CONTROLLING POST-OPERATIVE PAIN

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OBJECTIVES

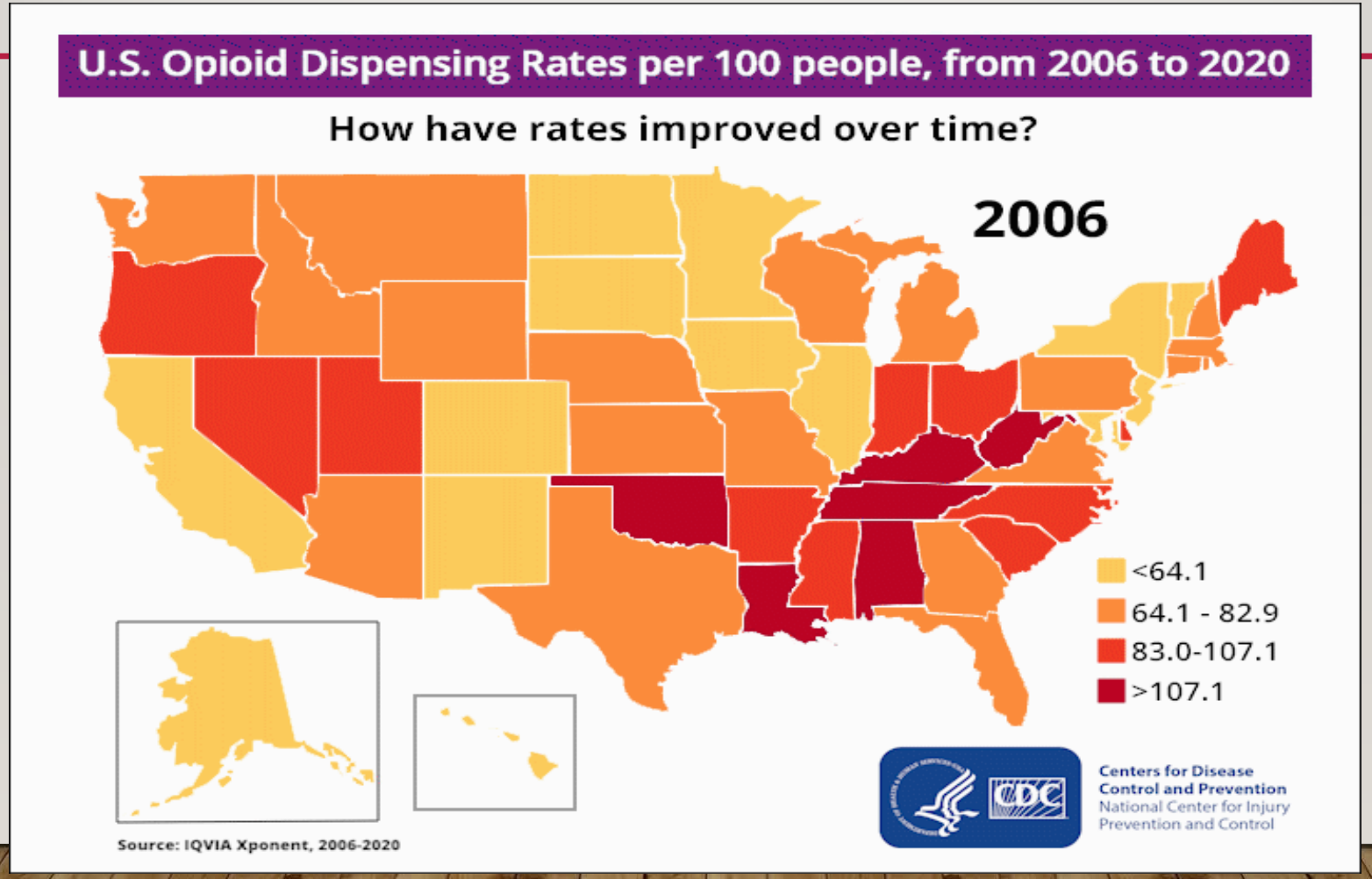
- Address the problems associated with post-operative pain treatment
- Differentiate the medication mechanisms of action that contribute to the multi-modal treatment of postoperative pain
- Discuss recommendations for treatment of postoperative pain

PROBLEM

- 75% of patients experience acute post-operative pain
- This pain is regarded as moderate-high intensity
- <50% of patients undergoing surgery report adequate pain control
- Severe persistent postoperative pain affects 2-10% of adults

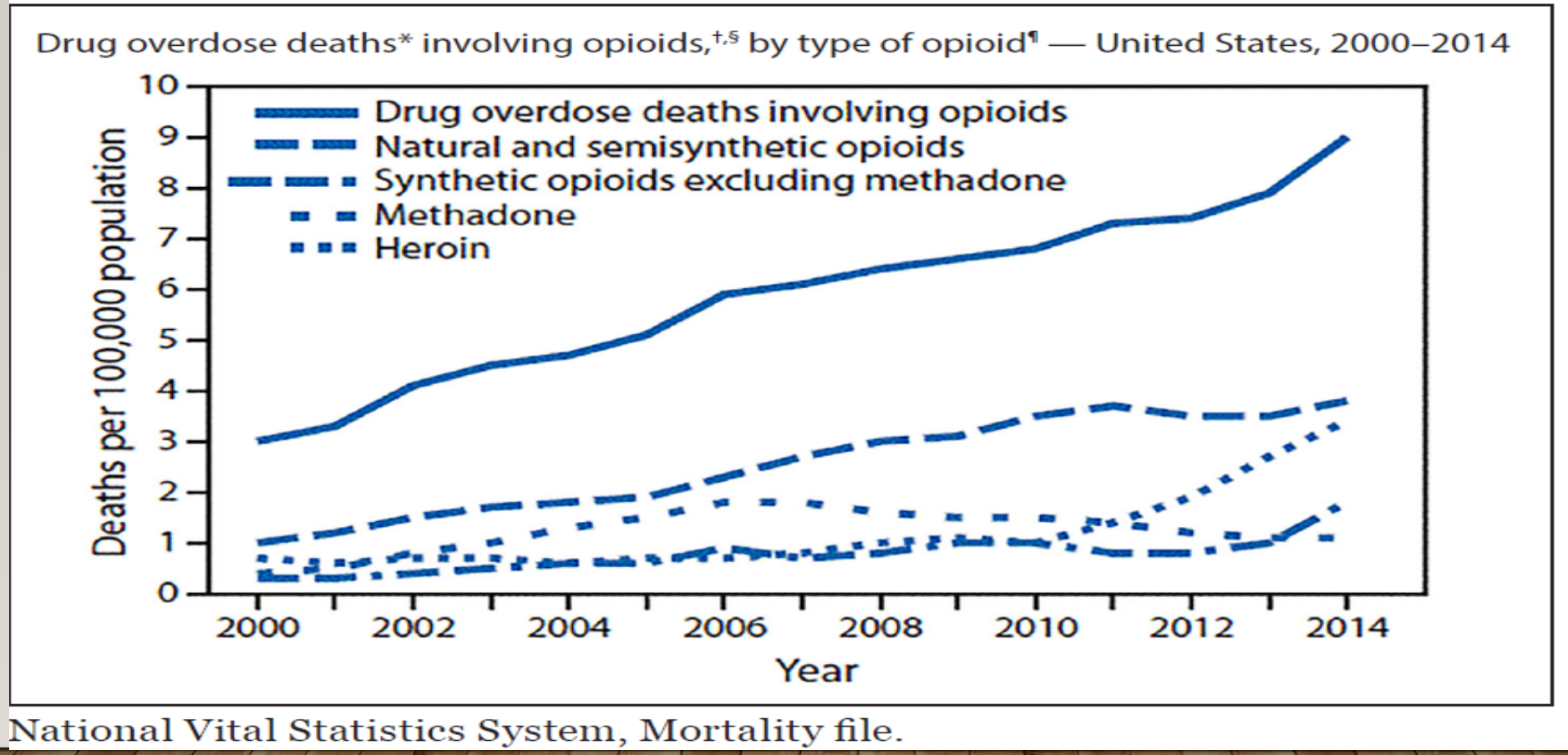
Horn R, Kramer J. Postoperative Pain Control. [Updated 2022 Sep 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK544298/

CHANGE IN OPIOID DISPENSING



Centers for Disease Control. U.S. Opioid Dispensing Rate Maps. https://www.cdc.gov/drugoverdose/rxrate-maps/index.html accessed on 1/15/2023.

DRUG OVERDOSE DEATHS



-Ansari A, Rizk D, Whinney C. The Society of Hospital Medicine's (SHM's) Mutlimodal Pain Strategies Guide for Postoperative Pain Management. Hospital Medicine. Accessed at https://safe.menlosecurity.com/doc/docview/viewer/docN50A3D03AE5BC789f0a982936a45c924663c07835347ad2039ab9244283265012259a92b02261e on 1/15/2023.

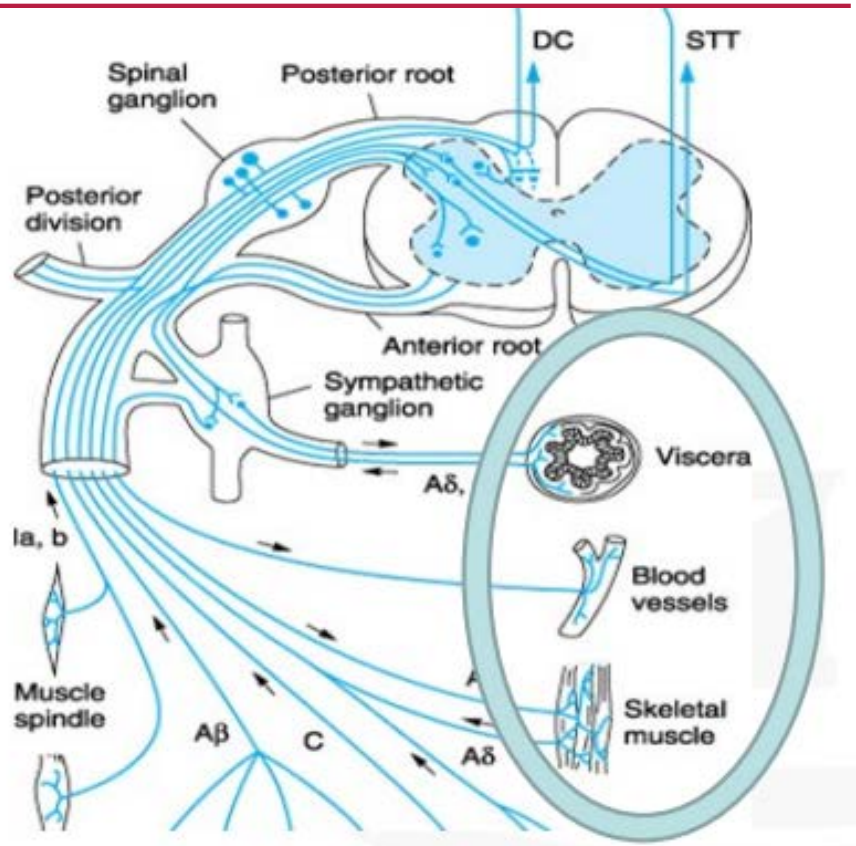
GOALS OF THERAPY

- Patient personalized approach to dealing with pain
- Increased patient understanding of what pain is considered "normal" and length of time for pain to occur
- Reduce negative consequences of postsurgical pain
- Improve patient transition to normal activities of daily living

- -Horn R, Kramer J. Postoperative Pain Control. [Updated 2022 Sep 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK544298/
- -Small C and Laycock H. "Acute postoperative pain management". British Journal of Surgery. Jan 2020. e1-e179.

PATHOPHYSIOLOGY

- **Nociceptor activation, sensitization, and hyperalgesia**
  - Surgical tissue trauma leads to nociceptor activation and sensitization.
  - Individuals suffer ongoing pain at rest and increased responses to stimuli at the site of injury (primary hyperalgesia)
- **Central sensitization during acute postoperative pain**
  - Noxious input during and after surgery can enhance the responses of nociceptive neurons in the CNS (central sensitization) thereby amplifying pain intensity
  - The magnitude of central sensitization depends on many factors, including the location of the operative site and the extent of the injury



Morgan and Mikail. *Clinical Anesthesia.*

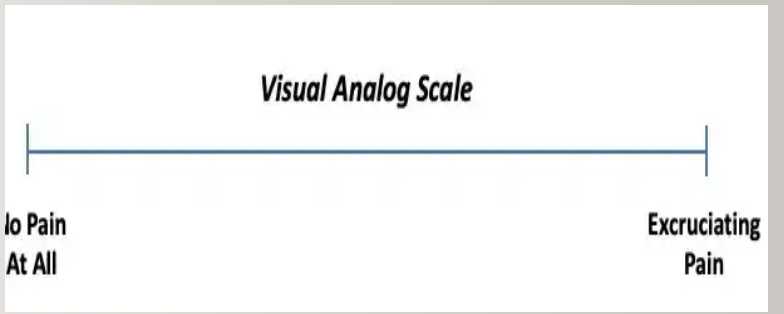
Kehlet H, Dahl JB. *Anesth Analg.* 1993;77:1048-1056 accessed at Medscape.com
-Pathophysiology of Acute Postoperative Pain. Brigham and Womens. Accessed at https://bcore.brighamandwomens.org/wp-content/uploads/2018/01/Pathophysiology-of-Acute-Pain_IASP-2017_3.pdf on 1/29/23

TYPES OF PAIN

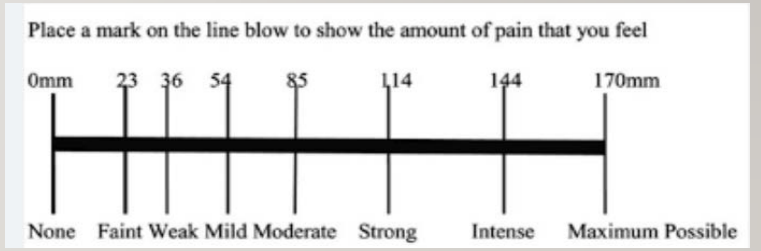
	Description	Localization	Description	Etiology	Management
Nociceptive	Tactile on skin and external soft tissues; musculoskeletal	Very localized	Variable but typically sharp, stabbing	Trauma, pressure	Anti-inflammatories, centrally acting agents; opioids as last resort
Visceral	Deeper origin, e.g., gut or brain (colic, obstruction)	Poorly localized (headache, abdominal pain, chest pain)	Dull, achy, colicky, intermittent	Injury or trauma to internal organs	Centrally acting; opioids as last resort, need to pursue cause
Neuropathic	Commonly peripheral extremities (spinal cord injury, herpes zoster, DM neuropathy)	Usually well localized	Burning, piercing, tingling; constant	Chronically damaged nerves from DM, ischemia,	Nerve stabilizers, antidepressants > anti-inflammatory; opioids as last resort
Inflammatory	Soft tissues and joints	Usually well localized	Burning, aching, worse with movement	Soft tissue or joint inflammation locally	Anti-inflammatory; ice, compression; opioids as last resort

-Ansari A, Rizk D, Whinney C. The Society of Hospital Medicine's (SHM's) Multimodal Pain Strategies Guide for Postoperative Pain Management. Hospital Medicine. Accessed at https://safe.menlosecurity.com/doc/docview/viewer/docN50A3D03AE5BC789f0a982936a45c924663c07835347ad2039ab9244283265012 59a92b02261e on 1/15/2023.

PAIN ASSESSMENT



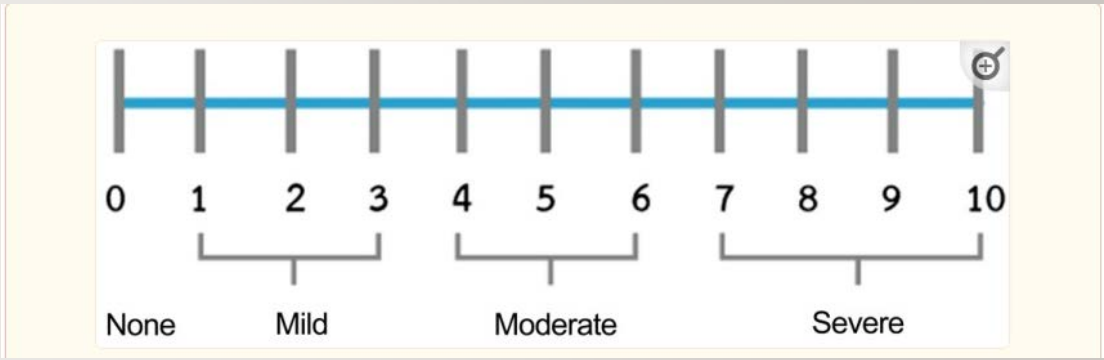
- Multiple Pain Scales available: None considered "Gold Standard"
  - Visual Analog Scale (VAS)
    - Developed by Hayes & Patterson (1921)
    - Pt mark on the scale & measure the distance between no pain & the pt mark
  - Heft-Parker VAS (HPS)
    - Like VAS but 170mm in length & contains various descriptors
  - Verbal Rating Scale (VRS).
    - Can range from 4-point scale to 15-point scales
    - Preferred in elderly patients
    - Less sensitive to treatment than VAS



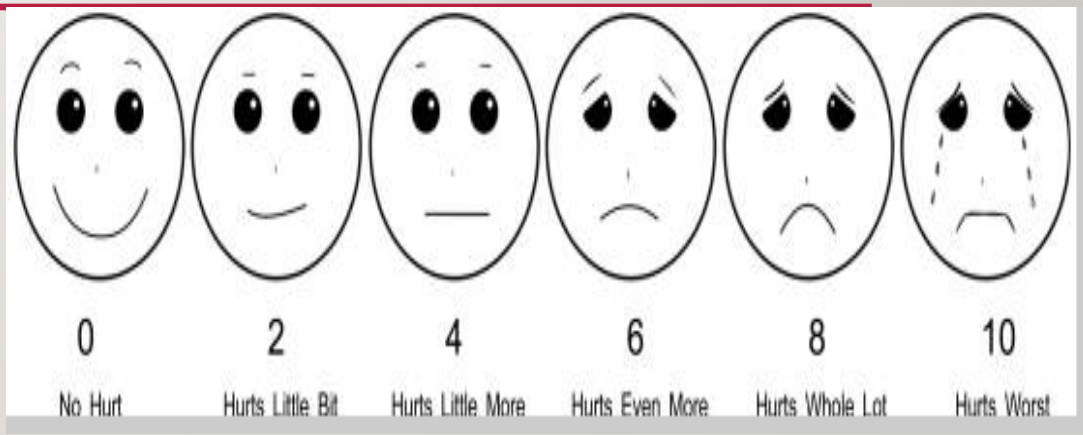
VRS (categories)
0 = no pain
1 = no pain at rest, slight pain on movement
2 = slight pain at rest, moderate pain on movement
3 = moderate pain at rest, severe pain on movement
4 = severe pain at rest and on movement

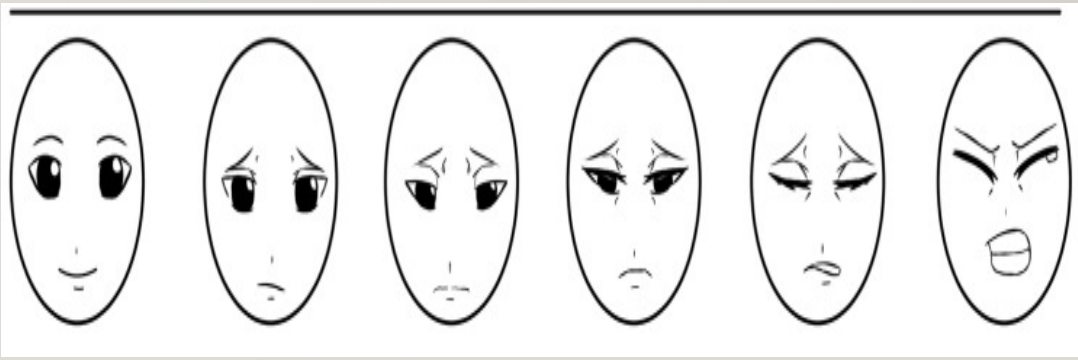
-Visual Analog Survey Scale-A Pain-ful Misnamed Scale. https://greatbrook.com/visual-analog-survey-scale/ accessed on 12/28/2022.
-Visual Analogue Scale. https://www.physio-pedia.com/Visual_Analogue_Scale accessed on 12/28/2022.
-Briggs, M and Closs, Jose. A Descriptive Study of the Use of Visual Analogue Scales and Verbal Rating Scales for the Assessment of Postoperative Pain in Orthopedic Patients. Journal of Pain and Symptom Management. Volume 18, Issue 7, P438-446. December 01, 1999.
-Heft MW, Parker SR. An experimental basis for revising the graphic rating scale for pain. *Pain.* 1984;19:153–161.

PAIN ASSESSMENT



- Multiple Pain Scales available:
  - Numerical Rating Scale (NRS)
    - Developed in 1978
    - Not suitable for elderly or very young children
  - Faces Pain Scale (FPS)
    - Originally a 7-point scale but changed to 10-point scale
    - Scored 0, 2, 4, 6, 8, 10
  - Wong-Baker Faces Pain Rating Scale (WBS)
    - Popular for pediatric pain assessment





-Downie WW, Leatham PA, Rhind VM, Wright V, Branco JA, Anderson JA. Studies with pain rating scales. *Ann Rheum Dis.* 1978;37:378–381
- Flaherty SA. Pain measurement tools for clinical practice and research. *AANA J.* 1996;64:133–140
-Sirintawat N, Sawang K, Chaiyasamut T, Wongsirichat N. Pain measurement in oral and maxillofacial surgery. J Dent Anesth Pain Med. 2017 Dec;17(4):253-263. doi: 10.17245/jdapm.2017.17.4.253.

TECHNIQUES FOR CONTROLLING PAIN

- Drugs, drugs, drugs
- Local, intra-articular, topical
- Regional anesthesia
- Neuraxial anesthesia
- Non-pharmacological:
  - Cognitive Behavioral Therapy (CBT)
  - Physical Therapy (PT)
  - Transcutaneous Electrical Nerve Stimulation (TENS)

-Horn R, Kramer J. Postoperative Pain Control. [Updated 2022 Sep 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK544298/

MEDICATION TREATMENT

- Acetaminophen/paracetamol (APAP)
- NSAIDs
- Alpha-2 agonists
- Gabapentin/pregabalin
- Ketamine
- IV Lidocaine
- IV Magnesium Sulfate
- Opioids

-Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, Carter T, Cassidy CL, Chittenden EH, Degenhardt E, Griffith S, Manworren R, McCarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thirlby R, Viscusi E, Walco GA, Warner L, Weisman SJ, Wu CL. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain. 2016 Feb;17(2):131-57.

ACETAMINOPHEN (APAP) (TYLENOL)

- Marketed under:
  - Acetaminophen (Japan/USA)
  - Paracetamol (Europe & everywhere else in the world)
  - Now marketed under Tylenol (Ortho McNeil) or Ofirmev
- Originally synthesized by HN Morse in 1878
- First marketed in 1950 under the brand name (Triagesic)
- MOA: not fully elucidated
  - Most likely related to activity at COX-3
  - May be due to activation of descending serotonergic inhibitory pathways in the CNS

-Molecule of the week-Acetaminophen. September 14, 2014. Accessed at https://www.acs.org/molecule-of-the-week/archive/a/acetaminophen.html on 1/28/2023
-Acetaminophen (Paracetamol): Drug information. Hudson, OH: Lexicomp, 1978-2023. http://online.lexi.com/. Updated date. Accessed 1/13/23.
-Tylenol. Accessed at ebay.com on 1/28/2023.

ACETAMINOPHEN (APAP) (TYLENOL)

- Dose: 500 to 1000 mg PO or IV every 6 hours
- No clear difference between IV & PO
  - PO will be less expensive
  - IV with faster onset of action
- Cochrane review (2015)
  - 50 RCTs of single-dose APAP 1g for acute postoperative pain in adults reported a NNT (evaluating the number of patients to treat to obtain a 50% of pain relief over 4-6 hours) of 3.6
  - NNT improves when combined w/ other analgesics
    - Ibuprofen 400 mg (NNT 1.5)
    - codeine 60mg (NNT 2.2)
    - oxycodone (NNT 1.8)
- Concern regarding APAP & the development of hepatotoxicity
  - Current data suggest this is unlikely to develop at therapeutic doses
  - Most of the cases of liver injury are associated with the use of APAP at doses that exceed the maximum daily limits & involve >1 APAP containing product

-Moore RA, Derry S, Aldington D, Wiffen PJ. Single dose oral analgesics for acute postoperative pain in adults – an overview of Cochrane reviews. Cochrane Database Syst Rev2015; (9)CD008659.
-Small C and Laycock H. "Acute postoperative pain management". British Journal of Surgery. Jan 2020. e1-e179.

ACETAMINOPHEN (APAP) (TYLENOL)

- Dose adjustments:
  - Max dose: 3 g/day in adults with normal liver function, particularly when used for longer durations (eg, >7 days) for pain
  - Max dose 2g/day or avoidance in adults with heavy alcohol use, malnutrition, fasting, low body weight, advanced age, febrile illness, select liver disease, and use of meds that interact with APAP metabolism (isoniazid, phenobarbital, rifampin, primidone)
  - When calculating total daily dose, confirm that all sources (eg, prescription, OTCs, combinations) are included
- BBW:
  - Prescribing, preparing, & administering APAP injection to avoid dosing errors that could result in accidental overdose/death.
  - Ensure the following:
    - Dose in mg & ml should not be confused
    - Dosing is based on weight for patients less than 50 kg
    - Infusion pumps are properly programmed
    - Total daily dose of APAP from all sources does not exceed maximum daily limits. (4g/day if less than 7 days)
    - APAP has been associated with cases of acute liver failure, at times resulting in liver transplant & death.

-Molecule of the week-Acetaminophen. September 14, 2014. Accessed at https://www.acs.org/molecule-of-the-week/archive/a/acetaminophen.html on 1/28/2023
-Acetaminophen (Paracetamol): Drug information. Hudson, OH: Lexicomp, 1978-2023. http://online.lexi.com/. Updated date. Accessed 1/13/23.
-Ofirmev. Accessed at https://www.empr.com/home/news/ofirmev-approved-for-management-of-pain-and-fever/ on 1/28/2023.

NSAIDS

Long history of use

- 400 B.C.-Hippocrates used willow bark and leaves to control fever & inflammation
- 1763- first published report of willow bark (salicilin, a prodrug)
- 1863-Salicylic acid mass produced by Kolbe in German
- 1897-ASA produced by Bayer-more palatable
- 1971- the mechanism of action was established
- 1974: Ibuprofen is FDA approved in U.S.
- 1990- the existence of two different cyclo-oxygenase isoforms was suggested
- 1998- the first COX-2 inhibitor was approved by the FDA

-Bindu S, Mazumder S, Bandyopadhyay U. Non-steroidal anti-inflammatory drugs (NSAIDs) and organ damage: A current perspective. Biochem Pharmacol. 2020 Oct;180:114147. doi: 10.1016/j.bcp.2020.114147. Epub 2020 Jul 10.
Vlachojannis J, Magora F, Chrubasik S. Willow species and aspirin: different mechanism of actions. Phytother Res. 2011 Jul;25(7):1102-4. doi: 10.1002/ptr.3386. PMID: 21226125.
-Connelly Dawn. The PHARMACEUTICAL JOURNAL. A brief history of ibuprofen. -https://pharmaceutical-journal.com/article/infographics/a-brief-history-of-ibuprofen accessed on 2/16/23.
-Rao PNP and Knaus E. J Pharm Pharmaceut Sci (www. cspsCanada.org) 11 (2): 81s-110s, 2008

NSAIDS

- Non-steroidal anti-inflammatory drugs (NSAIDs) are endorsed by the Enhanced Recovery After Surgery (ERAS) Society
- NSAIDs are reported to reduce IV PCA morphine consumption after major surgery
- Two observational studies explored NSAID-associated postoperative complications
  - 1st study: 1503 patients undergoing elective or emergency GI resection
    - Reported a risk-adjusted reduced incidence of postoperative complications following NSAID use (odds ratio 0·72, 95% c.i. 0.52 - 0.99)
    - Predominantly owing to a reduction in minor complications with high-dose NSAID use
  - 2nd observational cohort study: 9264 patients undergoing elective or emergency GI surgery
    - Use of NSAIDs was not associated with major complications, AKI or post-operative bleeding
    - Despite risk adjustment, these data are limited by selection bias in that NSAIDs are more likely to be administered to healthier patients

-Small C and Laycock H. "Acute postoperative pain management". British Journal of Surgery. Jan 2020. e1-e179

NSAIDS

- Some observational evidence of association
  - Between high-dose NSAIDs & nonunion in spinal fusion or fracture surgery
  - Between NSAID use & anastomotic leak in intestinal surgery
- Cochrane database systemic review
  - 45,000 subjects utilizing different NSAIDs & other analgesic (APAP & codeine)
  - Major advantage is the reduction of the relative risk of nausea & vomiting but does not result in reduction in other side effects as urinary retention, itch or respiratory depression
  - All NSAIDs, selective & non-selective, have the same analgesic effects & effectiveness in the postoperative period
  - Choice of NSAID guided by several factors: economic, pre-existing gastrointestinal bleeding, high-risk bleeding surgery, option to use the enteral route
  - Coxibs do not inhibit platelet aggregation & can be utilized in pre & postoperative period without increasing bleeding risk
  - COX-2 inhibitors do not increase GI toxicity
  - Study limitations on NSAIDs: mainly used in minor surgery with few studies regarding major surgery

-Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, Carter T, Cassidy CL, Chittenden EH, Degenhardt E, Griffith S, Manworren R, McCarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thirlby R, Viscusi E, Walco GA, Warner L, Weisman SJ, Wu CL. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain. 2016
-Cosmo1 GD, Congedo E (2015) The Use of NSAIDs in the Postoperative Period: Advantage and Disadvantages. J Anesth Crit Care Open Access 3(4): 00107. DOI: 10.15406/jaccoa.2015.03.00107

NSAIDS

- The difference of anti-inflammatory & analgesic activity between NSAIDs & Coxibs are minimal
  - One study reported superiority of a Coxib, celecoxib compared with a traditional NSAIDs (ibuprofen at low doses in patients undergoing minor oral surgery) BUT
  - Cochrane review of 8 RCTs of adults either receiving celecoxib 200mg, 400mg, or placebo
  - Author's conclusion: "Single-dose oral celecoxib is an effective analgesic for postoperative pain relief. Indirect comparison suggests that the 400 mg dose has similar efficacy to ibuprofen 400 mg"
- The number of patients needed to obtain a reduction of 50% of pain over 4-6 hours compared to placebo (NNT) has been introduced to compare the effects of NSAIDs
- A comparison of the efficacy of different anti-inflammatory drugs is reported in the Oxford league table
  - Diclofenac 100mg is 2.6
  - Ibuprofen 400mg/ketorolac 10mg is 2.6
  - Celecoxib 200mg: 4.2
  - Celecoxib 400mg: 2.5
  - Codeine 60mg is 16.7

-Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, Carter T, Cassidy CL, Chittenden EH, Degenhardt E, Griffith S, Manworren R, McCarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thirlby R, Viscusi E, Walco GA, Warner L, Weisman SJ, Wu CL. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain. 2016
-Cosmo1 GD, Congedo E (2015) The Use of NSAIDs in the Postoperative Period: Advantage and Disadvantages. J Anesth Crit Care Open Access 3(4): 00107. DOI: 10.15406/jaccoa.2015.03.00107

NSAIDS

- Pre-op dose of celecoxib
  - Associated with reduced opioid requirements after surgery, & some studies reported lower postoperative pain scores
  - Most common doses of celecoxib in the trials were 200 to 400 mg, administered 30 minutes to 1 hour preoperatively
  - Celecoxib is contraindicated in patients who undergo coronary artery bypass graft surgery, because of an increased risk of CV events
- Insufficient evidence to recommend a preoperative dose of nonselective NSAIDs
- No trial compared benefits or harms of nonselective NSAIDs versus celecoxib or placebo in patients who underwent nondental surgical procedures
- Postoperative dose is 200mg BID

-Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, Carter T, Cassidy CL, Chittenden EH, Degenhardt E, Griffith S, Manworren R, McCarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thirlby R, Viscusi E, Walco GA, Warner L, Weisman SJ, Wu CL. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain. 2016

GABAPENTINOIDS

- Gabapentin (Neurontin)
- Pregabalin (Lyrica)
- Atagablin
  - Pfizer development for insomnia: discontinued before approval
- 4-methylpregabalin
  - Enantiomer of pregabalin with 4x higher binding affinity to alpha 2 ligand channels
  - Unknown if further development will occur
- PD-217,014
  - Never developed

GABAPENTIN (NEURONTIN)

- Approval date: 1993
- MOA:
  - Structurally related to GABA
  - High affinity binding sites correspond to the presence of voltage-gated calcium channels specifically possessing the alpha-2-delta-1 subunit.
  - Presynaptically modulates the release of excitatory neurotransmitters which participate in epileptogenesis & nociception
- Pharmacokinetics
  - Onset of action: 2-4 hours, around the medication peak
  - Metabolism: None, primarily renal elimination
  - Dose adjustment
    - Renal: If CrCl is <50ml/min the dose adjustment necessary
      - 30-49ml/min: No more than 900mg/day
      - 15-29ml/min: No more than 600mg/day
      - <15ml/min: No more than 300mg/day
    - Hepatic: Child-Tucotte-Pugh score B&C: no more than 300mg/day

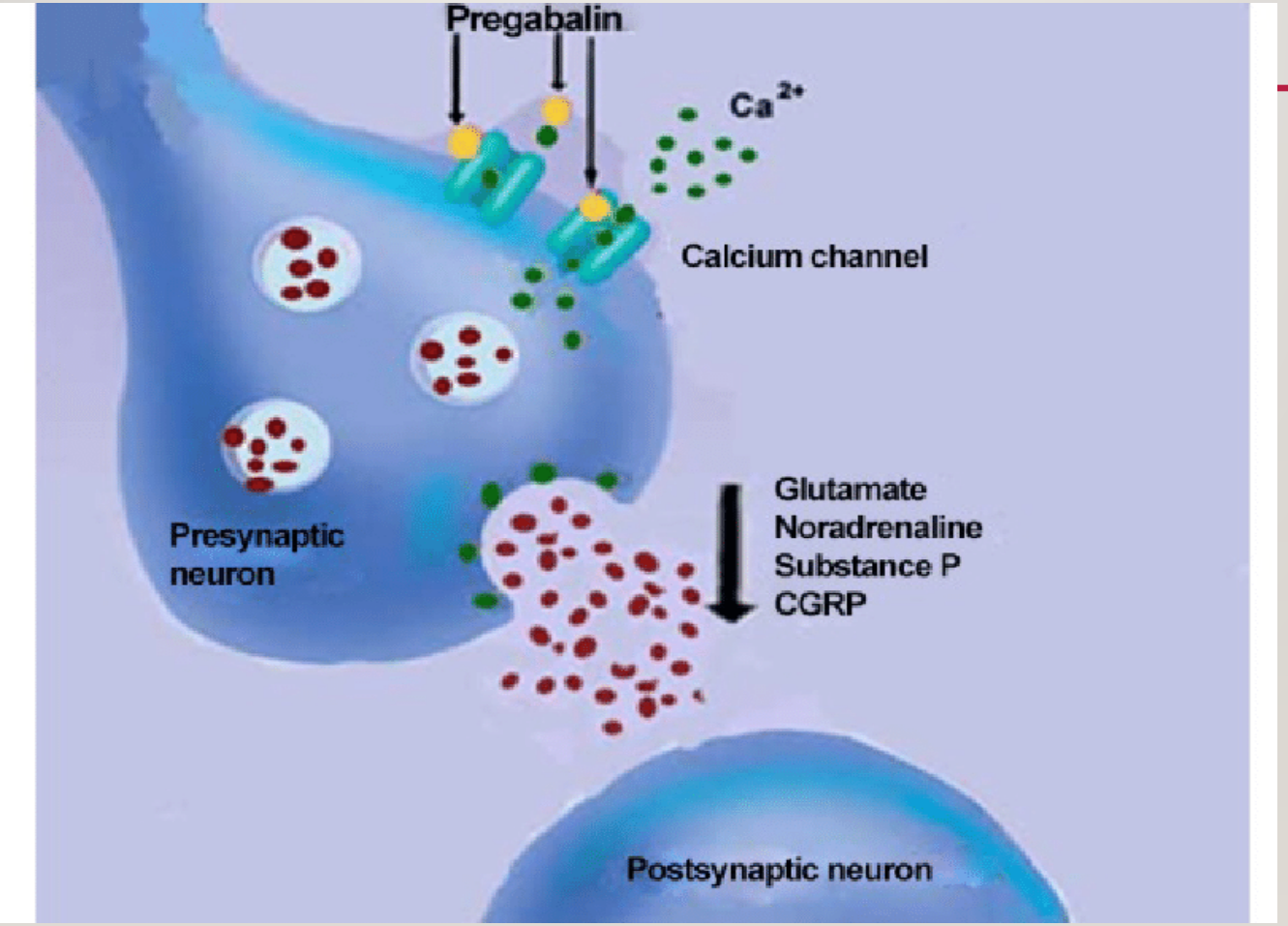
-Yasaei R, Katta S, Saadabadi A. Gabapentin. [Updated 2022 May 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK493228/
-NEURONTIN TABLETS Rx. MRP accessed at www.empr.com/drug/Neurontin-tablets/ on 1/23/23

PREGABALIN (LYRICA)

- Approval date: 2004
- MOA: Gabapentin S-enantiomer
  - Structurally related to GABA
  - High affinity binding sites correspond to the presence of voltage-gated calcium channels specifically possessing the alpha-2-delta-1 subunit
  - Presynaptically modulates the release of excitatory neurotransmitters which participate in epileptogenesis & nociception
- Pharmacokinetics
  - Onset of action: 1.5 hours as fasting
  - Duration of action: ~6 hours
  - Metabolism: Negligible
  - Dose adjustment
    - Renal:
      - 15-30ml/min: Do not exceed 150mg/day
      - <15ml/min: Do not exceed 75mg/day
    - Hepatic: None

-Yasaei R, Katta S, Saadabadi A. Gabapentin. [Updated 2022 May 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK493228/
-McKeage K, Keam SJ. Pregabalin: in the treatment of postherpetic neuralgia. Drugs Aging. 2009;26(10):883-92. doi: 10.2165/11203750-000000000-00000.
-www.alamy.com/stock-photo/lyrica.html accessed on 1/23/2023.

GABAPENTIN & PREGABALIN MOA



Hunis, Adrian. (2020). Neuropathic Pain and Fibromyalgia

GABAPENTINOIDS

- Both meds are associated with reduced opioid requirements after major or minor surgical procedures & some studies reported lower postoperative pain scores
- Both meds appear effective when administered as a preoperative dose 1-2 hours preoperatively
  - Gabapentin 600 or 1200 mg
  - Pregabalin 150 or 300 mg
- Postoperative dosing is effective
  - Gabapentin 600 mg as a single or in multiple doses every 6-8 hours
  - Pregabalin 150 or 300 mg after 12 hours
- Insufficient evidence to determine optimal dose (higher doses might be more effective but increased sedation)
- Potential adverse effects include dizziness and sedation that has not been linked to respiratory depression
- In a large observational study of 5.5 millions, U.S. hospital surgical admission, gabapentinoids did not increase the risk of opioid associated adverse effects, overall rate of overdose <0.1% of patients
- 1st Cochrane review in 2011, stated that a NNT of 11 for gabapentin 250mg solution was of limited clinical value compared to other analgesics

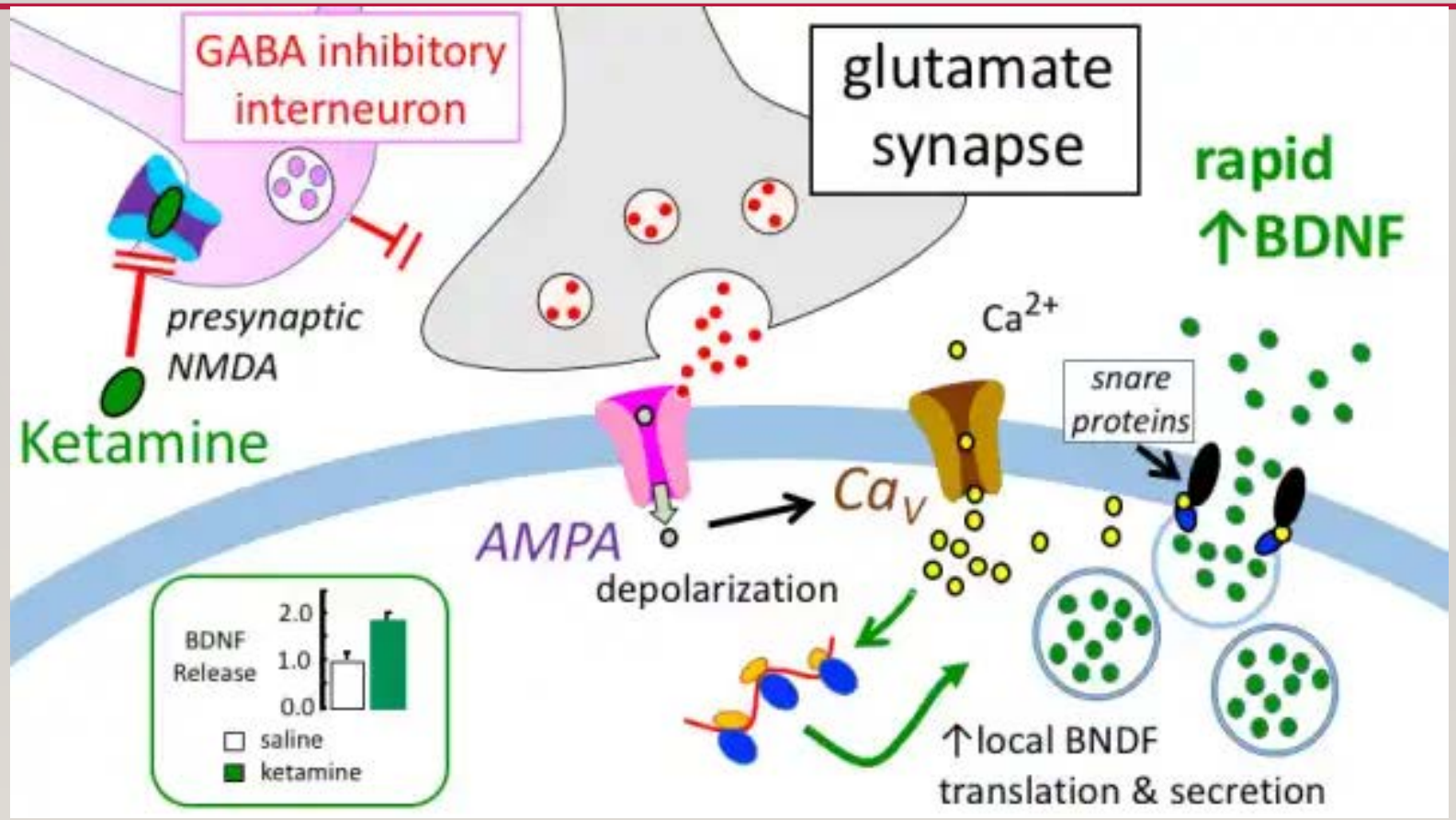
-Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, Carter T, Cassidy CL, Chittenden EH, Degenhardt E, Griffith S, Manworren R, McCarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thirlby R, Viscusi E, Walco GA, Warner L, Weisman SJ, Wu CL. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain. 2016
-Bykov K, Bateman BT, Franklin JM, Vine SM, Patorno E. Association of Gabapentinoids With the Risk of Opioid-Related Adverse Events in Surgical Patients in the United States. *JAMA Netw Open.* 2020;3(12):e2031647. doi:10.1001/jamanetworkopen.2020.31647

KETAMINE

- Approval date: 1970
- MOA: Phencyclidine (PCP) derivative that is a noncompetitive *N*-methyl-D-aspartate (NMDA) receptor blocker
  - NMDA receptor is involved in the amplification of pain signals, the development of central sensitization, & opioid tolerance
  - Analgesic action at sub-anaesthetic dose
- Dose: 0.25 to 0.5 mg/kg bolus (max bolus: 35 mg), followed by 0.05 to 0.25 mg/kg/**hour** continuous infusion for up to 48 to 72 hours
- Pharmacokinetics
  - Onset of action: 30 seconds
  - Duration of action: 5-10 mins
  - Metabolism: Hepatic via N-dealkylation (metabolite I [norketamine]), hydroxylation of the cyclohexone ring (metabolites III and IV), conjugation with glucuronic acid and dehydration of the hydroxylated metabolites to form the cyclohexene derivative (metabolite II); metabolite I (norketamine) is 33% as potent as parent compound.
  - Dose adjustment
    - Renal: None
    - Hepatic: None
- Pearls:
  - May be given IN if needed
  - Beware of emergent reaction: nightmares, HTN

-Bell RF, Kalso EA. Ketamine for pain management. Pain Rep. 2018 Aug 9;3(5):e674. doi: 10.1097/PR9.0000000000000674.
-Hydromorphone: Drug information. Hudson, OH: Lexicomp, 1978-2023. http://online.lexi.com/. Updated date. Accessed 1/29/23.

KETAMINE



Garrendale Pain and Wellness. Ketamine Infusion. https://drrickytubbs.com/?page_id=80. Accessed on 8/12/2022.

IV KETAMINE

- Adults & children, IV ketamine infusions associated w/ decreased postoperative pain med use compared with placebo, and in some studies with decreased postoperative pain scores
  - IV ketamine associated with decreased risk of persistent postsurgical pain
  - Insufficient evidence to determine the optimal method for dosing ketamine, but a recommendation is to use a preoperative bolus of 0.5 mg/kg followed by an infusion at 10 µg/kg/min intraoperatively, with or without a postoperative infusion at a lower dosage
- Clinicians who administer ketamine should be familiar with its use & adverse effects
  - Ketamine was associated w/ increased risk of hallucinations & nightmares
- Some situations in which ketamine might be particularly useful include management of highly opioid-tolerant patients or patients who have difficulty tolerating opioids

Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, Carter T, Cassidy CL, Chittenden EH, Degenhardt E, Griffith S, Manworren R, McCarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thirlby R, Viscusi E, Walco GA, Warner L, Weisman SJ, Wu CL. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain. 2016

IV LIDOCAINE

- Approval date: Discovered in 1943, marketed in 1949
- MOA: blocks both the initiation & conduction of nerve impulses by decreasing the neuronal membrane's permeability to sodium ions, which results in inhibition of depolarization with resultant blockade of conduction
- Pharmacokinetics
  - Onset of action: 3-20 mins
  - Duration: 2-2.5 hours
  - Metabolism: 90% hepatic via CYP1A2 and CYP3A4; active metabolites monoethylglycinexylidide (MEGX) and glycinexylidide (GX) can accumulate & may cause CNS toxicity
  - Dose Adjustment
    - Renal eGFR <30 mL/minute/1.73 m^2: Administer lower maintenance infusion rate with close monitoring for toxicity
    - Hepatic: Administer lower maintenance infusion rate with close monitoring for toxicity

-**Lidocaine: Drug information**. Hudson, OH: Lexicomp, 1978-2023. http://online.lexi.com/. Updated date. Accessed 1/6/23.
-Xylocaine. McGruff Medical Products. Accessed at https://www.mcguffmedical.com/xylocaine-lidocaine-hcl-mdv-50ml?productId=6213 on 1/28/23.
-Dental Instruments Past and Present. Accessed at https://exhibits.library.stonybrook.edu/s/dental-instruments-past-and-present/item/750 on 1/28/23.

IV LIDOCAINE

- Consider IV lidocaine infusions in adults who undergo open & laparoscopic abdominal surgery who do not have contraindications
  - Original studies showed perioperative or intraoperative IV lidocaine infusions were associated with shorter duration of ileus & better quality of analgesia compared with placebo
- Typical lidocaine dose is unknown but based on clinical experience
  - Typically administered as a bolus (100–150 mg or 1.5–2.0 mg/kg)
  - Followed by an infusion of 2 to 3 mg/kg/h through the end of surgery
- Continuation of lidocaine in the postoperative period has not been well studied

-Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, Carter T, Cassidy CL, Chittenden EH, Degenhardt E, Griffith S, Manworren R, McCarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thirlby R, Viscusi E, Walco GA, Warner L, Weisman SJ, Wu CL. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain. 2016

IV LIDOCAINE

- Cochrane review of continuous IV perioperative lidocaine infusion for postoperative pain in adults-68 RCTs
  - Insufficient evidence to demonstrate improvements in postoperative pain, or resolution of ileus, nausea, vomiting or side-effects compared with placebo, usual care or thoracic epidural anesthesia
- Current ERAS guidelines for elective colorectal surgery include perioperative lidocaine infusions but **these guidelines are based on the previous studies**
- Uncertainty regarding the use of IV lidocaine to aid postoperative analgesia
- There are several studies ongoing & publications that may change this conclusion are awaited

Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, Carter T, Cassidy CL, Chittenden EH, Degenhardt E, Griffith S, Manworren R, McCarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thirlby R, Viscusi E, Walco GA, Warner L, Weisman SJ, Wu CL. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain. 2016

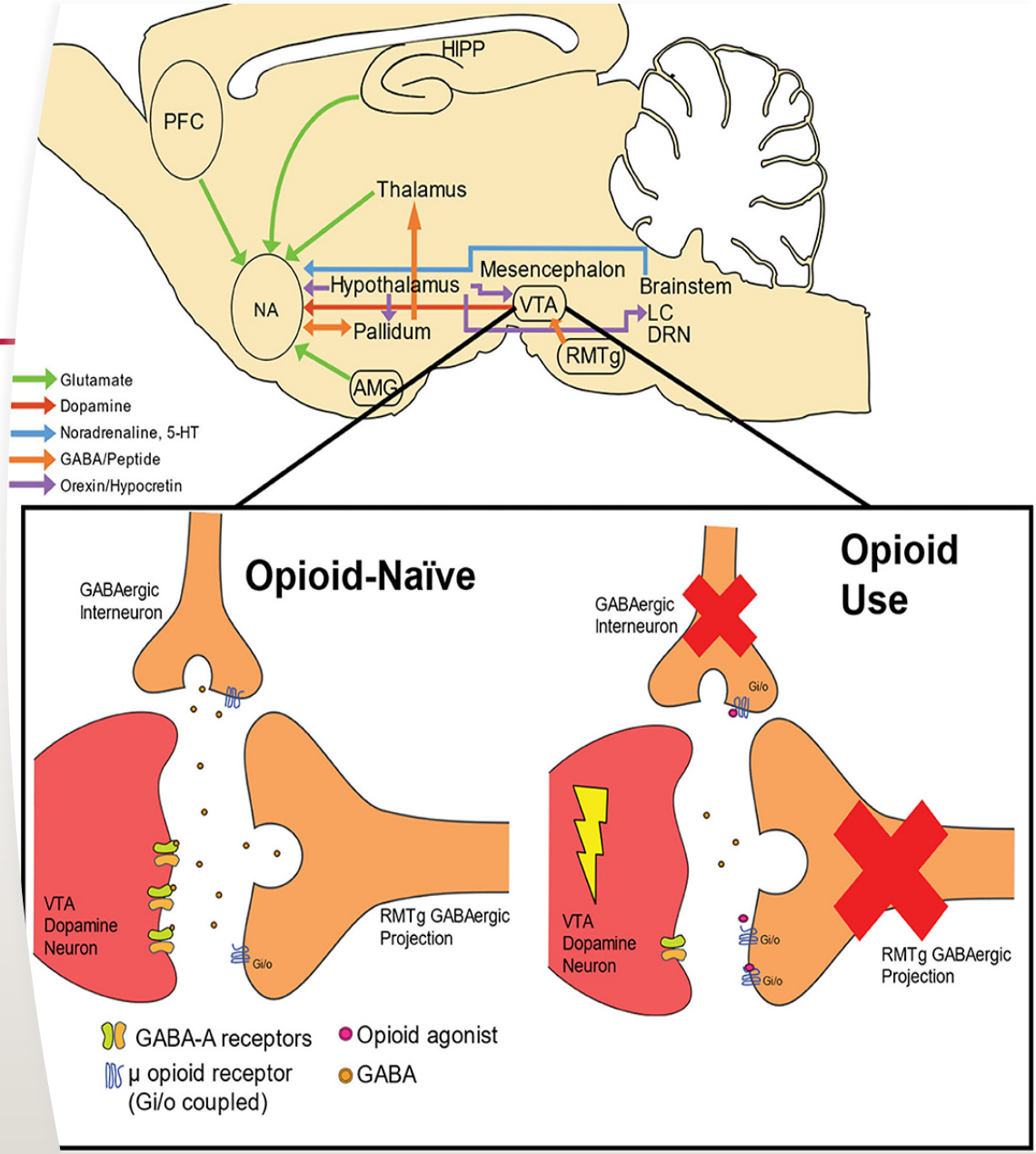
IV MAGNESIUM SULFATE

- NDMA receptor antagonist that competes with endogenous calcium, acts as a calcium channel blocker
  - Adjunct to morphine analgesia
  - Opioid-sparing effect and reduces pain scores
- Bolus doses(mostly 30–50 mg/kg) alongside an intraoperative lower dose or short postoperative infusions of magnesium (up to 48 h after surgery)
- In addition, two small RCTs suggested that intravenous magnesium extends the duration of sensory block with spinal anesthesia; reduces subsequent postoperative pain & opioid requirements
  - Kumar, et al randomly assigned patients to a $MgSO_4$ infusion with spinal anesthesia
  - The first rescue analgesia was required after 334 +/- 202 min in $MgSO_4$ group vs 233 +/- 141 min in NS group ($p < 0.05$)
  - The morphine required over 24 hours for analgesia was significantly less in $MgSO_4$ group (3.99 +/- 1.25 mg) as compared to NS group (7.13 +/- 2.68 mg) ($p < 0.000$)

-Small C and Laycock H. "Acute postoperative pain management". British Journal of Surgery. Jan 2020. e1-e179.
-Kumar M, Dayal N, Rautela RS, Sethi AK. Effect of intravenous magnesium sulphate on postoperative pain following spinal anesthesia. A randomized double blind controlled study. Middle East J Anaesthesiol. 2013 Oct;22(3):251-6. PMID: 24649780.

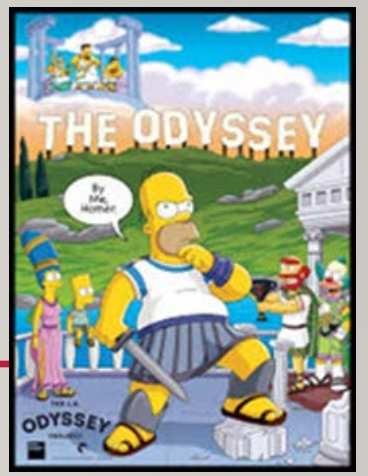
OPIOIDS

- Opiates: naturally occurring only
- Opioid: opiate + synthetic
- MOA:
  - Binds to opioid receptors in the dorsal horn at presynaptic & post synaptic neurons, causing inhibition of ascending pain pathways, altering the perception of and response to pain; produces generalized CNS depression
- Types of Opioid receptors
  - Mu (MOR)
    - Analgesia, dependence, euphoria, respiratory depression, miosis, constipation, vasodilation
  - Kappa (KOR)
    - Analgesia, diuresis, dysphoria
  - Delta (DOR)
    - Analgesia, diuresis, dysphoria
  - Nocieption (NOR)
    - Analgesia and hyperalgesia
  - Zetaception (ZOR)
    - Regulate developmental events in a variety of normal and tumorigenic tissues and cells



-Strickland JC, Gipson CD, Dunn KE.Dopamine Supersensitivity: A Novel Hypothesis of Opioid-Induced Neurobiological Mechanisms Underlying Opioid-Stimulant Co-use and Opioid Relapse . Frontiers in Psychiatry. VOL 13. 2022.
-Dhaliwal A, Gupta M. Physiology, Opioid Receptor. [Updated 2022 Jul 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK546642/

OPIOID HISTORY



- Derived from opium plant *Papaver somniferum*
- Cultivated by Sumeria (modern day Iraq) for religious ceremonies
- Greeks originally combined with hemlock to give a painless death
- 9th Century B.C.: 1st appearance in literature in The Odyssey, Homer
  - "Presently she cast a drug into the wine of which they drank to lull all pain and anger and bring forgetfulness of every sorrow
- 8th century A.D.: Arab traders introduced to India/China
- 16th century: drug abuse described in Turkey, Egypt, Germany, England
- Morphine discovered 1806 by Seturner & named after Morpheus, god of dreams
- Intensified by discovery of hypodermic needle in 1853
- 1898: Heroin (2-acetyl morphine) marketed
- 1939: Meperidine discovered
- 1946: Methadone discovered
- 1986: WHO addressed the under-treatment of postoperative and cancer pain with their Cancer Pain Monograph
- 1990: Ronald Melzack published an article in *Scientific American* that questioned why opioids were reserved solely for cancer pain and avoided entirely in chronic pain states

-Brownstein, Michael J. "A brief history of opiates, opioid peptides, and opioid receptors". Proc. Natl. Acad. Sci USA. Vol 90, pp 5391-5393. June 1993.
-Dhaliwal A, Gupta M. Physiology, Opioid Receptor. [Updated 2022 Jul 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan.
-Heroin bottle. Accessed at https://museum.dea.gov/museum-collection/collection-spotlight/artifact/heroin-bottle on 1/29/23.
-WHO . *Cancer pain relief.* Geneva: WHO; 1986.
-Melzack R. The tragedy of needless pain. *Sci Am.* 1990;262(2):27–33. doi: 10.1038/scientificamerican0290-27.

OPIOIDS USED FOR TREATMENT (MORPHINE)

- Approval date: 1941, U.S. approval
- Dose: 1-3mg every 5 mins until adequate pain control (max cumulative dose 20mg) then 1-4mg q 1-4 hours prn. If PCA is used: opioid naïve should not have a basal rate
- Pharmacokinetics
  - Onset of action: IV- 5 to 10 minutes
  - Duration of action : 3 to 5 hours
  - Metabolism: Hepatic via conjugation with glucuronic acid primarily to morphine-6-glucuronide (M6G) (active analgesic) morphine-3-glucuronide (M3G) (inactive as analgesic which contributes to CNS stimulation)
  - Minor metabolites: morphine-3-6-diglucuronide, normorphine, morphine 3-ethereal sulfate
  - Dose adjustment
    - Renal: Clearance is similar altered or normal renal function
      - M3G (CNS stimulant and lower seizure threshold) & M6G [active analgesic]) significantly accumulate in patients with reduced kidney function
      - M6G accounts for an increasing proportion of the analgesic effect & delayed steady state causing increased CNS depression, sedation, severe/prolonged respiratory depression
    - Hepatic: There are no dosage adjustments provided in the manufacturer's labeling. PK unchanged in mild liver
      - In cirrhosis, increases in half-life & AUC suggest dosage adjustment required
- Pearls:
  - High risk of pseudo allergy: vasodilation with itching
  - If true allergy to morphine, then usually allergic to other phenanthrene derivatives hydromorphone, hydrocodone, oxycodone, oxymorphone, codeine

-**Morphine: Drug information**. Hudson, OH: Lexicomp, 1978-2023. http://online.lexi.com/. Updated date. Accessed 1/29/23.

OPIOIDS USED FOR TREATMENT (FENTANYL)

- Approval date: FDA-1968
- Dose: 25- 50 mcg every 5 minutes (moderate pain) or 50-100 mcg every 2 to 5 minutes (severe pain) until pain is relieved or unwanted side effects
- Pharmacokinetics
  - Onset of action: IV-immediate
  - Duration of action: ½-1 hour
  - Metabolism: hepatic via CYP3A4
  - Dose adjustment
    - Renal: Fentanyl may be used is generally considered safe for use in patients with kidney impairment with low initial doses & careful monitoring
    - Hepatic: No dosage adjustments, use with caution
- Pearls:
  - 100x more potent than morphine
  - Low risk of pseudo allergy
  - If allergic, recommend against use of other phenylpiperidines such as meperidine

-Fentanyl citrate. Accessed at https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/016619s038lbl.pdf on 1/29/23.
-Fentanyl: Drug information. Hudson, OH: Lexicomp, 1978-2023. http://online.lexi.com/. Updated date. Accessed 1/29/23.

OPIOIDS USED FOR TREATMENT (HYDROMORPHONE)

- Approval date: Marketed in the U.S. in the 1920s
- Dose: **IV:** 0.2 to 0.5 mg every 2-4 hours as needed; adjust dose according to patient response under close monitoring. Usual dosage range: 0.2 to 1 mg every 2 to 4 hours as needed
- Pharmacokinetics
  - Onset of action: 5 mins
  - Duration of action: 3-4 hours
  - Metabolism: metabolized to hydromorphone-3-glucoronide
  - Dose adjustment
    - Renal:
      - 37% of hydromorphone metabolized to hydromorphone-3-glucuronide, a potentially neuroexcitatory metabolite, which can accumulate with kidney impairment
      - Careful titration of dosing with close monitoring of response and adverse reactions due to drug and metabolite accumulation is important with all degrees of kidney impairment
    - Hepatic:
      - Mild to severe impairment: Initiate with 25% to 50% of the usual starting dose depending on the degree of impairment. Use with caution and monitor closely for respiratory and CNS depression
- Pearls
  - 2-8x more potent than morphine

Hydromorphone: Drug information. Hudson, OH: Lexicomp, 1978-2023. http://online.lexi.com/. Updated date. Accessed 1/29/23.

OPIOIDS USED FOR TREATMENT (SUFENTANIL) (DSUVIA)

- Approval date: 2018
- Dose: SL tab: Initial: 30 mcg; may repeat every hour with a minimum of 1 hour between doses; max dose: 360 mcg/day; do not use for >72 hours
- Pharmacokinetics
  - Onset of action: IV 1-3 mins: SL: ~30 mins
  - Duration of action: SL: 3 hours
  - Metabolism: Primarily hepatic & small intestine via demethylation & dealkylation
  - Dose adjustment
    - Renal: None
    - Hepatic: None
- Pearls
  - Expensive
  - Must be specially trained to administer

-Sufentanil: Drug information. Hudson, OH: Lexicomp, 1978-2023. http://online.lexi.com/. Updated date. Accessed 1/29/23
-Dsuvia, single applicator. McKesson. Accessed on https://mms.mckesson.com/product/1139888/AcelRx-Pharmaceuticals-Inc-61621043011 on 1/29/23.

OPIOIDS USED FOR TREATMENT (OXYCODONE)

- Approval date: 1928, synthesized from thebaine in 1916
- Dose: 5-10 mg PO every 4 to 6 hours as needed
- Pharmacokinetics
  - Onset of action: 10-15 mins
  - Duration of action: 3-6 hours
  - Metabolism:
    - Hepatic via CYP3A4 to noroxycodone (has weak analgesic activity), noroxymorphone, and alpha- and beta-noroxycodol
    - CYP2D6 mediated metabolism produces oxymorphone (has analgesic activity; low plasma concentrations [<15%])
  - Dose adjustment
    - Renal:
      - No specific dose adjustments provided in the manufacturer's labeling
      - Oxycodone is excreted as parent drug (~10%) and active to weakly active metabolites (~47%) with varying degrees of analgesic activity
      - T1/2 is prolonged with accumulation of active metabolites
      - Use of other opioids may be preferred for management of severe pain in patients with kidney impairment
    - Hepatic:
      - Initiate therapy at 33% to 50% the usual dosage and titrate carefully
      - Severe impairment, consider extending the dosing interval based on response and tolerability (eg, every 6 to 12 hours)
- Pearls
  - Use caution if prescribing oxycodone/APAP combination due to APAP toxicity

-Oxycodone: Drug information. Hudson, OH: Lexicomp, 1978-2023. http://online.lexi.com/. Updated date. Accessed 1/29/23.

OPIOIDS FOR POSTOPERATIVE ANALGESIA

- Cornerstone treatment for moderate - severe acute pain
- Immediate postoperative phase, opioid-related adverse events (ORADE) were reported in 10% of surgical cohorts. More common in:
  - Older men with higher ASA fitness grades
  - Multiple comorbidities
  - History of alcohol or drug abuse
- ORADE associated with an increase in duration of hospital stay by 1.6 days
- In the U.S., 27% of chronic opioid therapy patients began after a surgery
- Systematic review found that <50% of opioid prescriptions issued after surgery are used by the patient following discharge
- Patients already on opioids, BZDs, or with SUD or another mental health disorder are at greatest risk of prolonged postoperative opioid use
- Risk of withdrawal if normal dose of opioids not continued at a baseline level
  - Pre-surgical history essential including PDMP use
- Other strategies to mitigate harm include:
  - Opioid rotation/switching
  - Regional analgesia
  - Ensuring that a 'reverse analgesic ladder' is used on dis-charge to return the patient to their preadmission opioid regimen

-Small C and Laycock H. "Acute postoperative pain management". British Journal of Surgery. Jan 2020. e1-e179.

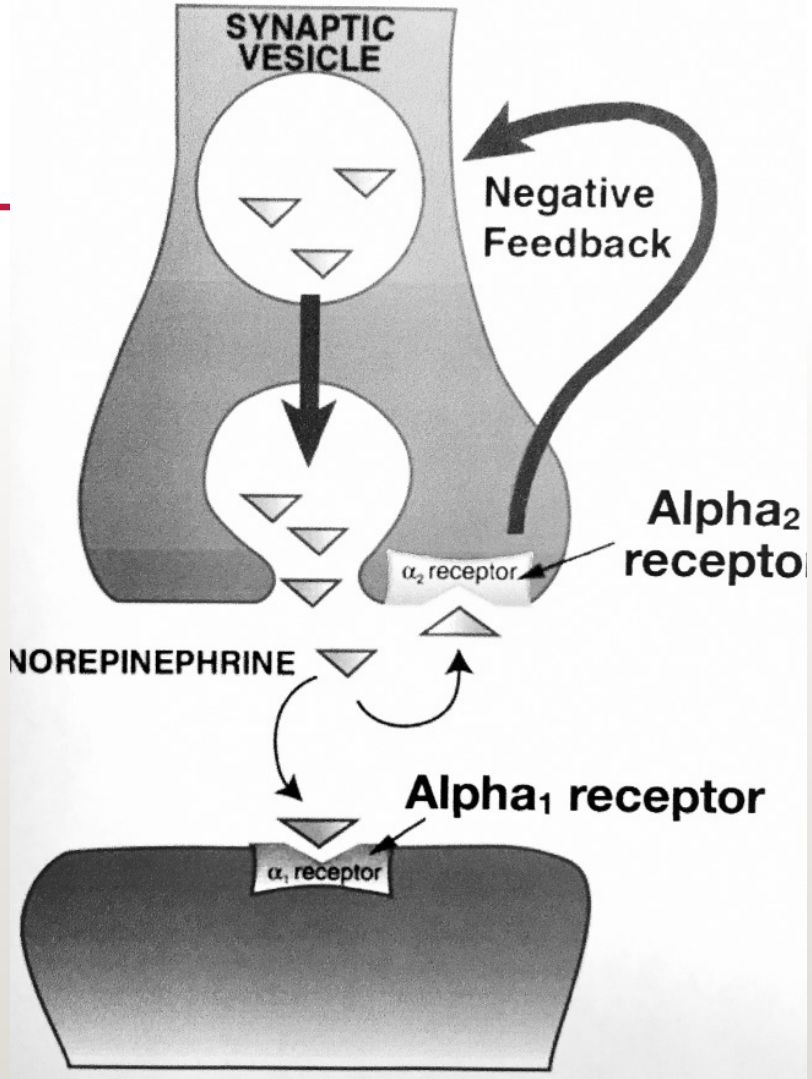
OPIOIDS FOR POSTOPERATIVE ANALGESIA

- Recommend PO over IV administration of opioids for postoperative analgesia
  - Evidence suggests that IV administration is not superior compared with PO
  - Postoperative pain may require round-the-clock dosing during the first 24 hours
  - Long-acting oral opioids are not recommended or labeled for use in the immediate postoperative period because of the need to titrate doses & the lack of evidence showing superiority over short-acting oral opioids, except for patients who receive long-acting opioids before surgery
- Preoperative administration of opioids is not recommended as an intervention to decrease postoperative pain or opioid consumption: no clear benefit from this practice
  - Clinicians should counsel patients to continue regularly prescribed opioids during the preoperative period unless there is a plan to taper or discontinue opioids
- Avoid intramuscular (IM) route
  - Discouraged due to significant pain & unreliable absorption, resulting in inconsistent postoperative analgesia
  - The IM route no clear advantages over other routes (eg, oral, i.v., rectal, or topical) of administration

-Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, Carter T, Cassidy CL, Chittenden EH, Degenhardt E, Griffith S, Manworren R, McCarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thirlby R, Viscusi E, Walco GA, Warner L, Weisman SJ, Wu CL. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain. 2016

ALPHA (A)-2 AGONISTS

- History: Clonidine was developed in 1961 by Boehringer Ingelheim while trying to make a decongestant
- Examples: clonidine, dexmedetomidine, tizanidine, guanfacine
- MOA (general): Stimulates α -2 adrenoceptors in the brain stem that result in reduced sympathetic outflow from the CNS, producing a decrease in peripheral resistance, renal vascular resistance, HR, & BP
- MOA of epidural α-2 agonists:
  - Produces pain relief at spinal presynaptic & postjunctional α -2 receptors by preventing pain signal transmission
  - Produces dose-dependent analgesia not antagonized by opiate antagonists
  - Analgesia is limited to the body regions innervated by the spinal segments where analgesic concentrations of clonidine are present
  - Produce analgesia at presynaptic & postjunctional alpha-2 adrenoceptors in the spinal cord by preventing pain signal transmission to the brain



-Giovannitti JA Jr, Thoms SM, Crawford JJ. Alpha-2 adrenergic receptor agonists: a review of current clinical applications. Anesth Prog. 2015 Spring;62(1):31-9. doi: 10.2344/0003-3006-62.1.31.
-Helmut Ståhle, A historical perspective: development of clonidine, Best Practice & Research Clinical Anaesthesiology,Volume 14, Issue 2, 2000,Pages 237-246,ISSN 1521-6896
-Clonidine: Drug information. Hudson, OH: Lexicomp, 1978-2023. http://online.lexi.com/. Updated date. Accessed 1/29/23.

ALPHA (A)-2 AGONISTS

- Clonidine
  - Administered orally, intravenously, intrathecally, or transdermal patch
  - Epidural clonidine is not recommended for obstetrical, postpartum, or perioperative pain management due to hemodynamic instability (especially hypotension & bradycardia). In rare instances, benefits may outweigh the possible risks
  - Avoid abrupt discontinuation
  - Associated with reduced opiate use & increased duration of nerve blocks
- Dexmedetomidine
  - Administered: intravenously, intrathecally, or perineurally
  - 7x the affinity for α -2 receptor compared to clonidine
  - Associated with reduced opiate use & increased duration of nerve block
  - Associated with sedation and hypotension
- Tizanidine:
  - Similar to clonidine, but has a shorter duration of action & less effect on HR & BP.
  - Study of 70 patients undergoing general anesthesia,
  - Tabori et al evaluated the effect of tizanidine vs placebo
  - Tizanidine reduced the propofol requirement by 25% & significantly reduced the incidence of postoperative shivering (11.4 vs 28.6%)
  - Concluded that tizanidine provides CV stability during induction of general anesthesia

-Clonidine: Drug information. Hudson, OH: Lexicomp, 1978-2023. http://online.lexi.com/. Updated date. Accessed 1/29/23.
-Dexmedetomindine: Drug Information. Hudson, OH: Lexicomp, 1978-2023. http://online.lexi.com/. Updated date. Accessed 1/29/23.
-Giovannitti JA Jr, Thoms SM, Crawford JJ. Alpha-2 adrenergic receptor agonists: a review of current clinical applications. Anesth Prog. 2015 Spring;62(1):31-9. doi: 10.2344/0003-3006-62.1.31
- Tabori M, Alipour M, Esalati H. Evaluation of oral tizanidine effects on (intraoperative) hemodynamic responses during direct laryngoscopy under general anesthesia. *Iran Red Crescent Med J.* 2013;15:541–546

NERVE BLOCKS

- See lecture on Perioperative Nerve Blocks

-Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, Carter T, Cassidy CL, Chittenden EH, Degenhardt E, Griffith S, Manworren R, McCarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thirlby R, Viscusi E, Walco GA, Warner L, Weisman SJ, Wu CL. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain. 2016

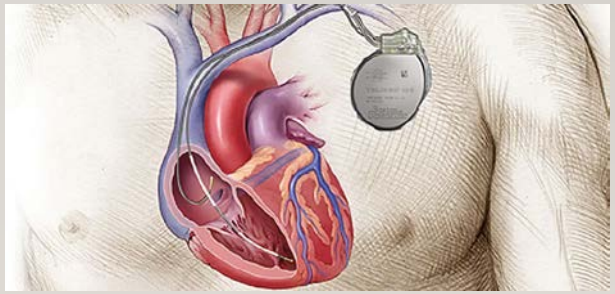
MEDS TO NOT ADMINISTER PER NEURAXIAL

- Evidence on the effectiveness of adjuvant medications administered using the epidural or spinal route with local anesthetics (with or without opioids) is limited
- Neuraxial administration of magnesium, benzodiazepines, neostigmine, tramadol, & ketamine in the treatment of postoperative pain is not recommended
  - No clear benefit of improvement
  - Insufficient evidence to determine safety
  - Medications are not available in a PF

Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, Carter T, Cassidy CL, Chittenden EH, Degenhardt E, Griffith S, Manworren R, McCarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thirlby R, Viscusi E, Walco GA, Warner L, Weisman SJ, Wu CL. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain. 2016

NONPHARMACOLOGICAL THERAPIES

- TENS unit
  - Systematic review of >20 RCTs found 25% less postoperative analgesic use compared to no TENS unit
  - TENS normally applied near surgical incision site or acupoint away from incision
- Contraindications to TENS use:
  - Pacemaker or implanted defibrillator
  - Lymphedema
  - Broken Skin



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•-**Bjordal J, Johnson MI, Ljunggreen AE.** Transcutaneous electrical nerve stimulation (TENS) can reduce postoperative analgesic consumption. A meta-analysis with assessment of optimal treatment parameters for postoperative pain. *Eur J Pain.* 2003; **7**: 181-188.

•-Digital TENS System. Essential Medical Supply. Accessed at https://www.essentialmedicalsupply.com/digital-tens-unit-complete on 1/30/23. .

•Moorman, Liza. Implantable cardioverter-defibrillator: Not just another device. American Nurse. Accessed at https://www.myamericannurse.com/implantable-cardioverter-defibrillator-not-just-another-device/ on 1/30/23

NONPHARMACOLOGICAL THERAPIES

- Insufficient evidence to recommend:
  - Acupuncture, massage, cold therapy, immobilization, bracing continuous passive motion or warm insufflation
  - These modalities are deemed safe
  - Lack demonstrated effectiveness
  - Equipment cost and provider time should be considered in relationship to low probability of patient benefit

-Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, Carter T, Cassidy CL, Chittenden EH, Degenhardt E, Griffith S, Manworren R, McCarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thirlby R, Viscusi E, Walco GA, Warner L, Weisman SJ, Wu CL. Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain. 2016

-Bjordal J, Johnson MI, Ljunggreen AE. Transcutaneous electrical nerve stimulation (TENS) can reduce postoperative analgesic consumption. A meta-analysis with assessment of optimal treatment parameters for postoperative pain. *Eur J Pain.* 2003; **7**: 181-188

SPECIAL POPULATIONS

- Chronic Kidney Disease
- Elderly
- Obesity
- Chronic Pain patient

CKD

- Issues:
  - Decreased clearance of medication
  - Medications that may cause further damage
- Depends on the stage of disease
  - Normally stage I & II have no change in function
  - Stage III & IV:
    - Impaired clearance of analgesia meds: increased risk of respiratory depression
    - Neuraxial or peripheral nerve blocks should be utilized to reduce postoperative pain
    - Avoid morphine, meperidine, codeine
  - Stage V: (Dialysis)
    - Impaired clearance of analgesia meds: increased risk of respiratory depression
    - Peripheral nerve blocks should be utilized to reduce postoperative pain
    - Gabapentinoids in neuropathic pain only

-Van den Bosch, C. Postoperative Pain Management in Special Population Groups. No. 26. 11/4/2016. accessed at https://safe.menlosecurity.com/doc/docview/viewer/docN287F9E27BF33b97aae582d65b5c21b0e08b4a940fbbbd23670dd51242d0431b5663dc14a3d72 on 12/28/2022

ELDERLY

- Issues:
  - Physiological & pathophysiological changes of aging
    - Decreased CO, hepatic/renal clearance, body comp, absorption
  - Alterations in the perception of pain
    - Experimental data suggest that elderly have a higher pain threshold inverse relationship with age
  - Assessment of pain, especially in those with cognitive decline
- Decreased sight, hearing, dementia may impact ability to assess
- Little evidence-based medicine d/t patient exclusion from clinical trials (>80yo, frail, multiple co-morbidities)

-Coldrey, J.C., R.N. Upton, and P.E. Macintyre, Advances in analgesia in the older patient. Best Pract Res Clin Anaesthesiol, 2011. 25(3): p. 367-78
-Van den Bosch, C. Postoperative Pain Management in Special Population Groups. No. 26. 11/4/2016. accessed at https://safe.menlosecurity.com/doc/docview/viewer/docN287F9E27BF33b97aae582d65b5c21b0e08b4a940fbbbd23670dd51242d0431b5663dc14a3d72 on 12/28/2022

ELDERLY

- Royal College of Physicians/British Pain Society/British Geriatric Society established guideline and pain ladder
  - Mild pain: acetaminophen, NSAIDs
  - Moderate pain: codeine, tramadol
  - Severe pain: opioids
    - 2-4 fold decrease in dose should be used compared to younger individuals
    - Recommend against use of meperidine or methadone
    - Recommend careful use of morphine, hydromorphone, & tramadol
    - Fentanyl & oxycodone usually work well

-Coldrey, J.C., R.N. Upton, and P.E. Macintyre, Advances in analgesia in the older patient. Best Pract Res Clin Anaesthesiol, 2011. 25(3): p. 367-78
-Van den Bosch, C. Postoperative Pain Management in Special Population Groups. No. 26. 11/4/2016. accessed at https://safe.menlosecurity.com/doc/docview/viewer/docN287F9E27BF33b97aae582d65b5c21b0e08b4a940fbbbd23670dd51242d0431b5663dc14a3d72 on 12/28/2022

CHRONIC OPIOID PATIENT

- Opioid tolerance with prolonged exposure to an opioid results in a reduced analgesic effect OR a higher dose is required to get the same analgesic effect
  - Opioids enhance the nociceptive response to painful stimulation i.e: Opioid Induced Hyperalgesia (OIH),
  - Diminished analgesic effect with the same prescribed dose
- Opioid tolerance is generally the result of receiving long-term opioids
  - Patients that misuse opioids or on opioid substitution programs many also fall into this category
- Physiology of opioid tolerance and OIH is not well understood; Distinct, but related
  - Opioid tolerance is often confused with physical dependance
  - Significant perioperative challenge in patients taking long term opioids
  - Patients with opioid tolerance may display 'pseudo-addiction' type behavior which may project as drug seeking behavior
  - Behavior will resolve when pain is adequately treated

-Van den Bosch, C. Postoperative Pain Management in Special Population Groups. No. 26. 11/4/2016. accessed at https://safe.menlosecurity.com/doc/docview/viewer/docN287F9E27BF33b97aae582d65b5c21b0e08b4a940fbbbd23670dd51242d0431b5663dc14a3d72 on 12/28/2022

OBESITY

- Goals are to provide comfort, early mobilization & improved respiratory function without causing inadequate sedation/respiratory compromise
- Pathophysiology of obesity, typical co-morbidities, high prevalence of OSA amongst obese patients make safe analgesic management difficult
- Pain control after bariatric surgery is a major challenge
  - Traditional opioid-centric pain management can often result in opioid-induced ventilatory impairment and increased morbidity and/or mortality
  - Multimodal analgesia strategies based on a step-wise, severity-based, opioid-sparing approach can improve patient safety and outcomes
- Advice on general management includes multimodal analgesic therapy, preference for regional techniques, avoidance of sedatives, non-invasive ventilation with supplemental oxygen, early mobilization and elevation of the head of bed to 30 degrees

-Schug SA, Raymann A. Postoperative pain management of the obese patient. Best Pract Res Clin Anaesthesiol. 2011 Mar;25(1):73-81. doi: 10.1016/j.bpa.2010.12.001. PMID: 21516915.
-Belcaid I, Eipe N. Perioperative Pain Management in Morbid Obesity. Drugs. 2019 Jul;79(11):1163-1175. doi: 10.1007/s40265-019-01156-3. PMID: 31256367.

OBESITY

- Meds:
  - **APAP:** no change in serum concentration between obese and non-obese
  - **NSAIDS:** no change but not used after bariatric surgery
  - **Opioids:** high risk of respiratory depression, hypoventilation: monitor closely
  - **Epidural:** no change
  - **Peripheral Nerve Blocks**: increased fat tissue, landmarks cannot be palpated or the image quality of U/S decreases, so peripheral nerve blocks may fail

-Schug SA, Raymann A. Postoperative pain management of the obese patient. Best Pract Res Clin Anaesthesiol. 2011 Mar;25(1):73-81. doi: 10.1016/j.bpa.2010.12.001. PMID: 21516915.
-Belcaid I, Eipe N. Perioperative Pain Management in Morbid Obesity. Drugs. 2019 Jul;79(11):1163-1175. doi: 10.1007/s40265-019-01156-3. PMID: 31256367.

CONCLUSION

- Adequate management of postoperative pain is a core determinant of the patient achieving DrEaMing (Drinking, Eating and Mobilizing) status
- Multimodal regimens for prevention of postoperative pain should be widely used but will vary depending on the patient, setting, & surgical procedure
- Optimal management begins in the preoperative period and it starts with assessment of the patient & development of a plan of care tailored to the individual
- Each of the biological, psychological & social dimensions of the pain experienced should be considered & understood in order to provide optimum pain management
- As part of a shared decision-making approach, it is appropriate for the clinician to inform the patient when a particular recommendation might not be applicable, after considering all circumstances pertinent to that individual

QUESTIONS