allycon 2022

"welcome home"

Pain and Neuropathy Management

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I have no disclosures to report for honoraria, payments, or other support from corporate entities.

All mentions of specific medications are provided as examples only; no endorsement is implied for any specific medication. Generic drug names are included unless no generic name is available.

Why I'm Here

A Disclaimer

- Please discuss your pain with your medical team. The advice in the following slides is not a replacement for the advice from the clinicians who know you the best.
- If you have struggled with pain or other symptoms despite interventions from your current team, ask your oncologist if a consultation with palliative care is possible. Palliative Care (or Supportive Care in some places) is a specialty dedicated to controlling symptoms *regardless of the stage of disease.*
- Discuss any supplements or over-the-counter medications you are considering before starting them. This includes medical cannabis (if legal in your jurisdiction), as some chemotherapy agents may have altered effects when used concurrently with cannabis products.

The Language of Pain

Definitions and Manifestations

What is Pain, Really?

"An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage."

The International Association for the Study of Pain recognizes that:

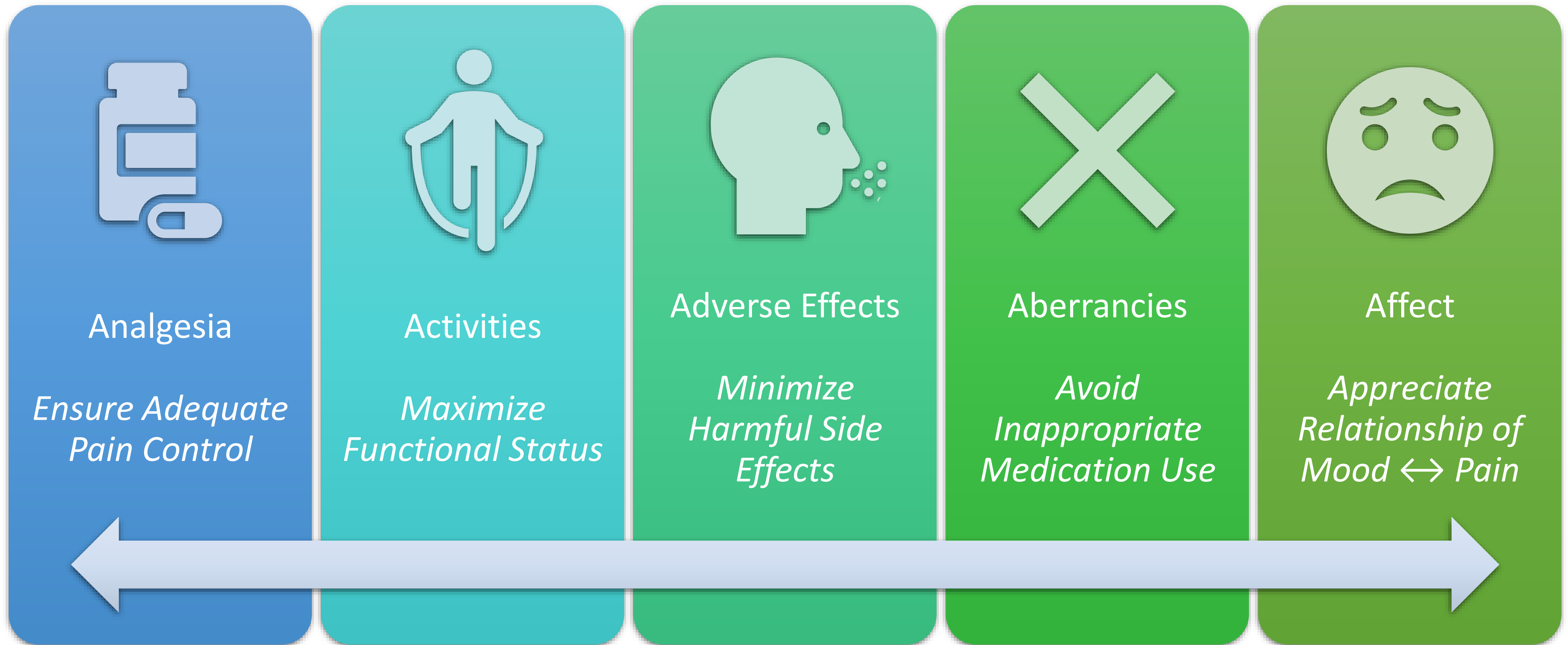
- Pain is always a personal experience that is influenced to varying degrees by biopsychosocial factors.
- Pain and nociception are different phenomena.
- Through their life experiences, individuals learn the concept of pain.
- A person's report of an experience as pain should be respected.
- Although pain usually serves an adaptive role, it may have adverse effects on function and psychological well-being.
- Verbal description is only one of several behaviors to express pain; inability to communicate does not negate the possibility that a human experiences pain.

Assessment of Cancer Pain, UpToDate.com; Accessed 9/4/22

Where Does Pain Come From?

- Tumor invasion
  - Primary pain: tumor directly invades pain-sensitive structures (e.g. bone)
  - Secondary pain: tumor causes obstruction of an organ or other structure (e.g. blood/lymph vessels)
- Radiation
- Surgery
- Chemotherapy
- Non-Cancer-Related Sources

The Five A's of Pain Management



Evaluation of Cancer Pain

Describing Intensity

- Verbal Rating
  - Mild, Moderate, or Severe?
- Numeric Rating
  - “On a scale of one to ten…”
- Visual Analog Rating
  - FACES
  - Pain ‘Thermometer’

Describing Timing and Provoking Factors

- Constant?
- Intermittent?
  - Triggering movements or biological functions
  - Time of day
  - Associated with a particular treatment

Examples for Visual Pain Scales

Visual analog scale (VAS) for pain

For assessment of pain using the VAS, the patient makes a mark on a 10 cm line that corresponds to the intensity of pain. The distance from the "no pain" end of the line to the mark is measured and recorded as the score.

VAS: Visual analog scale.

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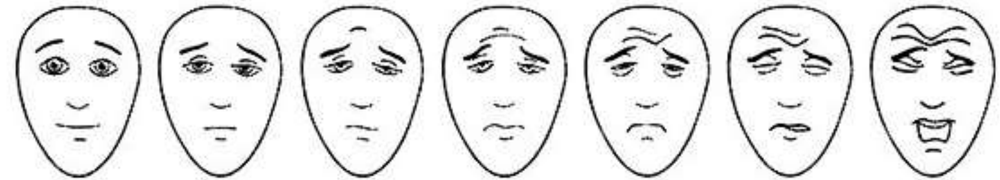
Faces pain scale



Schematic representation of the faces pain scale, rated from 0 to 6 left to right.

Bieri, D, Reeve, RA, Champion, GD, et al. Pain 1990; 41:139. Copyright © 1990 with permission from Elsevier Science.

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Intensity vs. Distress Caused

Memorial Symptom Assessment Scale - Short Form [MSAS-SF]

Patient's Name ___________________________ Date ___/___/___ ID#__________

Instructions:

I. Below is a list of symptoms. If you had the symptom DURING THE PAST WEEK, please check Yes. If you did have the symptom, please check the box that tells us how much the symptom DISTRESSED or BOTHERED you.

Check **all** the symptoms you have had during the PAST WEEK.	Yes [✓]	» IF YES: How much did it DISTRESS or BOTHER you? Not at all [0]	A little bit [1]	Some-what [2]	Quite a bit [3]	Very much [4]
Difficulty concentrating						
Pain						
Lack of energy						
Cough						
Changes in skin						
Dry mouth						
Nausea						
Feeling drowsy						
Numbness/tingling in hands and feet						
Difficulty sleeping						
Feeling bloated						
Problems with urination						
Vomiting						
Shortness of breath						
Diarrhea						
Sweats						
Mouth sores						
Problems with sexual interest or activity						
Itching						
Lack of appetite						
Dizziness						
Difficulty swallowing						
Change in the way food tastes						
Weight loss						
Hair loss						
Constipation						
Swelling of arms or legs						
"I don't look like myself"						
If you had any other symptoms during the PAST WEEK, please list them below, indicating how much the symptom DISTRESSED or BOTHERED you.						
1.						
2.						

II. Below are other commonly listed symptoms. Please indicate if you had the symptom DURING THE PAST WEEK, and is so, how OFTEN it occurred.

Check **all** the symptoms you have had during the PAST WEEK.	Yes [✓]	» IF YES: How OFTEN did it occur? Rarely [1]	Occasionally [2]	Frequently [3]	Almost constantly [4]
Feeling sad					
Worrying					
Feeling irritable					
Feeling nervous					

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What does pain *look* like?

Acute Pain

- Grimacing, tearing up
- Crying, grunting, vocalizations
- Unable to sit still *or* unable to move nearly at all
- Elevated heart rate
- Elevated blood pressure

Chronic Pain

- Lassitude
- Insomnia
- Lack of appetite
- Irritability
- Intermittent “flares” of acute pain, AKA *breakthrough pain*

Nociceptive? Neuropathic?

***Nociceptive* Pain**

- "Typical pain"
- Sharp, dull, throbbing, aching, or pressure-like.
- Associated with tissue damage or local inflammation, which is sensed by pain fibers and transmitted to the brain along traditional pain pathways.

***Neuropathic* Pain**

- "Dysesthesias"
  - Abnormal sensations: Burning, tingling, shock-like, electrical, or "uncomfortable numbness"
  - Hyperesthesia: painful stimulus is perceived as more painful than it should be.
  - Allodynia: non-painful stimulus is perceived as painful.
- Associated with direct pain fiber injury or altered signaling within the nerve structures that is interpreted by the brain as painful.

Visceral? Somatic?

Visceral Pain

- *Visceral: of or pertaining to an organ, usually of the abdomen though could apply to internal structures of the chest as well.*
- Visceral pain is often vague and does not necessarily manifest at the precise location of injury.
- Descriptors include *gnawing* or *cramping*, especially when related to the bowel.
- The liver is unique in that the outer capsule has pain-sensing fibers; capsule stretch due to an enlarged liver can present like somatic pain.

Somatic Pain

- *Somatic: of or pertaining to a structural component of the body, e.g. bone, connective tissue, or muscles.*
- Somatic pain is more localized and specific than visceral pain.
- Somatic pain may be associated with more visible inflammatory signs:
  - Redness
  - Swelling
  - Warmth

A Review of Pain Treatment

Elephant in the Room: Opioid Crisis

Physical Dependence

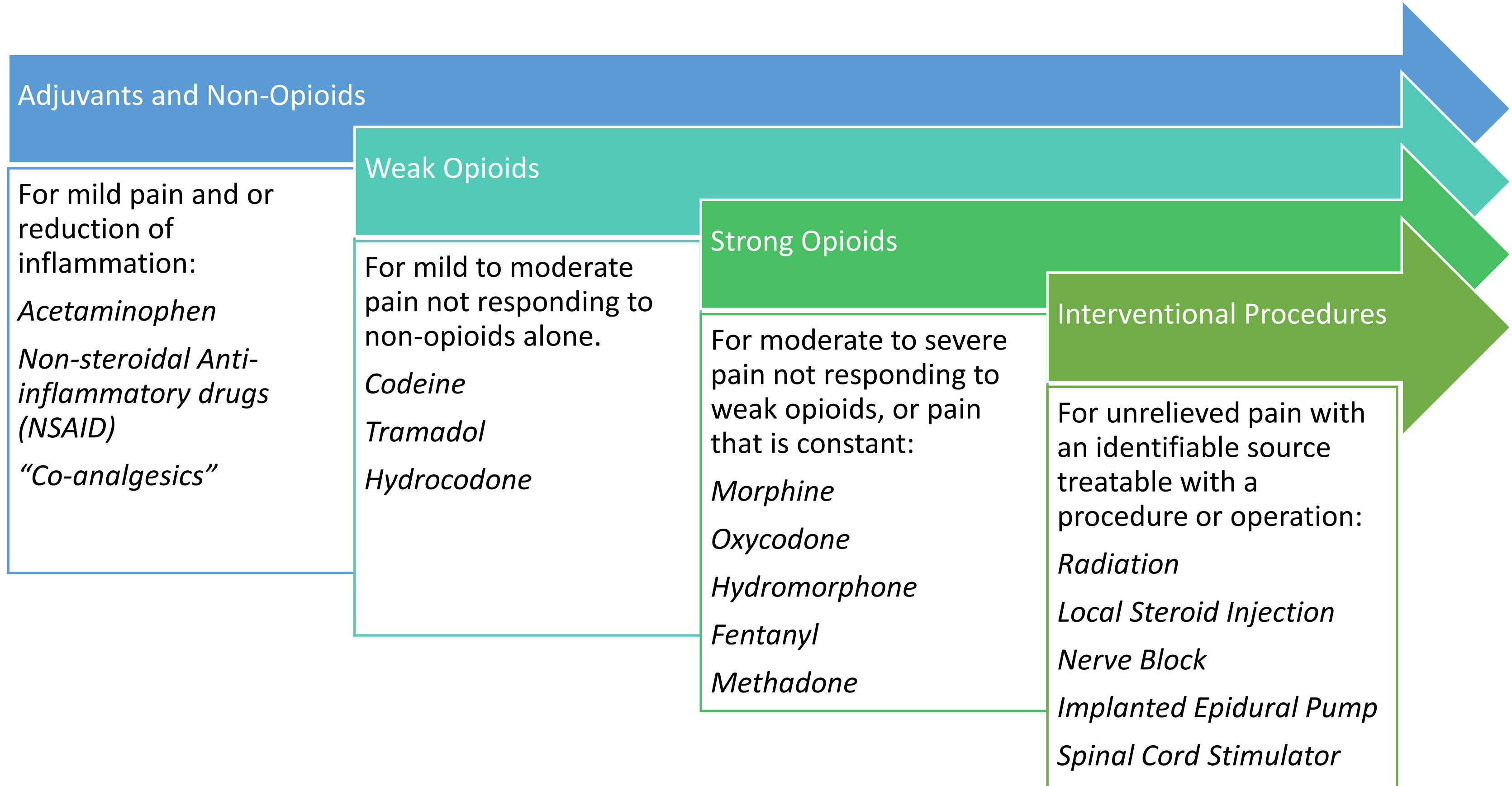
- A natural and expected physiologic (body chemistry) response to long-term use of several types of medication, including opioids.
- Primary cause of *withdrawal symptoms*.
- Managed with gradual tapering of medication.
- Does not imply or guarantee addiction.

Addiction

- A behavioral response to non-pain-relieving qualities of a medication.
- Use of medication is driven less by fear of withdrawal and more by seeking the “high”.
- Occurs *in addition* to physical dependence.
- Threatens social and professional relationships/responsibilities

The Pain Ladder

The World Health Association has maintained the WHO Pain Ladder Model, which has been revised to include minimally invasive and invasive procedures directed towards pain relief



W.H.O. 1990

Step 0: Adjuvant Medication

- Also known as “co-analgesics”; a supplemental medication or procedure, possibly without direct analgesic (pain-relieving) effects, but with potential to improve effect of other analgesic medications or a means of treating the source of the pain.
- These agents are implemented as tolerated through all later steps of the Pain Ladder
- Personal addition: *activity*
  - Remaining active during treatment can minimize progression of pain syndromes and lower need for medications.
  - Activity levels can be maintained with Physical Therapy (PT), Occupational Therapy (OT), and/or Osteopathic Manipulative Treatment (OMT).

- Clonidine
- Antidepressants
  - SNRI: Duloxetine, venlafaxine
  - TCA: Nortriptyline, amitriptyline
- Anticonvulsants
  - Gabapentin, pregabalin
- Anti-osteoporotics
  - Denosumab, zoledronic acid
- Steroids
  - Dexamethasone, prednisone
- Anesthetics
  - Topical lidocaine
  - Topical/infused ketamine

Step 1: Non-Opioid Analgesics

- Non-opioid analgesics include many medications that are available “over-the-counter” (OTC).
- OTC medication may be available in higher “prescription-strength” doses.
- Some forms of non-opioids will require a prescription
- All non-opioid medications require some form of monitoring for adverse effects, *even if they are available over-the-counter.*

- Acetaminophen (oral or IV)
- Non-steroidal anti-inflammatory drugs
  - Ibuprofen
  - Naproxen
  - Ketorolac (oral or IV)
  - Diclofenac (oral or topical)
  - Turmeric (curcumin)

Step 2: Weak Opioids

- Indicated for mild to moderate cancer-related or post-procedural pain
- Most agents are intended for intermittent use
  - Exceptions:
    - Tramadol hydrochloride ER (24 hr)
    - Hydrocodone bitartrate ER (24 hr)
    - Buprenorphine transdermal (weekly) or transmucosal (12 hr)

- Codeine (200 mg ≅ 25 mg morphine)
- Tramadol (120 mg ≅ 25 mg morphine)
- Tapentadol (100 mg ≅ 25 mg morphine)
- Hydrocodone (25 mg ≅ 25 mg morphine)
- Buprenorphine (It's complicated)

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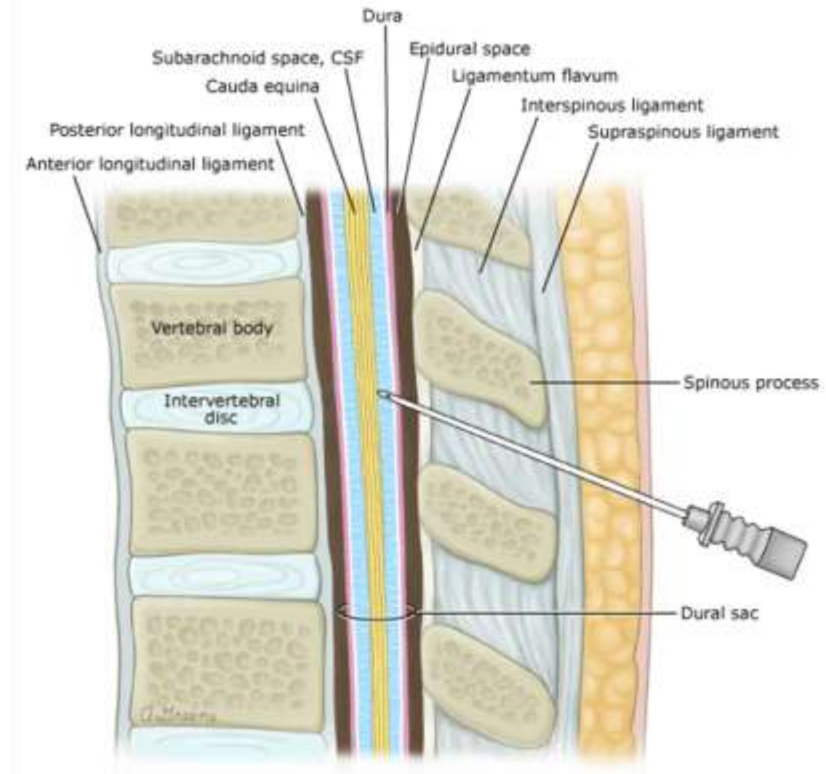
Step 3: Strong Opioids

- Indicated for moderate and severe pain.
- All are available in immediate-release formulations for acute pain, and in extended-release formulations to address constant pain.
- Methadone is unique as it has both immediate and extended-release properties, though it requires special training to dose appropriately.

- Morphine
- Oxymorphone
- Oxycodone
- Hydrocodone
- Fentanyl
  - Transdermal (patch)
  - Transmucosal (lozenge, spray, etc.)
- Methadone

Step 4: Interventional Procedures

- Steroid Injections
- Standard Nerve Blocks
  - Abdominal Pain
    - Celiac plexus
    - Splanchnic nerves
  - Pelvic/Perineal Pain
    - Hypogastric plexus
    - Ganglion Impar
- Lumbar Sympathetic Nerve Block
  - Rectal tenesmus (painful spasms)
- Kyphoplasty/Vertebroplasty
  - Pain due to compression fractures in spine
- Epidural Infusion
  - May be semi-permanent with an intrathecal (in the spinal cord) pain pump
- Spinal Cord Stimulator



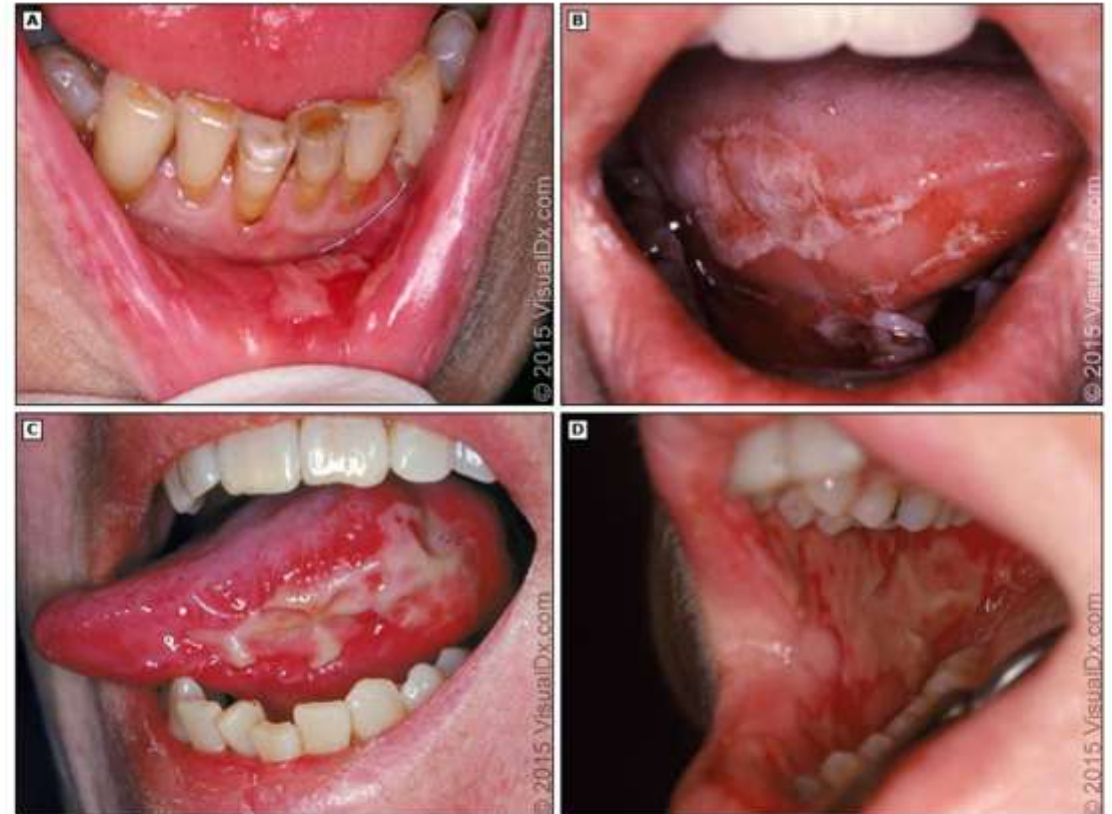
Targetable Sources of Pain

Acute Pain Crises: Things To Know

- Acute events can precipitate severe pain that can be refractory to medications on hand. Some of these events require prompt intervention to prevent further complications or threats to life.
- Examples
  - Pathologic fracture
  - Severe tumor bleeding
  - Obstruction (intestinal or bile system)
  - Deep vein thrombosis
- If you experience sudden, uncontrolled pain that is not responding to your medication seek urgent medical attention. Do not adjust your medication without first discussing with a clinician.

Mucositis

- Associated with multiple chemotherapy classes, including the those frequently used in colorectal cancers:
  - Fluorouracil
  - Capecitabine
  - Irinotecan
- Can affect the entire gastrointestinal tract, though most distressing symptoms are noted when it is present in the mouth and throat.
- Treatment is contingent on good oral hygiene practices. Chlorhexidine rinses without signs of active infection are not recommended.
- Symptoms may be controlled with multiagent topical rinses/washes, though these often require compounding and prescriptions are required.
- Cryotherapy can be useful for prevention in patients receiving 5-fluorouracil infusions
- Risk of diarrhea associated with gastrointestinal mucositis may be reduced with *Lactobacillus* probiotic.
- Painful rectal mucositis (proctitis) caused by radiation may benefit from treatment with hyperbaric oxygen.



Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology Clinical Practice Guidelines for Oral Mucositis; October 2021

Chemotherapy-Induced Neuropathy

- Strongly associated with agents used in colorectal cancer, including oxaliplatin
- Symptoms can be sudden in onset (e.g. pharyngolaryngeal spasm) or they may slowly build in intensity over time.
- There is an association between severity of symptoms, length of treatment, and dose of offending medication.
- Neuropathic symptoms can occur with a rash on the hands and feet, often called hand-foot syndrome (palmar-plantar erythrodysesthesia syndrome)

- Recommendations for treatment are primarily based on trials of medication for *non-cancer* neuropathy, though this has been improving.
- Specialists may recommend:
  - Anti-seizure medication
    - Gabapentin
    - Pregabalin
  - Anti-depressant medication
    - Duloxetine
    - Nortriptyline
  - Topical lidocaine
  - Combination topical compounded products
- Unknown if effective: alpha lipoic acid

National Comprehensive Cancer Network: Adult Cancer Pain Guidelines 2.2022

Radiation Enteritis and Proctitis

- Enteritis: inflammation of the small bowel
- Proctitis: inflammation of the rectum and sigmoid colon
- Pain is worsened with vomiting and/or with defecating
- Preventative use of anti-nausea medication may be considered
- Stool softeners can lower pain experienced with defecation, especially if opioid medications are contributing to constipation
- Persistent pain or pain with bleeding may require topical or endoscopic treatment

Summary

- Communication is essential
- Use functional status (abilities lost and/or desired) as a guide
- Opioid medication may be necessary for adequate pain control
- Physical Dependence is *not* equivalent to addiction
- Pain is subjective: no one can fully experience someone else's pain
- Pain may not be visible, especially if chronic
- The human body is incredibly adaptable

Further Reading

National Comprehensive Cancer Network

www.NCCN.org/patients

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