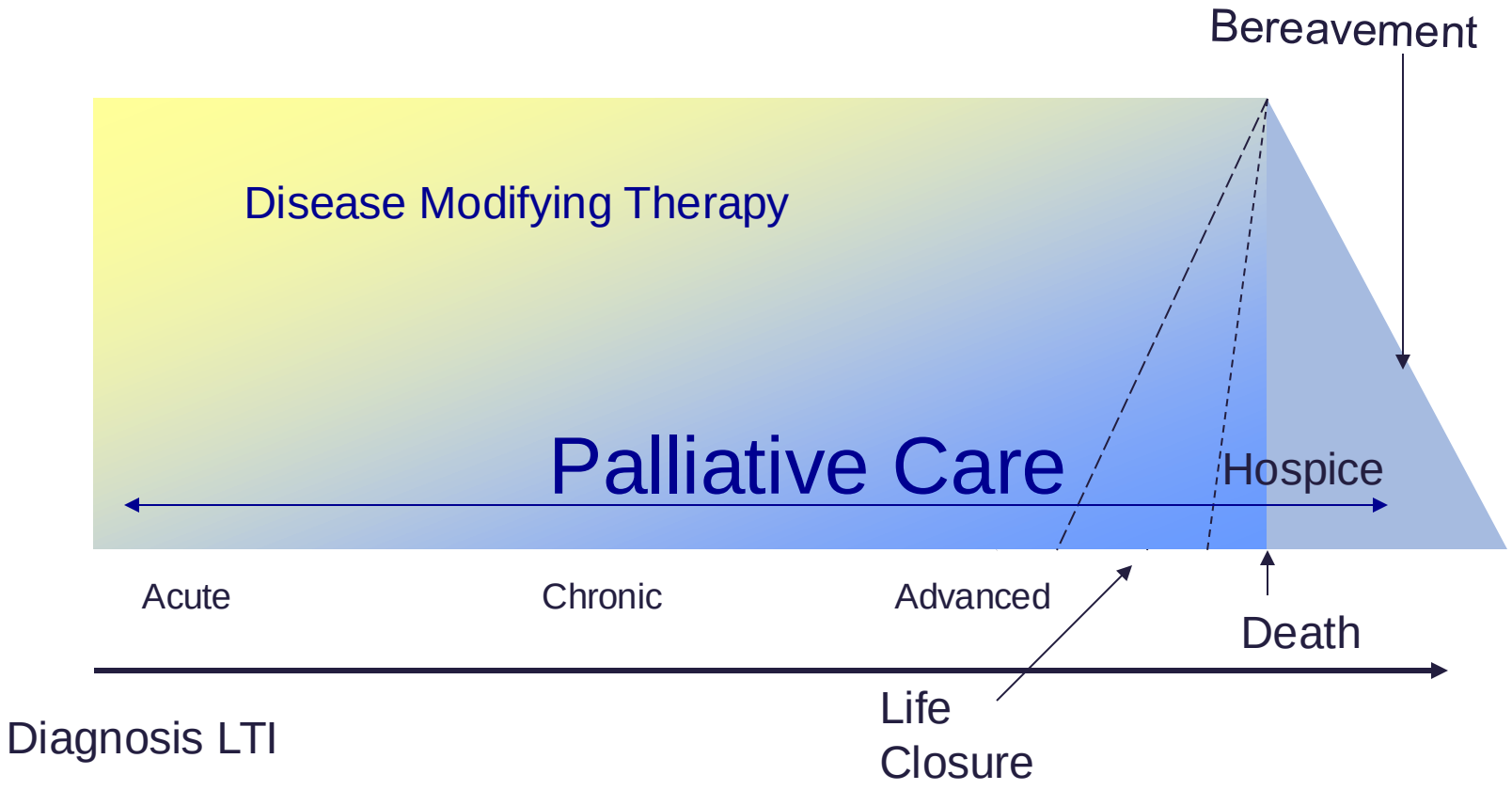
Radiofrequency ablation

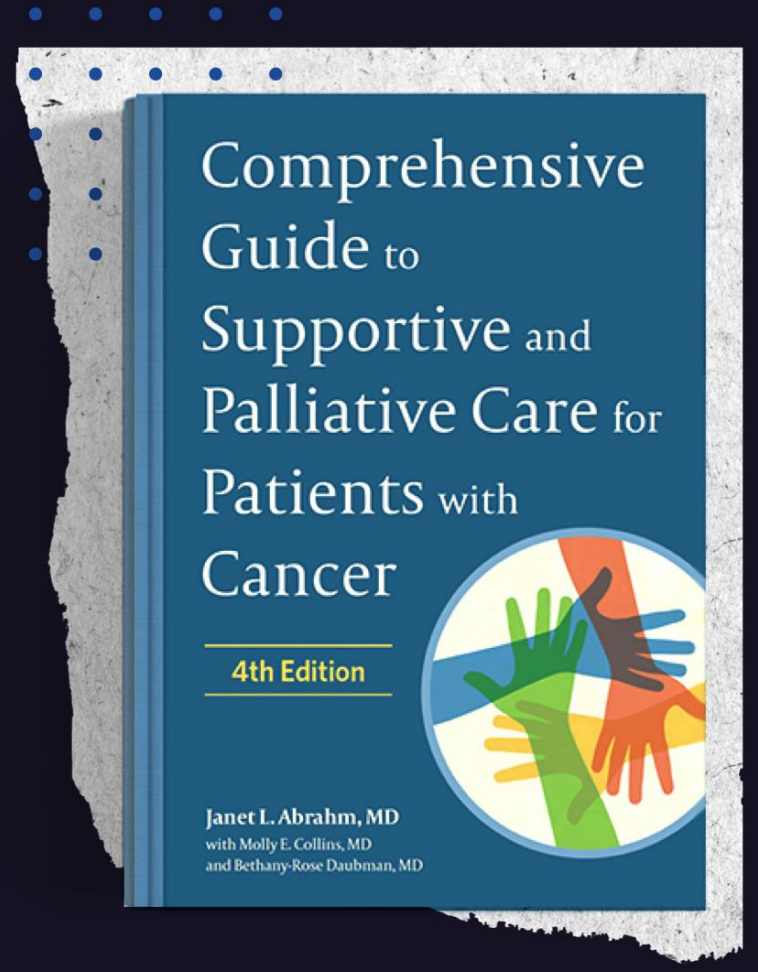
HEALING



Cassell EJ. The Nature of Healing, Oxford Univ Press, 2013

Palliative Care for Quality of Life




Comprehensive Guide to Supportive and Palliative Care for Patients with Cancer
4th Edition
Janet L. Abrahm, MD
with Molly E. Collins, MD
and Bethany-Rose Daubman, MD

Anticonvulsants

- **Gabapentin (Neurontin)**
  - Can be effective for patients with neuropathic pain from tumor, peripheral neuropathy from tumor or treatment, and PHN (FDA indication).
  - Most common side effects are sedation, dizziness
  - Binds to the alpha-2-delta subunit of the N-type calcium channels in neurons within the dorsal horn
  - Starting dose:100 mg three times daily or 300mg at bedtime. Dose increased as tolerated every 3 to 5 days until analgesia is achieved.
  - Effective dose varies between 900mg and 3600mg daily in divided doses.
  - Ceiling effect related to a saturable transport mechanism in the gut--effects of this drug may plateau during dose escalation.
  - Renally dosed

Anticonvulsants

- **Pregabalin (Lyrica)**
  - Same mechanism of action as gabapentin
  - Effective in patients with neuropathic pain (FDA approved for DPN, PHN and fibromyalgia)
  - Dosing: Start at 50mg BID or TID, with the usual effective dose between 150mg-300mg BID.
  - More efficiently absorbed through the gastrointestinal tract and the absorption is proportional to the dose throughout the effective dose range making titration simpler.
- **Other Anticonvulsants for neuropathic pain**: Some evidence for use of carbamazepine (Tegretol), lamitrogine (Lamictal), topiramate (Topomax), Levetiracetam (Keppra), oxcarbazapine (Trileptal)

Anti-depressants

- Duloxetine (Cymbalta)
  - Selective Serotonin and Norepinephrine Reuptake Inhibitor (SNRI)
  - FDA approved for: Diabetic Neuropathy, Fibromyalgia, Chronic Musculoskeletal Pain
  - Dose: Start 20-30mg daily, increase to 60mg daily
  - Risk in patients with hepatic dysfunction

*SSRIs lack significant efficacy in chronic pain

**All antidepressants and anticonvulsants carry warning about increase risk of suicidality.

Anti-depressants

- Tricyclic Anti-Depressants (TCAs)
  - Lowest numbers needed to treat of neuropathics
  - Lower doses for pain than as antidepressants

    (e.g., amitriptyline generally effective 50 to 100mg/day).
  - Anticholinergic side effects:

    2^o Amines (Nortriptyline) < 3^o Amines (Amitriptyline)
  - Risks of sedation, dry mouth, cardiac issues, falls, etc

Corticosteroids

- Bony Metastases, Cord Compression
- CNS Headaches 2/2 vasogenic edema/ICP
- Visceral inflammation (hepatic capsule stretch /RP lymphadenopathy)
- High doses (>16 mg/day) of dexamethasone are needed to in spinal cord compression, brain edema
- Lower doses (2 to 16 mg/day) can be helpful in patients with other types of cancer pain
- *Risk/Benefit Ratio*: increased infection risk, GI bleed, delirium, candida, insomnia, etc – may be helpful for other non-pain sx though

Topical Analgesics

- Local effect without systemic toxicity
- Local Anesthetics
  - Lidoderm patches/Ointment
  - Magic Mouthwash
  - Viscous Lidocaine
- Diclofenac cream/patch
- Topical Capsaicin
- 0.1% Morphine in Intrasite gel