Jackson HEALTH SYSTEM
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Dear Medical Staff,

The assessment and management of pain is a necessary and vital component in appropriate patient care. To that end, we seek to highlight a few points to consider.

1. **Evaluation:** Obtain a medical history and perform a physical exam, documenting these in the medical record, specifically noting the following:
    a. Nature and intensity of pain
    b. Current and past use of analgesics
    c. Underlying or coexisting diseases or conditions
    d. Effect of the pain on physical and psychological function
    e. History of substance abuse
    f. Presence of one or more recognized medical indications for the use of a controlled substance

2. **Informed consent and agreement for treatment:** Risks and benefits of controlled substance use should be discussed with the patient/designee/surrogate/guardian. The patient's agreement to receive prescriptions from a single physician and one pharmacy whenever possible should be strongly encouraged. A written agreement with the patient at high risk for medication abuse, or with a history of substance abuse should be developed and may include:
    a. Urine/serum medication level screening
    b. Number and frequency of all prescription refills
    c. Reasons for which drug therapy may be discontinued (e.g., violation of agreement)

3. **Consultation:** Refer as necessary for additional evaluation and treatment in order to achieve treatment objectives, paying special attention to patients who are at risk for medication misuse, abuse, or diversion.
    a. Provide extra care, monitoring, documentation and consulting with, or referring to, a pain specialist when treating patients with a history of substance abuse, or with comorbid psychiatric disorder

4. **Treatment plan** should be adjusted as needed according to the individual medical needs of the patient. It should also include other treatment modalities or a rehabilitation program depending on the etiology of the pain and the extent to which the pain is associated with physical and/or psychosocial impairment. Further, it should:
    a. State objectives that will be used to determine success, such as pain relief and improved physical and psychosocial function
    b. Indicate if any further diagnostic evaluations or other treatments are planned

5. **Medical records** must be kept accurate and should include the following:
    a. Medical history and physical examination
    b. Diagnostic, therapeutic, and laboratory results
    c. Evaluations and consultations
    d. Treatment objectives
    e. Discussion of risks and benefits
    f. Informed consent
    g. Treatments

h. Medications (including date, type, dosage, and quantity prescribed)
i. Instructions and agreements
j. Periodic reviews

6. **Periodic review:** Follow up regarding the course of pain treatment and any new information about the etiology of the pain or the patient's state of health should occur. The appropriateness of continuing the current treatment plan if the patient's progress is unsatisfactory should be assessed. Consideration of other therapeutic modalities may occur in this instance. Further, determine whether to continue or modify the use of controlled substances for analgesia. That decision may be based on progress toward treatment objectives according to the following factors:
   a. Satisfactory response, indicated by the patient's decreased pain, increased level of function, or improved quality of life
   b. Objective evidence of improved or diminished function, based on information from the family members or other caregivers who are monitoring treatment

7. **Compliance with controlled substance laws and regulations**: Registration with the Drug Enforcement Agency is required for a physician to prescribe, dispense, or administer controlled substances. Further he/she must be licensed in the State and comply with all applicable federal and state laws and regulations.

References: http://projects.hsl.wisc.edu/GME/PainManagement/index.html
http://www.fsmb.org/pdf/2004_grpol_Controlled_Substances.pdf

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Pain Management

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Objectives

- Identify pain characteristics
- Evaluate pain specific to the trauma population
- Review opioid pharmacology
- Define adverse drug profiles
- Determine appropriate dosing strategy
- Become familiar with converting between opioids

Epidemiology

- Annual cost in US: In the billions
- 25 million Americans experience pain
- Inadequate pain control in hospitalized patients
  - 45% of patients were dissatisfied with pain control

Pain Management

- Pain can be experienced by patients in the ICU for a variety of reasons
  - Surgery
  - Trauma
  - Mechanical ventilation
  - Routine care in the unit
- Pain control may also affect hemodynamic status
- Stress is associated with poor patient outcomes
  - Increase in catecholamine release that results in arteriolar vasoconstriction and impaired tissue perfusion

Trauma Population

- Inadequate analgesia can lead to:
  - Poor oxygenation
  - More frequent pulmonary emboli
  - Impaired tissue injury
  - Increased mortality
- Adequate analgesia postoperatively
  - More rapid recovery
  - Shorter hospital stays
  - Improved survival

Trauma Population

- Incidence of pain
- Within minutes of injury
  - Altered gene expression can lead to postsynaptic sensitization and neuronal remodeling
  - Cellular cascade initiated leading to chronic pain
- Early pain management can prevent or reverse the cascade

Blunt Thoracic Trauma

- Chest wall lesions
  - Rib fractures
  - Flail chest
  - Soft tissue contusion
- Intrapleural lesions
  - Hemothorax
  - Pneumothorax
- Parenchymal lung injuries
  - Pulmonary contusion
  - Lung laceration
- Mediastinal injury
  - Blunt cardiac injury

Chest Wall Trauma

- Most commonly seen after motor vehicle collisions
- Accounts for 8% of all trauma admissions
- Marker of severe injury
- Contributes significantly to morbidity and mortality

Chest Wall Trauma

- Rib fractures are the most common chest wall injury identified in 10% of patients
- Multiple rib fractures cause severe pain
  - May be more harmful then the injury itself
- Pain limits the patient's ability to cough and breathe deeply
  - Sputum retention
  - Atelectasis
  - Reduction in functional residual capacity

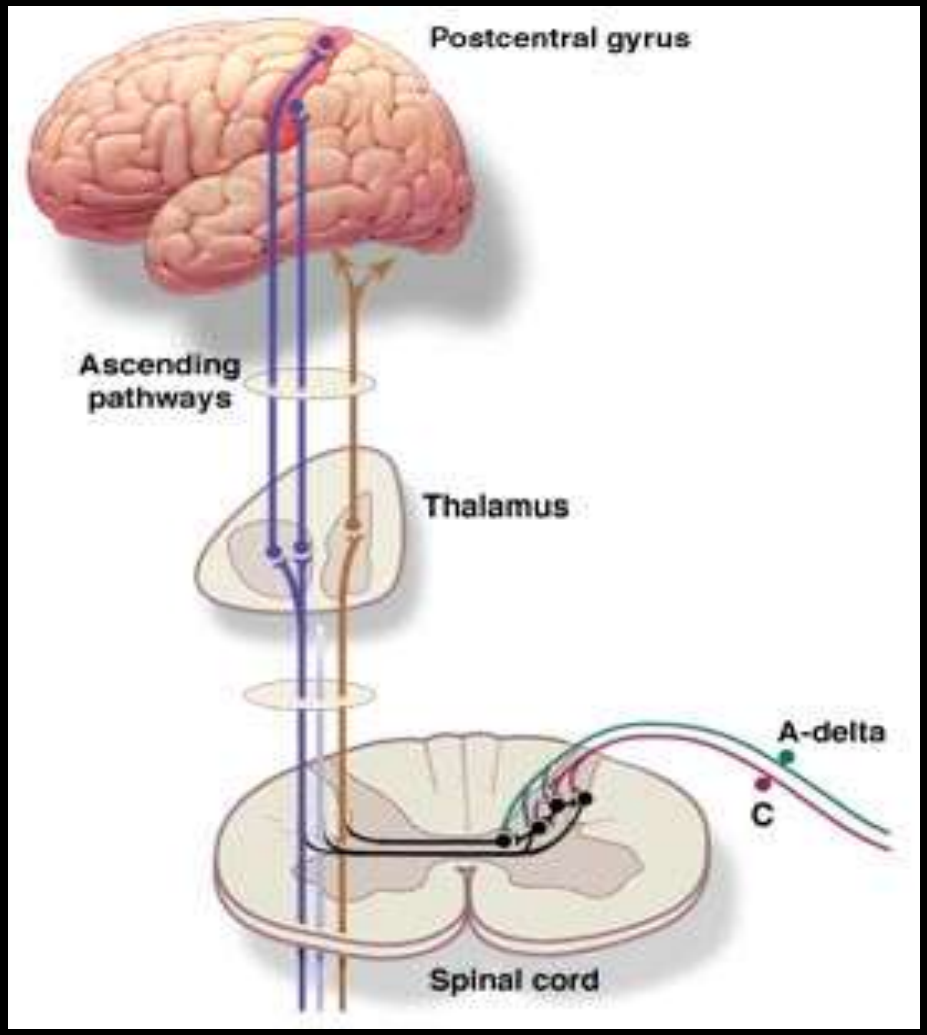
Pain Assessment

Critical Care Observation Tool (CPOT)		
Indicator	Description	Score
Facial Expression	No muscle tension observed	0, relaxed neutral
	Presence of frowning, brow lowering, orbit tightening and levator contraction or any other change (e.g. opening eyes or tearing during nociceptive procedures)	1, tense
	All previous facial movements plus eyelid tightly closed (the patient may present with mouth open or biting the endotracheal tube)	2, grimacing
Body movement	Does not move at all (doesn't necessarily mean absence of pain) or normal position (movements not aimed toward the pain site or not made for the purpose of protection)	0, Absence of movements or normal position
	Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements	1, protection
	Pulling tube, attempting to sit up, moving limbs/thrashing, not following commands, striking at staff, trying to climb out of bed	2, restlessness/agitation
Muscle tension	No resistance to passive movements	0, relaxed
	Resistance to passive movements	1, tense/rigid
	Strong resistance to passive movements or incapacity to complete them	2, very tense/rigid
Compliance with the ventilator (intubated patients)	Alarms not activated, easy ventilation	0, Tolerating ventilator or movement
	Coughing, alarms may be activated but stop spontaneously	1, Coughing but tolerating
	Asynchrony: blocking ventilation, alarms frequently activated	2, Fighting ventilator

Types of Pain

- **Nociceptive**
  - Somatic→ “throbbing”
  - Visceral→ referred pain
- **Neuropathic**
  - Nerve damage
  - Ex: Postherpetic neuralgia and peripheral neuropathy
- **Functional**
  - Abnormal operation of nervous system
  - Ex: fibromyalgia and IBS

Pathophysiology

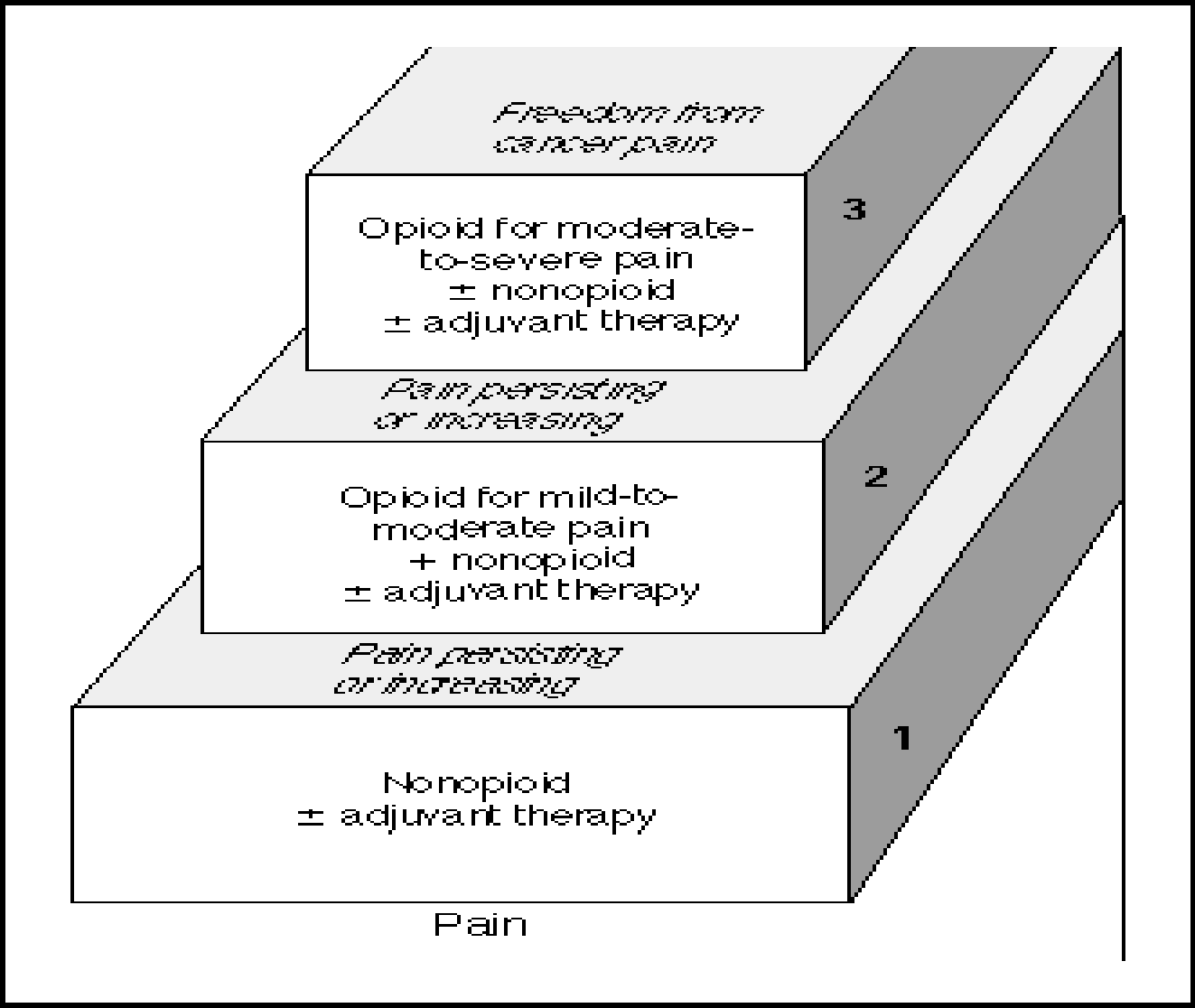


- Noxious stimuli→ depolarization at the peripheral nociceptors→ transmission to spinal cord via primary afferent nociceptive axons→ brain→ FEEL PAIN!!
- May involve acute or chronic inflammation

Clinical Presentation

- Palliative & provocative factors
  - What makes the pain better/worse?
- Quality
  - Description of the pain
- Radiation
  - Location
- Severity
  - How does the pain compare to pain you have experienced in the past?
- Temporal factors
  - Does the pain increase/decrease with time?

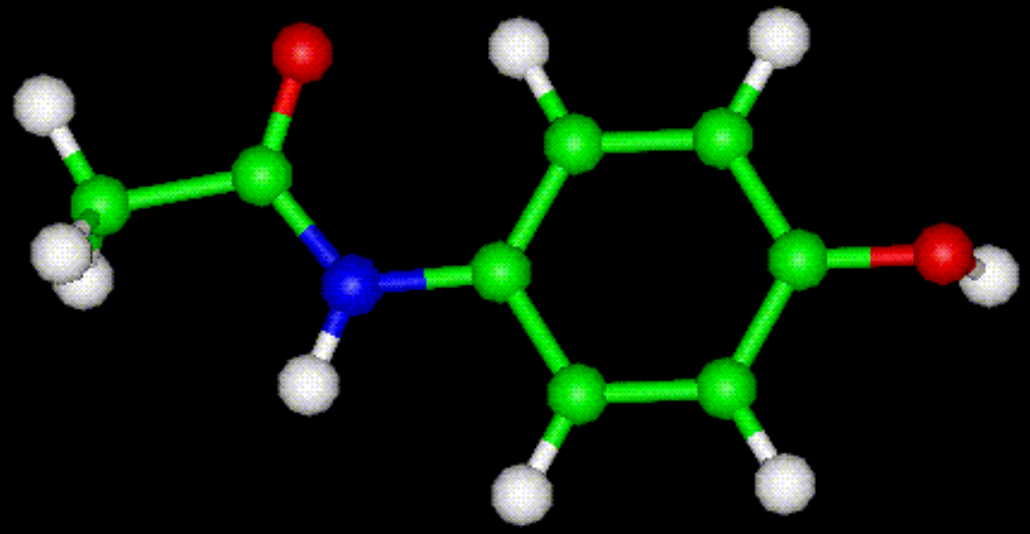
Management


Freedom from cancer pain
Opioid for moderate-to-severe pain
± nonopioid
± adjuvant therapy
3
Pain persisting or increasing
Opioid for mild-to-moderate pain
+ nonopioid
± adjuvant therapy
2
Pain persisting or increasing
Nonopioid
± adjuvant therapy
1
Pain

Therapy Options

- Nonopioids
  - Acetaminophen
  - NSAIDS
  - Aspirin
- Opioids
  - Morphine
  - Fentanyl
  - Oxycodone
  - Combinations
- Adjuvant
  - Steroids
  - Gaba Analogs
  - Anticonvulsants
  - Bisphosphonates
- Local Anesthetics
  - Lidocaine patch

NON-OPIOIDS



NON-OPIOIDS

Agent	Dose	AE	Other
Aspirin (ASA)	325-1000 mg PO q 4-6 h Max: 4 g/day	• Bleeding (GI) • Platelet dysfunction • GI ulcers • Hemolytic anemia • Pancytopenia	• Antipyretic •Onset: 0.5 h •Duration: 4-6 h •Half-life: 0.25 h
Acetaminophen (APAP)	325-650 mg PO q 4-6 h Max: 4g/day	• Hepatotoxicity • Pancytopenia • Rash	•Antipyretic •Onset: 0.5-1 h •Duration: 3-6 h •Half-life: 2-3 h

NSAIDS

Agent	Dose	AE	Other
Ibuprofen (Motrin® Advil®)	200-400 mg PO q 4-6 h Max: 3.2 g/day	•GI ulcers • Abdominal pain • Aplastic anemia • Thrombocytopenia • HTN • Edema • Renal insufficiency • Drowsiness	•Onset: 0.5 h •Duration: 4-6 h •Half-life: 2-2.5 h
Naproxen (Naprosyn®)	500 mg PO initially then 500mg PO Q 12h Max: 1 g/day		•Onset: 1 h •Duration: up to 12h •Half-life: 12-17 h
Celecoxib (Celebrex®)	Initial 400 mg followed by 200mg on day 1, then 200mg PO BID Max: 400 mg/day	•Thrombotic event •Stroke •MI	•Onset: 1 h •Duration:12-24 h •Half-life: 11 h

NSAIDS

Agent	Dose	AE	Other
Ketorolac (Toradol®)	IM/IV: 15-30mg q 6 h PO: 10mg q6h Max: 120mg/day Age >65, <50kg or Renal impairment→ Max: 60mg/d ONLY for 5 days	• Renal toxicity • Pancytopenia • Rash • Bleeding (GI) • Cardiac • Psychotic behavior	•Onset: 10 min (IM/IV) •Duration:6-8 h •Half-life: 5-6 h

OPIOIDS

Mechanism of Action

- Bind to opiate receptors in the PNS and CNS

Receptor	Effect
μ mu	Analgesic properties at spinal & supraspinal sites, dependence, euphoria, respiratory depression, sedation, miosis, tolerance
δ delta	Analgesia, euphoria
κ kappa	Analgesia, miosis, sedation, dysphoria

- Hyperpolarizing & inhibiting post-synaptic neurons by ↑ K^+ efflux or ↓ Ca^{++} influx into presynaptic nerve endings

Opioid Receptors

Receptors	Endogenous Agonist	Exogenous Agonist
μ mu	b-Endorphins	Morphine Meperidine Fentanyl
δ delta	Enkephalins b-Endorphins	Methadone
κ kappa	Dynorphins	Methadone Pentazocine Morphine (partial)

Classes

- Phenanthrenes (“morphine-like”)
  - Codeine, hydromorphone, oxycodone
- Phenylpiperidines (“meperidine-like”)
  - Fentanyl, sufentanil
- Phenylheptylamines
  - Methadone
- Agonist-antagonist derivatives
  - Pentazocine, butorphanol, nalbuphine

Formulations

- Intravenous
- Immediate-release
  - Acute pain
  - Dose finding for chronic pain
  - “Rescue” for break-through pain
- Extended-release
  - Good for chronic pain
  - Adherence

Adverse Events

- Constipation
  - ↓ GI motility
  - Docusate 100 mg + Senna 17.2 mg PO BID
- Nausea
  - Stimulation of CRT zone in the brain
  - Rule out constipation
  - Metoclopramide 10-20 mg PO q6h PRN
- Sedation
  - CNS depressant
  - Caffeine 100-200 mg PO q 3-4 h
  - Methylphenidate 10-15 mg PO BID

Adverse Events

- Pruritis
  - Diphenhydramine 25 mg PO/IV q4h PRN itching
  - Hydroxyzine 25 mg PO TID

- Respiratory Depression
  - ↑ opioid dose→ ↓ Respiratory center's response to CO_2
  - Can be avoided if properly titrated
  - Life threatening: Naloxone 40 mcg IV q30-60 min

Intravenous Opioids

	Onset after IV loading dose	Elimination Half-life	Intermittent dosing	Infusion rates
Morphine	5-10 minutes	3-4 hours	2-10mg IV q 1-4 hr	2-20mg/hr
Fentanyl	1-3 minutes	2-4 hours	25-100mcg IV q 0.5-1 hr	50-300mcg/hr
Remifentanil	~1-3 minutes	~20 minutes	Not recommended	5-200mcg/hr
Hydromorphone	5-10 minutes	2-3 hours	1-2mg IV q 1-4 hr	0.5-2mg/hr

Intravenous Opioids: Clinical Pearls

Morphine	• Histamine release upon administration • Hypotension • Accumulation of metabolite in renal failure
Fentanyl	• Preferred agent when rapid control is needed • Good agent for hemodynamically unstable patients • Rare adverse effect: chest wall rigidity • Also has sedative properties
Remifentanil	• Very fast onset of action • Continuous infusion for pain control • Good agent for hemodynamically unstable patient
Hydromorphone	• Approximately 7.5 times more potent than morphine • Good agent for hemodynamically unstable patients

Oral Opioids

Agent	Dose	AE	Other
Tramadol (Ultram®)	50-100 mg PO q 4-6 h Max: 400 mg/day CrCl<30 & cirrhosis: 50 mg PO q 12 h	• Diaphoresis • Palpitations • Orthostatic hypotension • Drowsiness	•Onset: ~1 h •Duration: 9 h •Half-life: 5-7 h •Weak opioid •Also available in Extended Release

Oral Opioids

Agent	Ingredients		Dose	Other
	APAP (mg)	Hydrocodone (mg)		
Vicodin®	500-750	2.5-10	1-2 tab PO q 4-6 h	Max: 4 g/day of APAP
Norco ®	325	5-10		
	APAP (mg)	Oxycodone (mg)		
Percocet ®	325	5	1-2 tab PO q 4-6 h	Max: 4 g/day of APAP
Tylox ®	500	5		
	ASA (mg)	Oxycodone (mg)		
Percodan®	325	5	1-2 tab PO q 4-6 h	Max: 4g/day of ASA
	APAP (mg)	Codeine (mg)		
Tylenol 3®	300	30	1-2 tab PO q 4-6 h	Max: 4 g/day of APAP
Tylenol 4®	300	60		

Opioid Dosing

Drug	Doses	Equianalgesic dose	
	Opioid Naïve	Oral	Parenteral
Morphine	PO: 5-30 mg q 3-4 h (IR) IV: 2- 5 mg q 3- 4 h	30 mg	10 mg
Hydromorphone-Dilaudid ®	PO: 2-4 mg q 3-6 h IV: 1-4 mg q 4-6 h	7.5 mg	1.5 mg
Oxycodone-OxyContin® (CR) Roxicodone® (IR)	IR: 5-15mg q 6 h CR: 10-20 mg q 12 h	20 mg	-
Codeine	IV/PO: 15-60 mg q 3-6 h	200 mg	NA
Levorphanol	PO: 2-3 mg q 6-8 h IV: 1-2 mg q 6-8 h	4 mg	2 mg

Opioid Dosing

Drug	Doses	Equianalgesic dose	
	Opioid naive	Oral	Parenteral
Meperidine (Demerol®)	PO: 50-150 mg q 3-4 h IV: 50-150 mg q 3-4 h	300 mg	75 mg
Fentanyl IV	IM: 0.05-0.1 mg q 1-2 h	-	0.1 mg
Fentanyl patch (Duragesic®)	TD: varies	-	-
Fentanyl oral buccal (Fentora®)	PO: 5-100 mcg q 1-2 h	-	-
Methadone	PO: 2.5-10 mg q 8-12 h IV:2.5-10 mg q 8-12 h PO: 5-20 mg q 8-12 h (chronic)	Varies	Varies

Suggested Conversion for Methadone

- **Use Caution when converting!!**

Oral Morphine Dose (mg/day)	PO Morphine: PO Methadone ratio
< 30	2:1
30-99	4:1
100-299	8:1
300-499	12:1
500-999	15:1
>1000	20:1

Opioid Dosing

Drug	Doses	Equianalgesic dose	
	Opioid naive	Oral	Parenteral
Pentazocine Talwin ®	IV/SQ: 30 mg q 3-4 h MAX: 360mg/day	-	-
Butorphanol Stadol ®	IV: 0.5-2 mg q 3-4 h IN: 1 spray in 1 nostril q 3-4 h	-	2 mg
Nalbuphine Nubain ®	IV/IM/SQ: 10mg q 3-6 h MAX: 160mg/day	-	10 mg
Buprenorphine Buprenex ® Butrans ®	IV: 0.3mg q 6-8 h TD: 5 mcg/h q 7 days SL: for opioid withdrawal	-	0.4 mg

Opioid Dosing Properties

Agent	Half-life (h)	Onset (min)	Duration (h)
Morphine	2	10-20	3-5
Hydromorphone	2-3	10-20	3-5
Codeine	3	10-30	4-6
Oxycodone	2-3	30-60	4-6
Meperidine	3-4	10-20	2-4
Fentanyl (IV)	2-4	2-5	1-2
Fentanyl (TD)	17	720-1440	72
Fentanyl (TB)	7	5-15	4-6
Methadone	15-30	10-20	4-5 (acute) >8 (chronic)
Pentazocine	2-3	IV: 2-3 PO: 15-20	2-3
Butorphanol	2.5-4	IV: <10 IN: 15	IV: 2-4 IN: 3-5

Morphine to Fentanyl patch

Oral Morphine 24h (mg)	Transdermal patch (mcg)
45-134	25
135-224	50
225-314	75
315-404	100
405-494	125
495-584	150
584-674	175
675-764	200
765-854	225
855-944	250
945-1034	275
1035-1124	300

Conversion Between Opioids

- Determine 24 hour opioid dose
- Multiply by conversion factor
- Divide 24 hour dose by number of doses given per day
- Example
  - PO hydromorphone to PO morphine

    4mg PO q4h= 24mg/day

    24mg/d x 5= 120mg → 120mg/2= 60mg

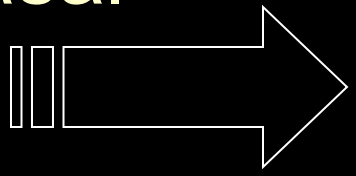
    (round to nearest tablet= 60mg CR q 12 hour)

Patient Controlled Analgesia (PCA)

Opioid Naïve

- Example: morphine
  - Determine basal dose
  - Determine demand dose (usually 25-50% of basal)
  - Determine dosing interval (range specific to medication)
  - Determine lockout dose

Example: Opioid Naïve

- 0.5 mg – 1mg Basal
- 0.5 mg – 1mg IV  Bolus dose
- Q 6 - 15 minutes
- Lock Out based on above parameters
  - 0.5 mg basal; 0.5 mg q 10min;
  - Lockout = 14mg / 4 hours

Example: Conversion to PCA

- Determine the 24 hour opioid dose of current regimen
- Convert to IV
  - Divide by 3
- Divide by 24 to get basal dose / hour
- Determine demand dose
  - Usually 25-50% of basal
- Determine interval based on opioid selected
- Determine lockout amount per 4 hours

Example: Conversion to PCA

- Determine the 24 hour opioid dose of current regimen
  - Morphine 60mg CR PO BID = 120 mg / 24 hr
- Convert to IV
  - divide by 3 120mg / 3 = 40 mg IV / 24 hr
- Divide by 24 to get basal dose / hour
  - 40mg / 24 =1.67mg/hr ~~2 mg/hr
- Determine demand dose
  - usually 25-50% of basal 1mg
- Determine interval based on opioid selected q 10 min
- Determine lockout amount per 4 hours 30 mg in 4 hours
- Order: Basal: 2mg/hr; bolus 1mg q10min; lockout 30mg in 4 hours

Adjuvant Therapy

Agent	Dose	AE	Other
Gabapentin (Neurontin®)	100 mg PO TID MAX: 3600 mg/day	•Somnolence •Fatigue •Edema •Mood Swings	Neuropathic
Pregabalin (Lyrica®)	75 mg PO BID MAX: 450 mg/day	•Somnolence •Weight gain •Edema •Xerostomia	Neuropathic
Venlafaxine (Effexor®)	37.5 mg PO daily (XR) 60 mg PO BID (IR)	•Somnolence •↑ appetite •Insomnia •Dyspepsia	Neuropathic

Adjuvant Therapy

Agent	Dose	AE	Other
Dexamethasone	4-10 mg PO BID	•Weight gain •Hyperglycemia •Osteoporosis •Leukocytosis •Cushing •Edema	Bone pain Nerve compression
Pamidronate (Aredia®)	90 mg IV TRO 2 h q month	• Osteonecrosis of the jaw • Hypocalemia • Headache • Fatigue	Bone pain Bone Mets
Zoledronic Acid (Zometa®)	4 mg IV TRO 15 min q month		Bone pain Bone Mets

Trauma Pain Management Clinical Pearls

- Propofol and benzodiazepines do not have analgesic properties

- Dexmeditomidine has weak analgesic properties and should NOT be used in place of other analgesic agents

Summary

- Pain is one of the most undertreated conditions in the hospital
- Choosing the appropriate agent and treatment plan is going to be individual
- Proper titration of opioids is essential in controlling chronic pain
- Don’t forget about the adverse effects of narcotics when counseling patients
- Be careful when converting between agents

References

1. Baumann TJ and Strickland J. Pain Management. In: Dipiro, JT, Talbert RL, et. al. eds. Pharmacotherapy: A Pathphysiologic Approach. 7th Ed: McGraw-Hill: 2008; 989-1003.
2. Curtis K, Henriques H, Fanciullo G, et al. A Fentanyl-Based Pain Management Protocol Provides Early Analgesia for Adult Trauma Patients. *J Trauma.* 2007; 63:819-826.
3. Patel D. Pain Mangement, Bone Metastases, and Spinal Cord Compression. BCOP Review Manual. 2010: 544-579.
4. Foley KM and Abernathy. Supportive care and quality of life. In: DeVitaVT, Lawerence TS, Rosenberg SA, et al., eds. Cancer: Principles & Practice of Oncology 8th Ed (2): Philadelphia: Lippincott Williams & Wilkins: 2008; 2757-2790.
5. Levy MH. Pharmacological Treatment of Cancer Pain. *N Eng J Med.* 1996;335(15): 1124-1131.
6. Chou R, Fanciullo GJ, Fine PG, et. al. Clinical Guidelines for the use of chronic opioid therapy in chronic noncancer pain: American Pain Society guidelines. *J of Pain*. 2009; 10 (2): 113-130.
7. Health Care Association of New Jersey (HCANJ). Pain management guideline. Hamilton (NJ): Health Care Association of New Jersey (HCANJ); 2006 Jul 18.
8. Bruera EB, Pereira J, Watanabe S, et. al. Systemic opioid therapy for chronic cancer pain: Practical guidelines for converting drugs and routes. *Cancer*. 1996; 78: 852-857.
9. National Comprehensive Cancer Network. Version 2.2011. Retrived on 10/12/2011. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp#supportive.
10. Ripamonti C, Groff L, Brunelli C, et al. Switching from morphine to oral methadone in treating cancer pain: What is the equianalgesic dose ratio? *J Clin Onc.* 1998; 19 (10):3219-3221.
11. Indelicato RA and Portenoy RK. Opioid rotation in the management of refractory cancer pain. *J Clin Onc*. 2002; 20 (1): 348-352.
12. Lexi-Comp OnlineTM , Lexi-Drugs OnlineTM , Hudson, Ohio: Lexi-Comp, Inc.; October 10, 2011.