Relief at last:

Pain management for the hospitalized patient

Hannah Farfour DNP, AGNP-c, ACHPN
Division of Palliative Medicine
Mayo Clinic Arizona

Objectives

- Describe types/classifications of pain
- Identify a variety of pharmacologic tools to manage acute and chronic pain.
- Review safe opioid practices in the hospital setting.
- Integrate non-pharmacologic interventions to help with pain management.

Pain

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

IASP, 1994

Pain

Pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors.

Pain and nociception are different phenomena. Pain cannot be inferred solely from activity in sensory neurons.

Through their life experiences, individuals learn the concept of pain.

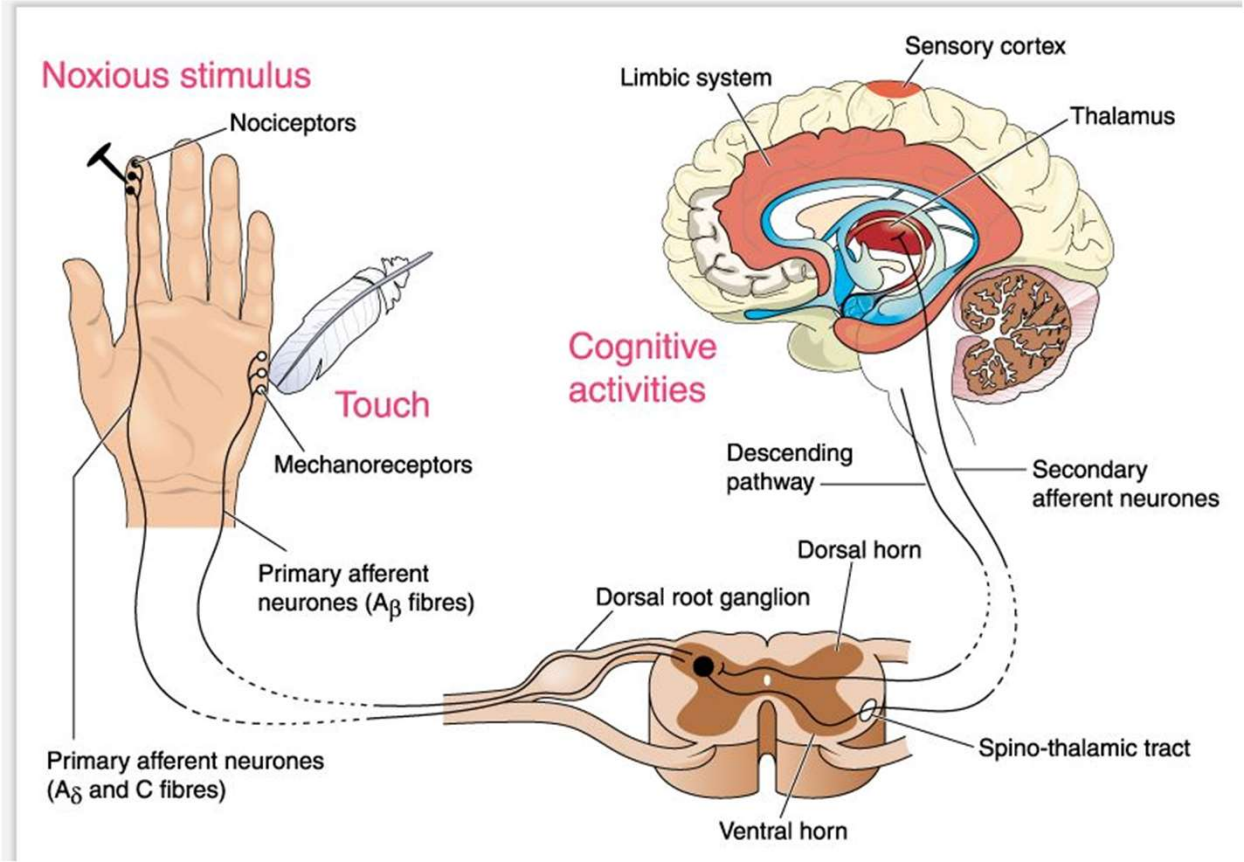
A person's report of an experience as pain should be respected.

Although pain usually serves an adaptive role, it may have adverse effects on function and social 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 or a nonhuman animal experiences pain.

IASP, 1994

PAIN is complex!



Types of pain

Acute pain: < 6 months, typically a cause/injury

Chronic pain: > 6 months, persists after original injury heals

Nociceptive pain: caused by stimulation of nociceptors (pain receptors for a tissue injury)

Visceral: internal organs
pressure/aching/squeezing/cramping

Somatic: skin, joints, connective tissues, bones
aching/gnawing sensation/ deep or superficial

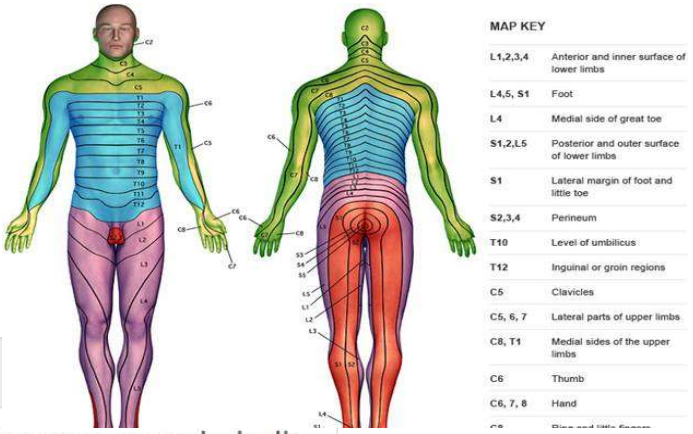
Neuropathic pain: damage to or dysfunction of the nervous symptom
burning/freezing/numbness/tingling/shooting/stabbing/electrical shocks

Assessment

Help me understand what your pain feels like.

- Where, when, why, how?
- Location, radiation, mode of onset, character, temporal pattern, exacerbating and relieving factors, intensity
- Impact on mood, usual activities, function, QOL, sleep
- Tools for pain assessments: NRS, VAS, verbal/categorical, FACES, pain drawings
- Expectations for pain management and current understanding
- Previous pain and treatment history
- Concurrent symptoms

Physical Assessment



Examination	Observation
Inspection	Cutaneous landmarks, symmetry, temperature, trauma, muscle bulk
Palpation/percussion	Tenderness, masses, trigger points, pulses Tinel sign, fractures
Range of motion	Described in degrees, reason for motion limitation
Strength	Graded 0–5
Sensation	Gain or loss of sensory function is tested and findings described in terms of dermatomal versus peripheral nerve distribution
Reflexes	Graded 0–4
Provocative maneuvers	Performed for appropriate symptomatic region to further narrow differential diagnosis

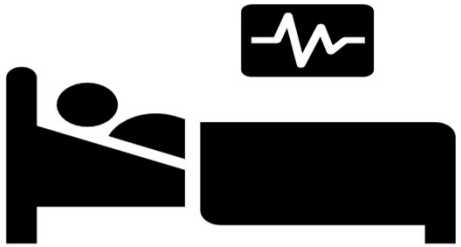
Management

Case 1: Mr. Johnson

Mr. Johnson is a 37-year-old male with a history of fibrotic, stenotic, Crohn's disease with multiple resections admitted with a 3 days history of severe abdominal pain, nausea and vomiting.

Pertinent clinical information:

CT of abdomen shows an acute Crohn's flare and possible stricture/obstruction
CBC significant for mild anemia
Renal and liver function WNL
No BM in 4 days



Current pain management:

Steroids
NSAIDS
Acetaminophen

Physical exam:

Diaphoretic, appears uncomfortable, tachycardic, abdomen distended and tender

CASE 1: Mr. Johnson

Pain characteristics:

Sharp, stabbing, with crampy components, radiating diffusely across lower abdomen, currently an 8/10, improves to a 6/10 with Toradol. Acetaminophen not helpful. Pain relief goal 2/10.

Pertinent history:

What has worked for you in the past for pain management?

Develops pruritus with morphine
PDMP reviewed
Intermittent acetaminophen or ibuprofen use at home
Gabapentin 900 mg tid for chronic visceral pain

Actions:

Frame expectations
Manage concomitant symptoms (nausea/anxiety)
Initiate IV opioids in addition to present management
Consult surgery

Commonly used pain medications

Medication	Usual dose	Max dose	Characteristics
Acetaminophen	Weight ≥50 kg: 650 mg IV/PO every 4-6 hours or 1000 mg PO/IV every 6-8 hours Weight <50 kg: 12.5 mg/kg IV every 4 hours or 15 mg/kg IV every 6 hour	Weight ≥50 kg: 4000 mg IV Weight <50 kg: 75 mg/kg per day up to 3750 mg IV	• Short-term treatment of mild to moderate acute pain and febrile conditions. • Onset 5 to 10 minutes. • Minimal alteration of platelet functioning. • Less risk of GI bleeding, renal, and cardiovascular toxicity than nonselective NSAIDs. • Lacks antiinflammatory activity. • Patients should be well hydrated. • Avoid or use a lower total daily dose (maximum 2000 mg per day) in older adults, patients at risk for hepatotoxicity (regular alcohol use, malnourished) or with significant renal or hepatic impairment.

Commonly used pain medications

Medication	Usual dose	Max dose	Characteristics
Ketorolac	Age <65 years and weight ≥50 kg: 15 to 30 mg IV every 6 hours Age ≥65 years or weight <50 kg: 15 mg IV every 6 hour	Age <65 years and weight ≥50 kg: 120 mg IV per day for up to five days Age ≥65 years or weight <50 kg: 60 mg per day IV for up to five days	• Onset ~30 minutes. • Duration of platelet dysfunction ~24 hours. • Risk of gastropathy and renal failure is related to dose and duration of use. • Patients should be well hydrated and without significant kidney disease (CrCl >60 mL/minute). • Avoid use in patients with a history of ischemic heart disease, stroke, or heart failure.

Commonly used pain medications

Medication	Usual dose	Max dose	Characteristics
Ibuprofen	400 to 800 mg PO/IV every 6 hours	3200 mg PO/IV	• Onset ~30 minutes. • Duration of platelet dysfunction ~8 hours. • Patients should be well hydrated and without significant kidney disease (CrCl >60 mL/minute). • Recommended infusion regimen requires 30 minutes and administration in 100 mL volume per 400 mg dose or 200 mL per 800 mg dose. • Avoid use in patients with a history of ischemic heart disease, stroke, or heart failure.

Additional Medications

Muscle relaxers

- methocarbamol, baclofen, cyclobenzabrine

Gabapentin/pregabalin

SNRIs/SSRIs

- Duloxetine/desvenlafaxine/milnacipran/desvenlafaxine

Starting doses for opioid naïve patients

Drug Name	Oral dose	Intravenous Dose
Morphine	5 mg PO/SL 7.5 mg (15 mg pill cut in half)	2 mg
Hydromorphone	1 mg (2 mg pill cut in half)	0.2 mg
Oxycodone	2.5 mg (5 mg pill cut in half)	-
Hydrocodone	5 mg	-

(CAPC,2020)

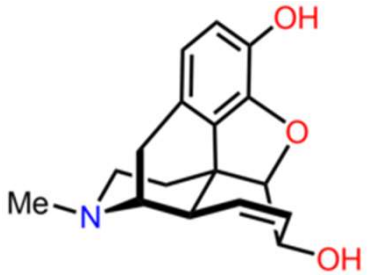
Opioid conversions

Equianalgesic doses

Morphine	Oxycodone	Hydromorphone	Fentanyl
PO 30mg IV 10mg	PO 20mg	PO 7.5mg IV 1.5mg	IV 100mcq

(CAPC,2020)

Opioids



Time to peak effect / Duration of Action

PO Opioids: 30-60 minutes / 3-4 hours

IV Opioids: 5-15 minutes / 2-4 hours

Time to peak effect is the same for analgesia, relief of dyspnea, and sedation

<u>Other Opioid Principles</u>:

If initial dose of IV opioid is ineffective after 2 doses at least 15 minutes apart, double the dose

Typically **need 6-8 hours of controlled symptoms to calculate a continuous opioid infusion**
If starting a continuous infusion, do not change more often than every 6 hours. Adjust infusion dose based on the 24-hour sum of PRNs

(CAPC,2020)

Case 1- Mr. Johnson

Day 2:

Start hydromorphone IV 0.2 mg IV q 2 hours prn for pain
Surgery does not want to take to OR for stricture
GI continues to manage Crohn's flare

Day 3:

24- hour review:
Hydromorphone IV 0.2 mg q 2 hours x 4 doses
Increased dose to 0.4 mg q 2 hours x 8 doses
Pain continues to be sharp, cramping, rated 6/10, relief from IV administration lasts about 90 mins
Surgery elects to take him to OR later today for exploratory lap

Time to start a PCA?

Case 1- Mr. Johnson

PCA Initiation:
IV Hydromorphone use in 24 hours = 4 mg
4 mg/24 hour = 0.167

PCA settings:
CI 0.1 mg hr w/ 0.1 mg q 15 mins PRN, lockout 2.0 mg

Mr. Johnson goes for an exploratory laparotomy and ended up doing a bowel resection.

Case 1- Mr. Johnson

Day 17:
Transfers back to your service, remains on PCA due to several complications but doing and feeling better. Tolerating a soft diet. Eager to discharge home ASAP.

Current settings:
0.4 mg CI with 0.2 mg q 15 min bolus
Total usage in 24 hours, 10.6 mg (5 boluses)
Dose conversion 1 mg hydromorphone IV = 20 mg of oral morphine
MME 212

Remains on prn acetaminophen
Of note, on ketamine infusion during surgical and post-surgical stage

Next steps?

Case 1- Mr. Johnson
The Science and Art of the Taper

Day 17- until discharge:

- Engage in shared decision making
- Write an opioid exit strategy, plan for taper continue to work together until discharge
- Initiate 6 mg of oral hydromorphone q 3-4 hours prn or oxycodone 10 mg q 3-4 hours prn (can dose reduce for non-cross tolerance)
- Educate on and monitor for symptoms of withdrawal
- Schedule acetaminophen or other appropriate non-opioid medications
- Maximize other non-pharmacologic tools: breathing, guided imagery, etc.
- Goal is to drop a dose/reduce dose over days to weeks.

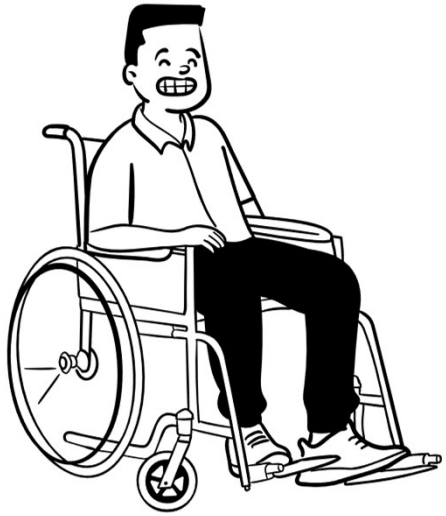
Case 1- Mr. Johnson
Plan for success

Discharge Planning:

Goal is to drop a dose/reduce dose over days to weeks. Patient led.

Ensure proper prescribing for a taper at discharge, including **naloxone** script.

If any barriers, ensure that there is follow-up for patient for continued prescribing/taper.



Case 2- Mrs. Robbins

Mrs. Robbins is an 82-year-old with history of Alzheimer's dementia, osteoporosis, and severe OA admitted due to a fall. She has multiple contusions, a subdural hematoma, 2 rib fractures, and a fractured wrist.

Pertinent clinical information:
Engaged in advance care planning/serious illness communication
Outcome: Conservative management
Agitated, crying, per family, more confused than baseline
1:1
Creatinine 1.9

Current pain management:
Tramadol 50 mg q 6 hours prn ordered
Acetaminophen prn ordered

Physical exam:
Diaphoretic, guarding wrist/chest, restless, brow furrowed, dilated pupils

Case 2- Mrs. Robbins

Pain Characteristics

FACES scale 10/10

Pertinent history

Care facility notes and family report

Pain managed with prn acetaminophen and CBD creams

PDMP reviewed

Received 4 mg of morphine IV for pain and a dose of 1 mg lorazepam for agitation in ED

Actions

Treat pain with multimodal interventions

Schedule acetaminophen 1000 mg q 8 hours

Topicals/lidocaine patch

Treat other symptoms (ie, constipation)

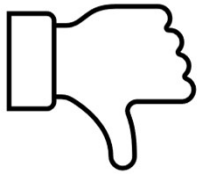
Consult pain colleagues (? intercoastal block)

Discontinue tramadol

Hydromorphone 1 mg PO or oxycodone 2.5 mg PO q 4 hours prn

Avoid morphine due to renal function

Trama“Don’t”



- SNRI and opioid effects
- Unpredictable kinetics
- Risk for seizures and hypoglycemia
- Drug-drug interactions

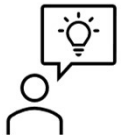
https://geripal.org/tramadont-dangers-of-tramadol/#summary

Case 2- Mrs. Robbins

Day 3:

Remains confused, restless/agitated
Not taking in PO
FACES Scale
Consider IV versus something transdermal
Nursing interventions in place for the non-pharmacologic management of delirium and dementia
Goal: Return to memory facility ASAP

Fentanyl patch OR Buprenorphine???



BUPRAWHAT??

Common formulations

Pain

OUD

Drug	Formulation	Doses	Indication	Administration
Buprenorphine patch (Butrans)	Weekly patch	5/7.5/10/15/20 mcg/hr	Pain Chronic pain at high risk of an unintentional OD and < 80 mg/d of oral morphine	• Rotate patch sites • Apply to fatty location • Can titrate Q 72 hours, but usually Q 7 days • Max dose is 20 mcg
Buprenorphine (Belbuca)	Buccal film	75/150/300/600/750/900 mcg	Pain	Dissolves inside of mouth in 30 mins (no chewing/swallowing)
Buprenorphine/naloxone (Suboxone)	Buccal film SL tablet	Film: 2/0.5 mg 4/1 mg 8/2 mg 12/3 mg SL Tablet: 2/0.5 mg 8/2 mg	OUD Off-label for pain	Dissolves under tongue in 5-7 mins
Buprenorphine (Subutex)	SL tablet	2 mg 8 mg	OUD Off-label for pain	Dissolves under tongue in 5-7 mins

True or false??

BUP is a schedule 2 medication

An “X-waiver” is required to prescribe BUP for <u>pain</u>

An “X-waiver” is no longer required to prescribe BUP for <u>OUD</u>

PRN opioids are contraindicated with BUP

BUP just as likely to cause respiratory depression as other opioids

Receptor pharmacology: Why bup is so unique…….

Receptor	Action	Effect(s)
mu opioid receptor (spinal >>> brain binding)	“partial” agonist with very high affinity and slow dissociation (trend toward no longer deeming "partial" agonist)	• analgesia • lower risk of respiratory depression (because of spinal vs. brain binding propensity)
kappa opioid receptor	antagonist	• antidepressant • lower abuse potential • slows opioid tolerance • potentially reduced hyperalgesia
opioid receptor-like 1 (ORL-1)	agonist	• diminished nociception • enhanced mu receptor expression
G-coupled protein receptor (Gi pathway; alpha subunit)	promotes dissociation of alpha subunit	• reduced nociceptive action potentials • reduced presynaptic substance P
voltage gated sodium channels	inhibitor	• local anesthetic effect

BUP pharmacokinetics

	IV	Transdermal	Sublingual	Buccal
Time to peak	5 mins	3 days	30 mins to 1 hour	2.5-3 hours
Half life	2.2-3 hours	Approx. 26 hours	Approx. 37 hours	27.6 hrs (+/- 11.2 hrs)
Duration of action	6-8 hours	7 days	6-8 hours	12 hours

BUP pharmacokinetics ADME

Bioavailability

- Oral bioavailability of buprenorphine is very low, roughly 15% due to extensive first pass metabolism
- Sublingual bioavailability of buprenorphine is average, roughly 50%
- Buccal bioavailability varies between 28-65%
  - Increased if wounds / mucositis → avoid
- Transdermal bioavailability is 15%

Distribution

- Large volume of distribution
- Buprenorphine is approx. 96% protein bound

Metabolism

- Primarily hepatic → reduce initial doses in severe impairment
- CYP3A4 interactions exist

Elimination

- 70% fecal 30% urine → does not require renal dose adjustments

Adverse effects:for better, or worse

- Similar to other opioids, but **less**:
  - Euphoria / abuse potential
  - Constipation
  - Respiratory depression
    - Rare, but can still occur, esp. if concomitant CNS depressants
    - More difficult to reverse with naloxone
  - Immune suppression
  - Tolerance
  - Depression with long-term use
  - Adrenal insufficiency
- QTc interval prolongation (dose related, less significant in patch, film)
- Transdermal:
  - Erythema and pruritus at patch site (15%); do not re-use application site for at least 21 days
- Buccal / sublingual: dental problems (decay, cavities, infection, tooth loss)
  - After completely dissolved, rinse / swallow with water

Butrans/Buprenorphine Transdermal

Route: Once a week transdermal patch
Strengths: 5/7/10/15/20 mcg/hr
Indication:

- Pain
- Patients with chronic pain that are at high risk of unintentional overdose and use < 80 mg/d of oral morphine

Butrans/Buprenorphine Transdermal

Administration considerations:

- Rotate patch sites Q 7 days
- Apply to a fatty location
- Titration can occur every 72 H
- OK to use 2 patches at one time to achieve dose
- May not appear in UDS
- OK to tape patch down
- If patch falls off, apply a new one and start 7-day cycle over
- Don’t use patch in hot tub / sauna

Titrating Buprenorphine Transdermal

- May increase every 72 hours- (may double patches)
- If max out on Butrans, can rotate to Belbuca versus a full opioid agonist

Oral Morphine Milligram Equivalent Conversion Factors

Opioid (strength in mg except where noted)	Oral MME Conversion Factor*
Buprenorphine, buccal film (mcg)	N/A†
Buprenorphine, tablet or film‡	N/A†
Buprenorphine, transdermal patch (mcg/hr)	N/A†

Initiating Butrans Transdermal

- Opioid Naïve <30 MME
  - Buprenorphine 5 mcg/hr applied once Q 7 days

- Opioid Tolerant 30-80 MME
  - Buprenorphine 10 mcg/hr applied once Q7 days
  - Consider taper the current OTC opioid to less or equal to 30 mg/day for up to a week to mitigate withdrawal **impractical**
  - Consider continuing with prn use of current immediate release opioid

Case 2- Mrs. Robbins

Day 5:

- Ended up starting a 5 mcg/hr q 7 day buprenorphine patch
- Continue with scheduled acetaminophen and topical lidocaine patch (rib fractures)
- S/p intercostal nerve block (able to sit still to tolerate procedure)
- Eating, starting to be more active
- Cleared to go back to Memory Care Center and comfortable with use of patch

Case 3- Mrs. Jones

Mrs. Jones is a 46- year-old with a history metastatic triple negative breast cancer, s/p L breast removal and radiation with recurrence, now on 3rd line systemic treatment with chemotherapy and immunotherapy. She is admitted with intractable abdominal/chest pain.

Pertinent clinical information:
CT Chest/Abdomen shows new large liver lesions and a R sided large pleural effusion in lung
Creatinine 0.68
Cardiac workup negative
LFTs slightly elevated

Current pain management:
ED ordered 4 mg of IV morphine q 4 hours PRN

Physical exam:
Crying, guarded, tachycardic, dyspneic (no supplemental O2 required)

Case 3- Mrs. Jones

Pain characteristics:

Constant, sharp, stabbing, radiating diffusely across right upper quadrant through back, currently an 9/10, improves to a 7/10 with IV morphine. Pain relief goal 4/10.

Pertinent history:

What has worked for you in the past for pain management?

PDMP reviewed
Morphine 60 mg PO q 12 hours for chronic cancer associated pain
Taking morphine 30 mg immediate release 5 x a day MME 270
Intermittent acetaminophen (not helpful) or ibuprofen (holding due to chemo) use at home
Gabapentin 1200 mg tid for neuropathy

Actions:

Frame expectations
Manage concomitant symptoms
Initiate IV opioids
Consult IR/Pulm for evaluation of thoracentesis

Severe cancer pain is a medical emergency and should be addressed promptly!

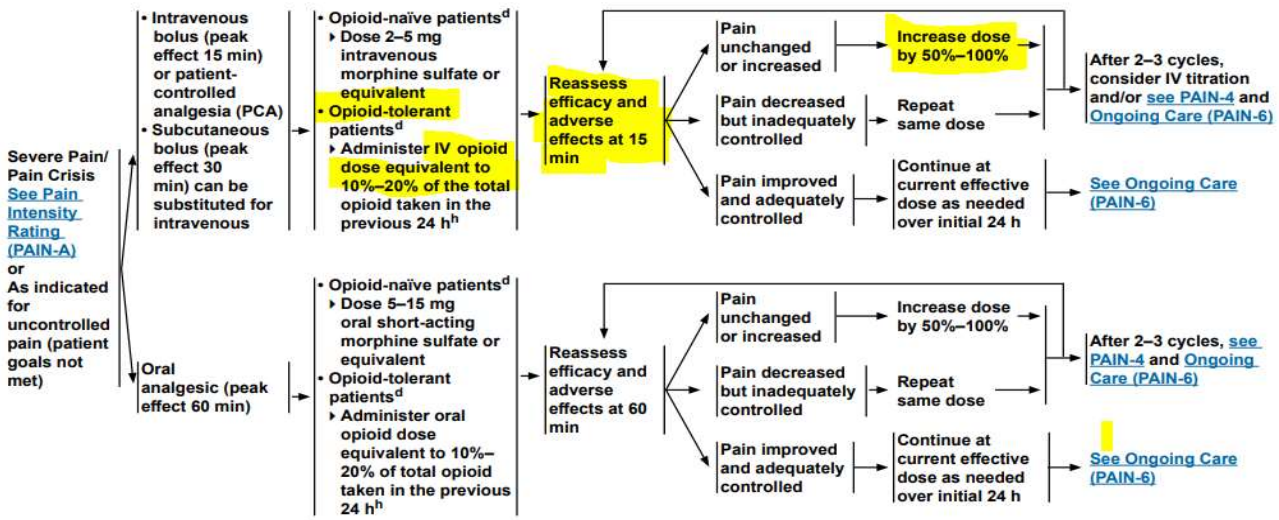
National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2021
Adult Cancer Pain

NCCN Guidelines Index
Table of Contents
Discussion

MANAGEMENT OF PAIN CRISIS

Monitor for acute and chronic adverse effects. See Management of Opioid Adverse Effects (PAIN-H)



[d] Opioid-naïve patients are those not chronically receiving opioid analgesic on a daily basis and therefore have not developed significant tolerance. Opioid tolerant includes patients who are chronically receiving opioid analgesic on a daily basis.The FDA identifies tolerance as receiving at least 25 mcg/h fentanyl patch, at least 60 mg of morphine daily, at least 30 mg of oral oxycodone daily, at least 8 mg of oral hydromorphone daily, or an equianalgesic dose of another opioid for a week or longer.
[g] Dose and titrate with caution in patients with risk factors such as decreased renal/hepatic function, chronic lung disease, upper airway compromise, sleep apnea, and poor performance status.
[h] Not including transmucosal fentanyl dose.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

NCCN Guidelines Adult Cancer Pain. Retrieved from pain.pdf (nccn.org) on 1/18/22

Case 3- Mrs. Jones

Plan:

MME: 270
IV morphine: PO morphine 1:3
10-20% for initial dose
Administer 10 mg of IV morphine x 1 and evaluate for response after 15 mins

After 15 mins, pain reduced to 7/10
Repeat the same dose x 1-2 x
Initiate a PCA

PCA Settings:
MME 270/3= 90 mg of IV morphine/24= 3.75
4 mg CI with 2 mg of IV morphine q 15 mins prn
Evaluate relief after 4-6 hours and adjust dosing accordingly
Monitor closely for relief/accumulation of medication and titrate accordingly

Also, may choose to continue to 60 mg of extended- release morphine and use a bolus only PCA

Case 3- Mrs. Jones

Plan:

- Initiated PCA
- Address any modifiable symptoms
- Consult Palliative Care/Oncology/Pain if available
- If not available, consult with prescriber to collaborate on a plan

FINAL PEARLS

Understand the complex physiology of pain and types of pain.
Acute and chronic pain require a multimodal approach to management.
Know your pharmacology for opioids and non-opioids.
All patients deserve to have their pain treated with the right tools.

References

"Part III: Pain Terms, A Current List with Definitions and Notes on Usage" (pp 209-214) Classification of Chronic Pain, Second Edition, IASP Task Force on Taxonomy, edited by H. Merskey and N. Bogduk, IASP Press, Seattle, ©1994. Foster, Bethany et al. Buprenorphine. Journal of Pain and Symptom Management 2013; 45:5 939-949.

Calderon, Raul et al. Buprenorphine for Chronic Pain. Journal of Pain & Palliative Pharmacotherapy. 2013; 27:4 402-405

Chan, C. (2021, October 11). Approach to Management of Acute Pain. (299) In Curbsiders. https://thecurbsiders.com/podcast/299

Arbuck, Dmitry. Buprenorphine: A Promising Yet Overlooked Tool. Practical Pain Management. Accessed June 11 2019

Hans, G, Cruciani, R.A. Knotkova, H (eds.). Handbook of Methadone Prescribing and Buprenorphine Therapy. 2013 Chapter 10; 109-137.

Giron, S et al. Demystifying buprenorphine with current evidence-based practice in acute and chronic pain management, *AANA Journal*, 2022; 90(3): 225-33.

Golcic, Marin et al. Differences Between Transdermal Fentanyl and Buprenorphine in the Elderly Hospice Patients. Pain Research and Treatment. Volume 2018. October 2018.

Induru, Raghava et al. Buprenorphine for Neuropathic Pain – Targeting Hyperalgesia. American Journal of Hospice and Palliative Medicine. 2009. Vol 26(6) 470-473.

Childers, Julie, Arnold, Robert. Treatment of Pain in Patients Taking Buprenorphine for Opioid Addiction. Fast Facts and Concepts #221. January 2018.

Johnson, Rolley et al. Buprenorphine Considerations for Pain Management. Journal of Pain and Symptom management. 2005 Vol 29(3) 297-326.

Matthias R., Dougherty, P., Raja, S. (Ch.1, 3-10.e1). Essentials of Pain Medicine. Elsevier. E-book. Accessed 7/28/2022.

Poulain, Philippe et al. Efficacy and Safety of Transdermal Buprenorphine: A Randomized Placebo Controlled Trial in 289 Patients with Severe Cancer Pain. Journal of Pain and Symptom Management. 2008. Vol 36 (2) 117-125. Prommer, Eric. Buprenorphine for Cancer Pain: Is it Ready for Prime Time. American Journal of Hospice and Palliative Medicine. 2015. Vol 32(8) 881-889.