Chapter 3 – Pain Management

NOTE: CONTENT CONTAINED IN THIS DOCUMENT IS TAKEN FROM ROSEN'S EMERGENCY MEDICINE 9th Ed.

Italicized text is quoted directly from Rosen's.

Key Concepts:

1. *Acute pain is an urgent condition requiring rapid assessment and treatment*
2. *Treatment of acute pain is different than treatment of chronic pain. Management of chronic pain should be done in consultation with the provider responsible for the patient's long-term management.*
3. *Titrated opioid IV analgesics are the main treatment approach for moderate and severe acute pain. SC administration is preferable to IM administration in when IV access is not established, and if patient is not tolerating oral routes.*
4. *Oral opioids can be used for moderate pain when the IV route is not otherwise needed.*
5. *Outpatient opioids should be confined to the period of acute pain. Consider a 3-5 day supply after which the patient should be reassessed and/or transitioned to non-opioid analgesia for most uncomplicated acute painful complaints with a natural history of expected resolution.*
6. *Acetaminophen and NSAIDS should be used for pain therapy, when not contraindicated. The analgesic effects are additive to the effects of opioids and to each other.*
7. *Morphine, fentanyl, and hydromorphone are the preferred parenteral opioids for use in the ED. Do not use meperidine.*
8. *There is no evidence to support that administration of analgesia impairs diagnostic accuracy of physical exam findings.*
9. *There is no evidence to suggest that morphine causes more smooth muscle spasm than other opioids. Morphine is a safe drug for patients with biliary colic and nephrolithiasis.*
10. *Patients who are known to be diverting or abusing opioids* ***should not be prescribed opioids for use as outpatients.*** *When possible, opioids should be avoided in chronic pain.*
11. *Topical and local anesthetics can be used to treat pain associated with most ED procedures.*
12. *Low tissue pH (5 or 6) in infected tissue impairs local anesthetic function.*

Core Questions:

1. Define the following terms (Box 3.1):
    - Allodynia
    - Amnesia/amnestic
    - Local anesthesia
    - Analgesia
    - Hypnotic
    - Narcotic
    - Nociceptor
    - Noxious stimulus
    - Opiate
    - Opioid
    - Pain
    - Procedural Sedation
    - Sedative
2. Describe a practical approach to stepwise management of pain in the ED.
3. Describe the adult parenteral and oral doses for:
    - Morphine
    - Hydromorphone
    - Fentanyl
    - Aside - don't use IM opioids (Box 3.5)
4. Differentiate between opioid side effects and opioid toxicity.
5. How do you manage opioid toxicity?
6. Describe relative safety profiles for the NSAIDS.
7. List the classes of local anesthetics. How do they work?
8. List the toxic doses for each local anesthetic
    - Lidocaine
    - Lidocaine with Epi
    - Bupivicaine
9. List 5 techniques to reduce pain of injection of local anesthetic
10. List agents that can be used for topical anesthesia of:
    - Intact skin
    - Mucous membrane
    - Open skin/lacerations

Wisecracks:

1. What agents can be used as a substitute in cases of anaphylaxis to local anesthetic?
2. Why should you avoid use of the following agents:
    a. Tramadol
    b. Demerol
3. How does local anesthetic toxicity present?

Rosen's in Perspective

Pain is something we deal with on a daily basis in the ED. This is something that we need to be really damn good at managing. As we mentioned above, acute pain is an emergent condition for the patient that requires rapid assessment and management. Tylenol, NSAIDS, and opioids for the basis for ED management of acute pain. Additionally, we have access to a whole armamentarium of local and topical anesthetics, and we need to be well-versed in their use.

We'll try and keep the pathophysiology to a minimum, but there's a few things we should cover:

1. Describe how a pain signal travels to the brain (Fig 3.1, 3.2, 3.3)

See figure 3.1, 3.2. and 3.3 in Rosen's 9th Edition Chapter in Pain Management

- Spinal tracts associated with pain transmission are spinothalamic, spinomesencephalic, spinoreticular tracts, located in anterolateral aspect of cord.

2. Describe the 6 types of opioid receptors (Table 3.2)

See table 3.2 in Rosen's 9th Edition Chapter in Pain Management

Opioid Receptor Class	**Effects**	**Associated Endogenous Endorphin**
Mu 1	Euphoria, supraspinal analgesia, confusion, dizziness, nausea, low addition potential	Beta-endorphin
Mu 2	Respiratory depression, CV and GI effects, miosis, urinary retention	Beta-endorphin
Delta	Spinal anagesica, CV depression, decreased brain and myocardial oxygen demand	Enkephalin
Kappa	Spent analgesia, dysphoria, psychomimetic effects, feedback inhibition of endorphin system	Dynorphin, beta-endorphin
Epsilon	Hormone	Beta-endorphin
Gamma	Dysphoria, psychomimetic effects	Beta-endorphin

3. Types of peripheral nerve fibers can be found in table 3.1 in Rosen's 9th Edition Chapter in Pain Management. We won't go through these for sake of time.

Core Questions:

[1] Define the following terms:

- See table 3.2 in Rosen's 9th Edition Chapter in Pain Management
  i. Allodynia – pain from a stimulus that does not normally provoke pain
  ii. Amnesia/amnestic – an agent that suppresses the formation of memories
  iii. Local anesthesia – creates an area of insensibility to pain by injection of a local anesthetic agent
  iv. Analgesia – relief from pain
  v. Hypnotic – agent that promotes the onset of sleep
  vi. Narcotic – term with legal implications describing opioid agents together with various central nervous system depressants drugs of abuse
  vii. Nociceptor – receptor that is sensitive and responsible for transmitting joint stimuli
  viii. Noxious stimulus – stimulus that is damaging or potentially damaging and results in sensation of pain
  ix. Opiate – naturally occurring derivative of opium alkaloid that binds opiate receptors and produces effects similar to those of endogenous endorphins
  x. Opioid – naturally occurring or semisynthetic derivative of opium alkaloid (includes all opiates) that binds opiate receptors and produces effects similar to those of endogenous endorphins
  xi. Pain – unpleasant sensory and emotion experience arising from actual or potential tissue damage or described in terms of such damage
  xii. Procedural Sedation – pharmacologic induction of a state of sedation or dissociation with amnesia for pain control during a painful procedure
  xiii. Sedative – agent that decreases a patient's level of awareness

[2] Describe a practical approach to stepwise management of acute pain in the ED.

This is pretty straightforward for most patients.

For Mild/Moderate Pain:
Tylenol and NSAIDS (providing there are no contraindications) are reasonable first steps. If this is not sufficient, consider addition of PO opiates.

For Severe Pain - parenteral opioids are the mainstay of treatment.
There are specific situations where adjuncts or regional anesthesia may be appropriate for you patient (e.g. - ?fascia iliac block in hip fracture)

For discharging patients with acutely painful conditions (e.g. burn or fracture), consider scheduled Tylenol and Advil q6h with a short supply (3-5 days) of opioids for breakthrough pain.

This obviously does not apply across the board.

- NSAIDS - caution or avoid in elderly or hx gastritis, renal insufficiency, GI bleeds, etc.
- Acute on chronic pain - be aware that some patients may become opioid tolerant and may be on multiple additional agents.
- Methadone - be aware of non-linear morphine equivalence with higher doses
- Suboxone - stronger affinity for mu opioid receptors means that conventional opioids will likely have little to no effect (this is why it's useful for treating opioid abuse, but poses interesting issues if a suboxone patient comes in to the ED with an acutely painful condition)

[3] Describe the adult parenteral and oral doses for:

- Morphine.
    i. Rosen's - IV 0.1mg/kg PO 0.5 mg/kg
    ii. I go a bit lower and titrate. IV 2.5 -5 mg. PO 5 -10 mg. Q4h typically.
    iii. Duration 3-4h.
    iv. Issues - histamine release and preload, accumulation of metabolites in renal insufficiency
- Hydromorphone
    i. Rosen's - 0.015 mg/kg IV and 0.075mg/kg PO.
    ii. Again, a bit lower than this and titrate up. IV - 0.5-1mg (0.25mg if elderly or at risk). 2-4mg PO.
    iii. Morphine equivalence: 5:1
    iv. Duration 2-4h.
- Fentanyl
    i. Rosens: 1.5µg/kg IV and 3 µg/kg PO
    ii. Practically - I just use IV 50-100 mcg and titrate
    iii. Synthetic opioid, highly lipophilic, Shorter acting - duration 30 - 60 minutes.
- Aside – See box 3.5 in Rosen's 9th Edition Chapter in Pain Management
    i. Disadvantage of Intramuscular Opioid Administration
        1. Pain on injection
        2. Delayed onset of action
        3. Inability to predict therapeutic effect
        4. Inability to titrate dosage
        5. Diurnal variation in level achieved
        6. Disease state may affect level achieved
        7. Level dependent on intramuscular injection site

If you prescribe an opiate in the ED, leave an antiemetic order + stool softener as needed (inpatients or outpatient Rx).

[4] Differentiate between opioid side effects and opioid toxicity.

Opioid Toxidrome - we all know this. Respiratory Depression, Depressed LOC, Miosis; below are additional findings from UpToDate.

- Vital Signs:
  - Heart rate decreased or increased
  - Blood pressure decrease or unchanged
  - Respiratory rate decreased
  - Temperature decreased or unchanged
- Gastrointestinal:
  - Decreased bowel sounds
- Neurological:
  - Sedation or coma
  - Seizure (Meperidine, propoxyphene, tramadol, or as a result of hypoxia)

Vs. Side effects (multiple)

- New: risk factor for invasive pneumococcal disease and other infections

Ann Intern Med. 2018 Mar 20;168(6):396-404. doi: 10.7326/M17-1907. Epub 2018 Feb 13.

Opioid Analgesic Use and Risk for Invasive Pneumococcal Diseases: A Nested Case-Control Study.

Wiese AD[1], Griffin MR[2], Schaffner W[1], Stein CM[1], Greevy RA[3], Mitchel EF Jr[1], Grijalva CG[2].

- Constipation (reduced peristalsis and longer transit times)
- Sedation (typically with dose escalation or initiation)
- Nausea and vomiting
- Myoclonus (often associated with opiate mediated neurotoxicity and sedation)
- Neuroendocrine effects - adrenal suppression and hypogonadism
- Sleep disordered breathing
- Pruritis
- Rare - true opioid allergy
- Urinary retention due to peripheral effect on nerves that innervate bladder and regulate tone
- Weight gain
- Hyperalgesia

[5] How do you manage opioid toxicity?

- Prevention is key - know your safe doses (and then cut them in half if you've got an at risk patient - elderly or frail especially)!
- Recognition (we've talked about this) - triad of respiratory depression, coma, miosis
- ABC's plus naloxone!
- IV, IM, SubQ: Initial: 0.4 to 2 mg; may need to repeat doses every 2 to 3 minutes. A lower initial dose (0.1 to 0.2 mg) should be considered for patients with opioid dependence to avoid acute withdrawal or if there are concerns regarding concurrent

stimulant overdose (Mokhlesi 2003). After reversal, may need to re-administer dose(s) at a later interval (ie, 20 to 60 minutes) depending on type/duration of opioid. If no response is observed after 10 mg total, consider other causes of respiratory depression. **Note:** May be given endotracheally (off-label route) as 2 to 2.5 times the initial IV dose (ie, 0.8 to 5 mg) (AHA [Neumar 2010]).

[6] Describe relative safety profiles, interactions, and at risk populations for NSAIDS.

See box 3.6 in Rosen's 9th Edition Chapter in Pain Management

NSAID	Relative Risk of Serious GI Toxicity
COX2 Inhibitor	0.6
Ibuprofen	1.0
Diclofenac	1.8
Sulindac	2.1
Naproxen	2.2
Indomethacin	2.4
Tolmetin	3.0
Piroxicam	3.8
Ketoprofen	4.2
Ketoprofen	24.7
RISK REDUCTION WHEN ADDED TO IBUPROFEN	
Proton Pump Inhibitor	0.09
Misoprostol	0.57

- Patients at Risk for Adverse Events During Nonsteroidal Anti-Inflammatory Drug (NSAID) Therapy
    - Patients with dehydration, hypovolemia or who have impaired renal function are at increased risk for decreasing renal function or renal failure
    - Patients with liver disease or CHF – in particular, those who already taking ACEi, ARBs, or diuretics – in who liver or heart conditions may worsen
    - Older patients are at enhanced risk for GI and renal events
    - Patients with asthma and known aspiration hypersensitivity are increased risk of bronchospasm
    - Women in the third trimester of pregnancy – NSAIDs may prolong gestation or prematurely close the ductus arteriosus
    - Patients who use tobacco or ethanol with a history of gastritis or peptic ulcer disease are at increased risk for peptic ulcer or GI bleed

Interactions

- OAC's - add to anticoagulant properties of warfarin, displace protein bound warfarin.
- ACEI - may impair renal function and impair antihypertensive effects of ACEI's
- Diuretics - increased risk of renal failure as NSAIDS decrease renal blood flow
- Glucocorticoids - increased risk of peptic ulcer disease
- Lithium - NSAIDS enhance lithium reabsorption and reduce excretion, leading to increased lithium levels.

No NSAID is more effective as an analgesic than ibuprofen, 400 mg, including ibuprofen, 600 and 800 mg.

[7] List the classes of local anesthetics. How do they work?

- Esters and Amides - Local anesthetics work by reversibly blocking sodium channels in the nerve cell membrane which prevents the generation of action potentials
    - Amides - Lidocaine, bupivicaine, and co. Hepatic metabolism
    - Esters - Cocaine, procaine, tetracaine and others. metabolized by plasma cholinesterase

[8] List the toxic doses for each local anesthetic

- Lidocaine - 3-5mg/kg
- Lidocaine with Epi - 5-7mg/kg
- Bupivicaine - 1.5 mg/kg
- Bupivicaine with Epi - 3mg/kg

These are approximate guides - some patients could become toxic below the threshold and some may receive doses in excess of the thresholds and be fine.

Say we have a 70kg adult and we want to figure out the max amount of 1% lidocaine we can safely give.
Step 1 - Find max dose. 70kg x 5mg/kg = 350 mg
Step 2a - Find amount of lidocaine to use. 1% Lidocaine = 10mg/mL
Step 2b - 350mg x 1mL/10mg = 35mL of 1% Lidocaine

Don't podcast but have as add'l example for shownotes
Max dose of 1% lidocaine with epinephrine for 20kg child
Step 1 - max dose = 20kg x 7mg/kg = 140mg
Step 2a - 1% lidocaine = 10mg/mL (1% x 10)
Step 2b - 140mg x 1mL/10mg = 14mL of 1% lido with Epi

[9] List 5 techniques to reduce pain of injection of local anesthetic

See box 3.6 in Rosen's 9th Edition Chapter in Pain Management

- Techniques to Reduce the Pain of Injection
    - Buffering of local anesthetic agents
    - Counterirritation
    - Slow rate of injection
    - Use of topical anesthetics
    - Warming of solution
    - Distraction techniques

How to make a buffered solution according to Rosen's: take a standard solution of bicarb (8.4% in 50mL) and add to a syringe containing lidocaine in a ratio of 1:10.

[10] List agents that can be used for topical anesthesia of:

- Intact skin
  - EMLA - eutectic mixture of local anesthetics. Mixture of lidocaine and prilocaine in an alkaline oil mix which allows diffusion through intact skin.
  - Ethyl chloride and fluoromethane sprays
- Mucous membrane
  - Cocaine. Potent vasoconstrictor along with anesthetic activity. Generally, avoid doses >200mg and avoid in patients with known CAD (we know all about that vasospasm)
  - Lidocaine (gel and spray formats). Applications to nasal procedures, Foley catheter placements, temporization for awake intubation, etc.
  - Tetracaine - cornea
  - Benzocaine - oral procedures. Almost insoluble in water and remains on mucous membranes in the mouth.
- Open skin/lacerations
  - LET (lidocaine, epinephrine, tetracaine). Can apply to open wound and let it sit for 10-20 minutes to achieve superficial anesthesia. Note - tetracaine toxicity from application to mucous membranes (eye, nose) has been documented so avoid this.

Wisecracks:

[1] What agents can be used as a substitute in cases of anaphylaxis to local anesthetic?

- Very rare. Often the offending agent is the preservative used. In this case, you could substitute an agent from a different class - the preservatives don't typically cross- react.
- However - if the patient has a true anaphylactic allergy to all 'caine anesthetics - you can locally inject diphenhydramine (dilute 1 mL of a 50mg/mL ampoule with 5 or 10 mL of saline to make a 1% - 0.5% solution)

[2] Why should you avoid use of the following agents:

- Tramadol
  - Tramadol is a dirty drug! By this I mean it acts on multiple receptors. Weak mu agonist with some effects on serotonin and norepi. Unpredictable kinetics due to individual variations in CYP2D6 which produces active metabolite ODT. Also lowers seizure threshold, can precipitate serotonin syndrome in conjunction with other serotonergic drugs, and can precipitate hypoglycemia. https://emcrit.org/toxhound/tramadont/
- Demerol
  - Rosen's - "No indication for use in the ED." metabolized by cytochrome P450 to normeperidine which can cause CNS toxicity at therapeutic doses.
  - Half-life is 12-16h, and blocks muscarinic receptors, which can result in anticholinergic effects like agitation, delirium, etc.

- Can precipitate seizures. Can precipitate serotonin syndrome in conjunction with SSRIs, SNRIs, or MAOIs

[3] How does local anesthetic toxicity present?

Local toxicity vs. systemic toxicity.

- Local toxicity - theoretical risk of the reduction in blood flow to end organs (classic teaching of finger, nose, penis, toes don't get epi). However, this has not really been borne out by the evidence. For example, it is safe to use epinephrine for ring blocks.
- Systemic Toxicity - Has a typical progression of symptoms. Circumoral paresthesias, dysarthria, tinnitus, decreased LOC/confusion, seizures, coma, and cardiac arrest.

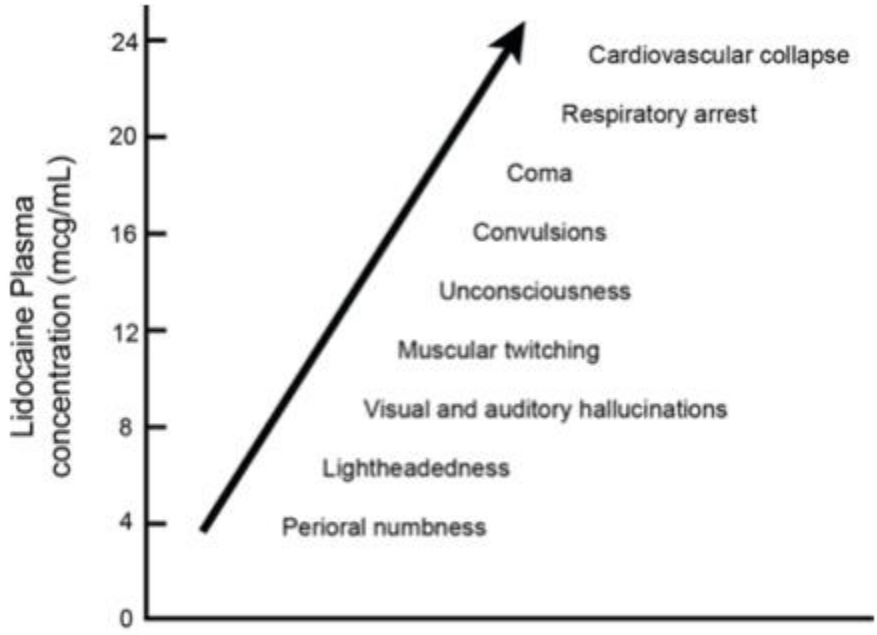

Fig. 15.5 Lidocaine systemic toxicity and plasma concentrations. Adapted from Neural Blockade. Cousins MJ, Bridenbaugh PO. 2nd Edition 1980. JB Lippincott.

Management

- ABCs
- Manage seizures with Benzos
- ACLS as needed
- The main antidote is intralipid - theoretically extracts lipid soluble molecules from cardiac tissues