ECD and Pain Management

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Background

- Erdheim Chester disease (ECD) is a rare non-Langerhans cell histiocytosis, commonly involving the musculoskeletal system.
- Other tissue can also be involved, including the central nervous system, cardiac, lung resulting in a wide spectrum of clinical features, at times being nonspecific
- ECD should be considered as a differential diagnosis in patients presenting with bony pain and nonspecific features of multiorgan involvement.

Background

- Clinical presentation can vary from asymptomatic tissue infiltration, bony pains to multiorgan failure
- ECD presents commonly with skeletal symptoms, diabetes insipidus (DI), neurological, and constitutional symptoms
- Bone involvement occurs in about 96% of the cases.
- Classically involves appendicular long bones (distal femur, proximal tibia, and fibula, and less commonly the ulna, radius, and humerus)
- The most common presenting symptom is persistent bone pain (50% of patients) in lower limbs, especially around knees and ankles.

Key Points of Comprehensive Assessment

- Recognize pain and its location, subjective quality, and severity
- Assess not only the type and intensity of pain but how it impacts life of patient
- Use pain assessment to determine the pathophysiology and select treatment strategies
- Determine the best time(s) to assess and reassess the pain
- Establish comfort/function goals with the patient

Pain management

- Pharmacotherapy
  - analgesic ladder
    - opioid analgesics, non-opioid analgesics, adjuvant analgesics
- Adjuvant Techniques
  - Non-invasive
    - Relaxation techniques, distraction techniques, biofeedback, psychosocial interventions
  - Invasive
    - Nerve blocks, surgical or chemical ablation, spinal opioid infusion

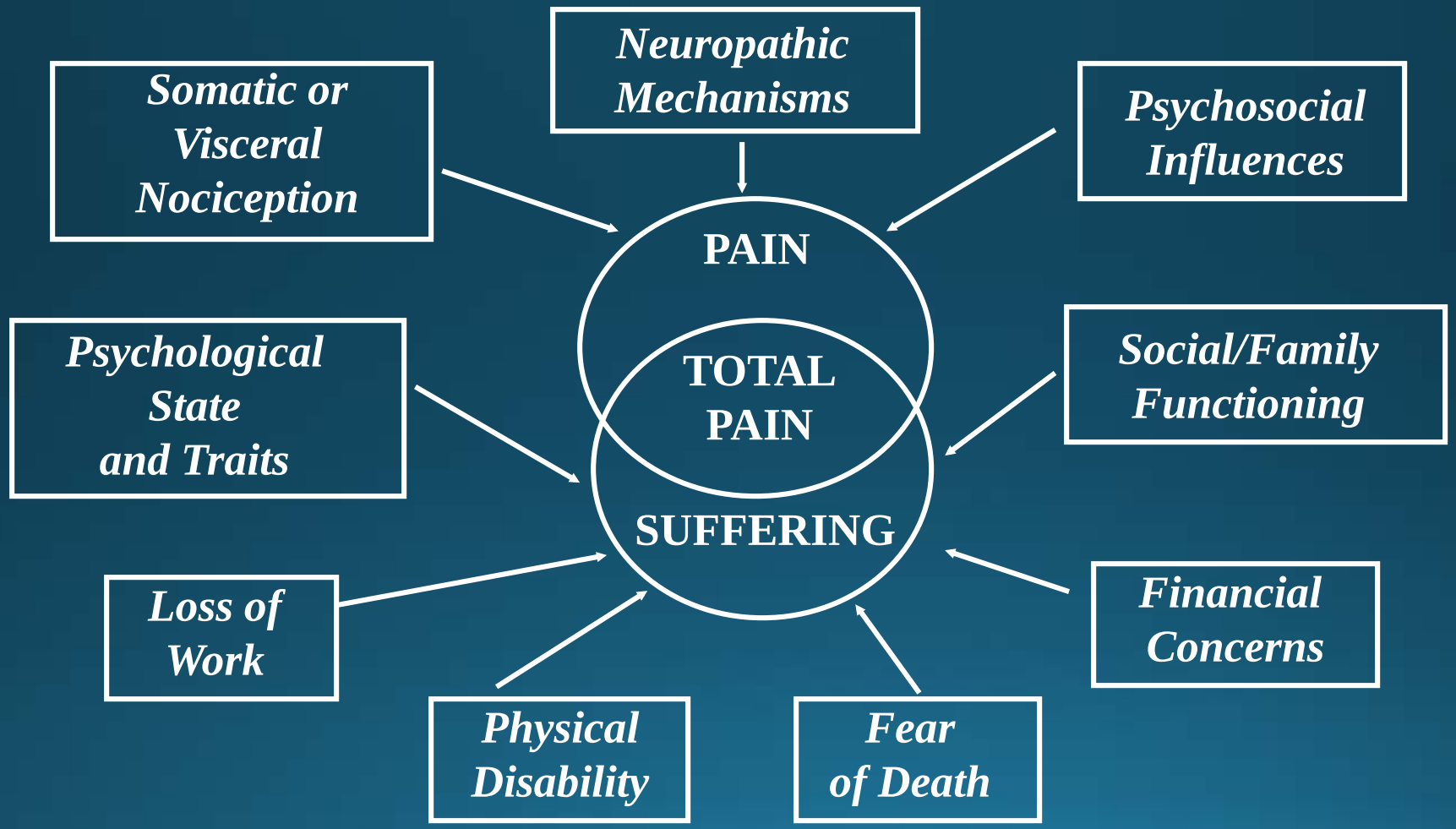
Treatment of Bone Pain

- Limited evidence regarding medications for treating bone pain
- Bisphosphonates have shown partial success by reducing bone pain.
- Radiation therapy
- Steroids
- Opioids

Pain Definitions and Pathophysiology

- …sensory and emotional experience associated with tissue damage or described in terms of such damage –IASP
- Acute / Chronic
- ***Nociceptive pain: somatic / visceral***
- Neuropathic pain
- Basal pain / Breakthrough pain
- Psychogenic pain
- Idiopathic pain

Multifactorial Nature of Pain

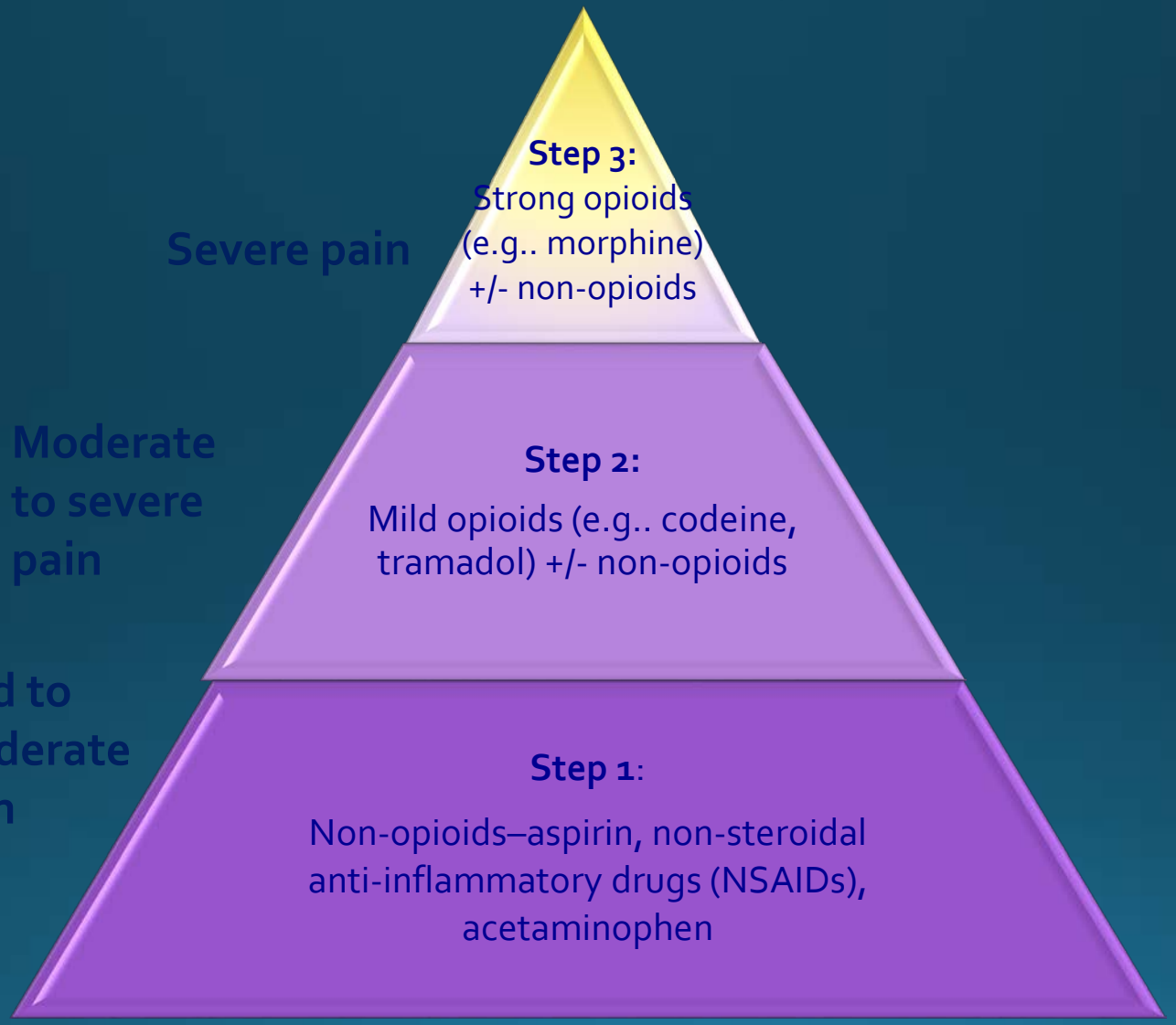


(Adapted from Portenoy, 1988)

Therapeutic Approaches

- Pharmacotherapy
- Rehabilitative
- Psychological
- Anesthesiologic / Surgical
- Complementary and alternative
- Lifestyle changes

Pain Ladder


Severe pain
Step 3:
Strong opioids
(e.g.. morphine)
+/- non-opioids
Moderate to severe pain
Step 2:
Mild opioids (e.g.. codeine, tramadol) +/- non-opioids
Mild to moderate pain
Step 1:
Non-opioids–aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen

Opioid Therapy: Drug Selection

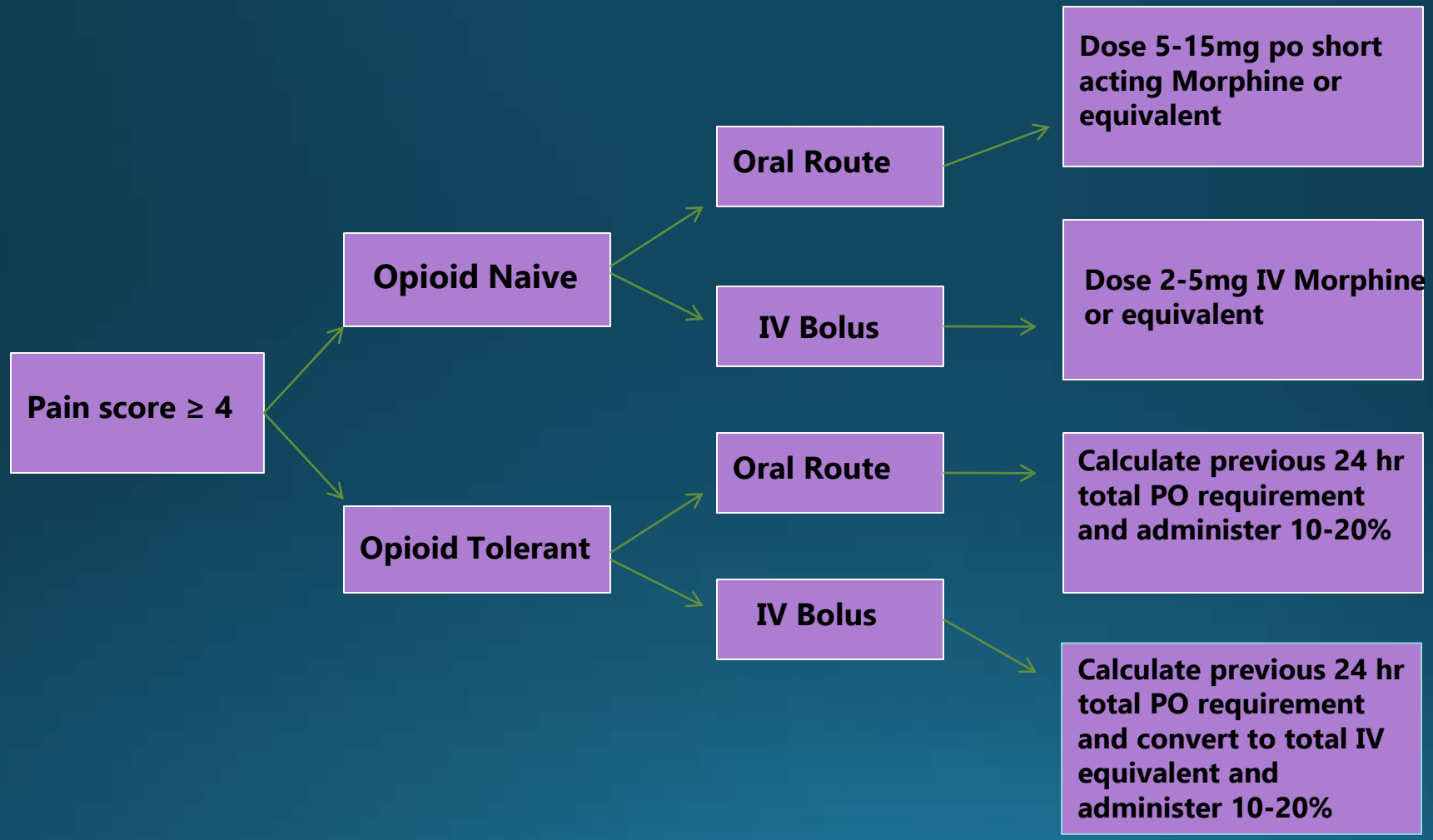
- **Long-acting opioid around-the-clock plus a short-acting opioid rescue dose prn**
  - Preferred approach for patients with cancer pain and selected others with chronic pain
  - Rescue dose may or may not be appropriate for all patients, depending on syndrome and ability to use the drug responsibly
  - Rescue is 5%-15% of total daily dose; usually prescribed "q4h prn" when oral

Portenoy, JCO 2014: Principles of Opioid Use in Cancer Pain

Overview of STRONG Opioids

Opioid	Onset (minutes)	Peak effect (hours)	Duration (hours)	Initial scheduled dose	Available Oral/TD Formulation	Comments
Hydrocodone/ Acetaminophen Hydrocodone ER	PO: 30 PO: 60	1-1.5 5	IR: 4 LA: 12	5/325 mg po q4h 10mg po q12h	Tablet, Liquid, Tablet	Co-ingestion with alcohol increases peak concentration
Morphine	PO: 30	0.5-1	IR: 3-6 LA: 12	LA: 15 mg po q12h, IR: 7.5mg po q 4 hrs prn	Tablet, cap, liquid	Kadian® can be given via PEG tube (16Fr or larger)
Oxycodone	PO: 10-15	0.5-1	IR: 3-6 LA: 12	LA:10 mg po q12h IR: 2.5-5mg po q 4 h prn	Tablet, Liquid	Long acting formulation reformulated to minimize drug abuse
Hydromorphone	PO: 15-30	0.5-1	IR: 3-5 LA: 24	LA: 8mg po once daily IR: 1-2 mg po q4h	Tablet, Liquid	ER Hydromorphone available in 8mg, 12mg, 16mg, 32mg
Methadone	PO: 30-60	1-7.5	Variable	PO: 2.5 mg po q12h	Tablet, Liquid	Multiple drug interactions, monitor electrolytes, QTc
Oxymorphone	PO: 10-15	0.5	8 (IR) 12 (ER)	ER: 10 mg po q12h IR: 5mg po q 6-8h prn	Tablet	Co-ingestion with alcohol and food increases peak concentration
Fentanyl Transdermal	TD: variable, typically takes >5 hours	24-48	72	12mcg patch Q 72 hours	patch	Adjust dose after 3 days. May take up to 2 applications to reach steady state

NCCN Guidelines: Adult Cancer Pain



Adult Cancer Pain. V.1.2010. NCCN Clinical Practice Guidelines. Available at http://www.nccn.org.

Opioid Management

- Opioids are the preferred medications to treat cancer related pain
- Challenges still exist
  - Inadequate pain control
  - Common side effects like nausea and constipation
  - Opioid induced neurotoxicity

Opioid Induced Neurotoxicity (OIN)

- Caused by accumulation of the parent opioid and its metabolites
  - Excessive sedation
  - Hallucination
  - Confusion
  - Myoclonus
  - Seizures

Opioid Rotation (OR)

- Substituting one opioid with another using equianalgesic ratios
- Indications
  - Uncontrolled pain
  - Opioid induced neurotoxicity
  - Common side effects
  - Route of administration
  - Opioid availability

Treatment of OIN

- Opioid rotation
- Dose reduction or discontinuation
- Hydration
- Discontinuation of other contributing drugs
- Symptomatic treatment with neuroleptics

Opioid Rotation for Uncontrolled Pain

- Balance between analgesia and side effects to allow dose escalation
- Large individual variation in response to different mu-agonists
- Incomplete cross tolerance between opioids
- Higher cross tolerance to adverse effects than to analgesic effects

- 31% of cancer out patients and 34% of cancer inpatients required OR by the palliative care team
- Uncontrolled pain most common indication for OR in out patients and adverse effects such as OIN most common indication in inpatients

- 65% of cancer outpatients had successful OR

- 81% of cancer inpatients had a successful OR

- MEDD significantly decreased in patients with successful OR and also in patients with OIN as reason for OR

Reddy 2013; Mercadante 2009

Neuropathic pain

- Tricyclic antidepressants
- Anticonvulsants
- Clonidine
- Corticosteroids
- Local anesthetics

Non Pharmacological Methods of Pain Management

- Distraction
- Relaxation
- Guided Imagery
- Art Therapy

Hypnosis

Exercise

Acupuncture

Music Therapy

Meditation

Biofeedback

Pet Therapy

Reiki


THANK YOU