

# **Issues of Pain: Further questions, and Summary**

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A.M.B.E.R. clinic  
Albuquerque Multidisciplinary Behavioral Evaluation for Recovery and  
Resiliency

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# Overview

- **Pain presentations**
- **Great mimicry**
- **Pain-related behavior**
- **Summary**

# Multiple Dimensions of Pain

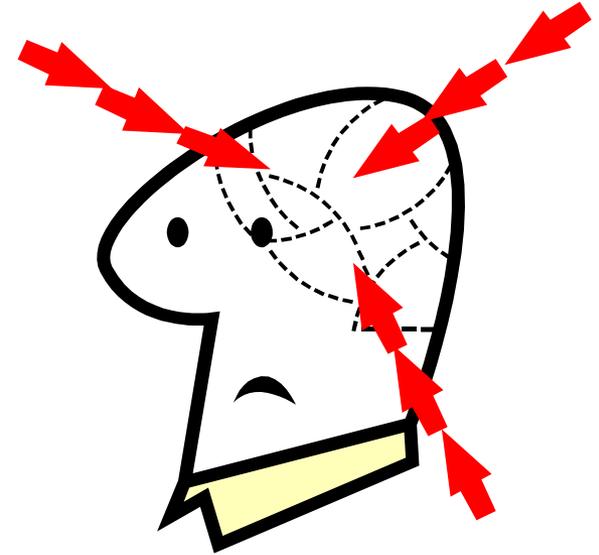
## The ABCs of Pain

**A**ffective Dimension

**B**ehavioral Dimension

**C**ognitive Dimension

**P**hysiological-Sensory Dimension



# Definition of Pain

**“Unpleasant sensory and emotional experience arising from actual or potential tissue damage or described in terms of such damage (IASP)**

# Types of Pain

- **Nociceptive vs Neuropathic**
- **Physiologic vs pathophysiologic**
- **Acute vs chronic**
- **Malignant vs nonmalignant**
- **Pain syndromes**

# Medication Management-- Analgesics

**Analgesics**  
Three Types

**Nonopioids**  
(acetaminophen,  
NSAIDS)

**Opioids**  
(mu agonist,  
agonist-antagonist)

**Adjuvants**  
(multiple examples)  
& Anesthetics

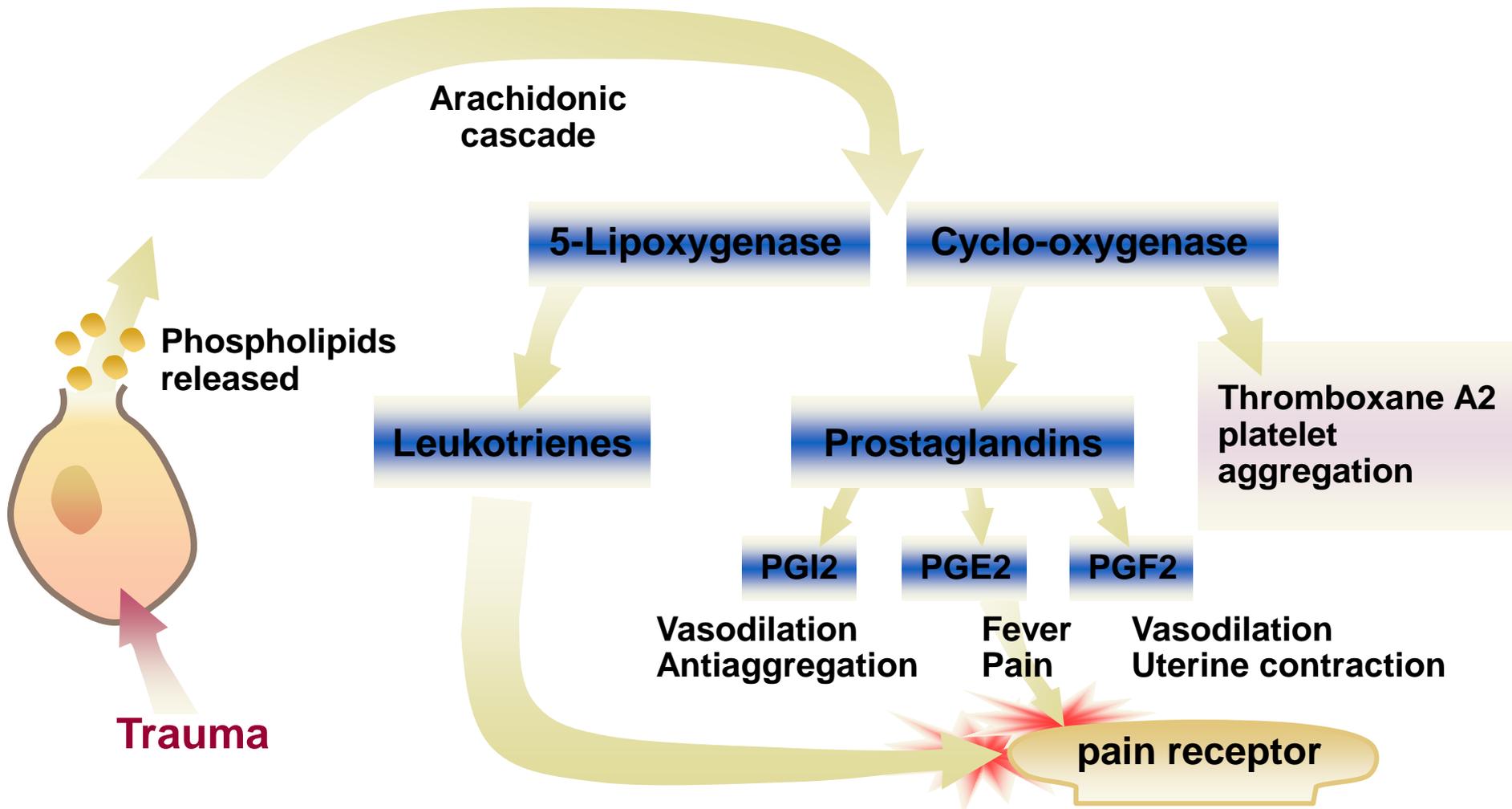
# Acetaminophen

- **Mechanism of action is not certain**
- **Probably centrally acting—?cox-3 inhibitor**
- **Acetaminophen toxicity**
  - **Hepatotoxicity**
    - Toxic metabolite (NAPQI)
    - Several other mechanisms lead to hepatotoxicity
    - Mechanism not completely understood
  - **Nephrotoxicity >4g/day for long periods**
    - Uncertain cause
    - May be caused by activity of NAPQI in renal microsomes
    - Increase frequency to 6-8 hrs in renal failure

# NSAIDS

- **NSAIDS—Anti-inflammatory, antipyretic, analgesic**
- **Mechanism of action—prostaglandin inhibition by way of COX-1**
  - **Prostaglandins**
    - important in maintaining integrity of GI and duodenal mucosa; important in modulating renal plasma flow
- **Inhibit formation of thromboxane—  
affecting platelet aggregation**
- **Use with *caution* in pts. with history of asthma**
  - Inhibits prostaglandin E—responsible for bronchodilation

# Transduction: Nociceptive Chemical Stimuli



Class	Generic name	UAD	Brand name
<b>Propionic acids</b>	<b>Naproxen</b>	500 mg initially- followed by 250mg q6-8h	<b>Naprosyn,</b> <b>Anaprox, Alleve</b>
	<b>Flurbiprofen</b>		<b>Ansaid</b>
	<b>Oxaprozin</b>		<b>Daypro</b>
	<b>Ibuprofen</b>	400-800mgQ6-8h	<b>Motrin</b>
	<b>Ketoprofen</b>	25-75 mg Q6-8h Max 120mg/d	<b>Orudis, Oruvail</b>
	<b>Ketorolac</b>	(parenteral)	<b>Toradol</b>
<b>Indoleacetic acids</b>	<b>Sulindac</b>	200mg Q12h	<b>Clinoril</b>
	<b>Indomethacin</b>	25-50mg q8h	<b>Indocin</b>
	<b>Etodolac</b>	200-40mg q6-8h	<b>Lodine</b>

Class	Generic name	UAD	Brand name
Phenylacetic acids	Diclofenac	50 mg/q8h	Cataflam, Voltaren
Salicylic acids (nanacetylated)	Salsalate Choline magnesium trisalicylate	1000-1500 mg/q12h 1000-1500 mg/q12h	Disalcid Trilisate
Naphthylalkanone	Nabumetone	1000-2000 mg/day	Relafen
oxicam	Piroxicam		Feldene

# COX-2 Inhibitors

- **May have fewer GI effects than COX-1 inhibitors**
- **Should be avoided in patients with creatinine clearance <30ml/min**
  - **Carry same risk as traditional NSAIDs**
- **Celecoxib—Celebrex**
  - **UAD=100-200 mg q12h max=400 mg/d**

# Opioids

## Mu-agonists

**Bind to mu opiate receptors blocking transmission of pain**

- Morphine
- Fentanyl
- hydromorphone
- oxycodone
- hydrocodone
- Codeine
- \*Methadone
- \*meperedine
- \*tramadol

# Morphine

- **Hydrophilic—delayed onset and longer duration**
- **Two metabolites but only one active at opioid receptor—morphine-6-glucuronide (M6G)—analgesic**
- **Patients with renal impairment should start at  $\frac{1}{4}$  dose and titrate as needed**
  - **Accumulation results in neurologic side effects as well**
  - **Removed with dialysis**

# Hydromorphone (Dilaudid)

- **Hydrophilic—similar to morphine**
  - **IV**—1.5 mg:10 mg morphine/PO—7.5 mg:30 mg morphine  
Onset 5 min; peak in 8-20 min. duration ~ 4 hrs
  - **Oral**
    - 60% bioavailable; onset 30 min. duration 3-4 hrs
  - Metabolized in the liver; Several metabolites
- **Use decreased amounts in renal impairment due to possible sensitivity to hydromorphone-3-glucuronide → possible neuroexcitation**
  - there is no 6-glucuronide so may have fewer SEs
- **May be safer than morphine in renal insufficiency**

# Fentanyl

- **Lipophilic → Short half-life, short duration of action**
  - **UNLESS given regularly—then half-life is extended**
- **No active metabolites**
- **Safer in renal and liver failure**
- **Fewer side effects**
- **Half-life extends with continuous use**
- **Multiple formulations**
  - **transdermal, oral transmucosal, buccal**

# Oxycodone

- **Available in combination or single-entity**
  - Short and Long-acting
- **More potent than morphine**
- **Metabolized in the liver by cytochrome CYP2D6**
  - Multiple metabolites
- **Binds at  $\mu$  and  $\kappa$  receptors—may be better in chronic pain states**
  - Half-life and bioavailability slightly longer than MS
  - One active metabolite—oxymorphone
  - Women may have a greater effect
  - Excretion impaired in uremic patients and
    - Elimination half-life is severely impaired in these patients
  - May cause CNS toxicity and sedation in renal failure

# Hydrocodone (Vicodin)

- **Only available in combination with acetaminophen, ibuprofen, aspirin**
  - **Onset 20 min. peak by 60 min; half-life 3.8 hrs**
- **Metabolized in the liver**
  - **Several metabolites**
- **Significant renal excretion of active forms**
- **Should be avoided in patients with renal failure**
- **Adverse effect –hearing loss**

# Demerol (meperidine)

- Half-life is 2-3 hrs (parenterally)
- Bioavailability from p.o. is  $\frac{1}{4}$  that of parenteral
- Onset 10 minutes; peak effect 30 min. duration up to 4 hrs
- More likely than other opioid drugs to cause delirium in postop pts of all ages
  - More nausea and vomiting
- Limit use to 600 mg/d and no more than 48 hours due to metabolite—normeperidine
- Observe for signs of neuroexcitation—restlessness, shakiness, tremors, twitching and jerking
- Misconception—produces less biliary spasm than other opioids—all opioids can produce this

# Normeperidine

- **Only active metabolite of meperidine**
  - toxic metabolite
  - half-life 15-20 hrs
  - causes neuroexcitation—hyperreflexia, myoclonus, agitation and grand mal seizures
  - half analgesic potency but twice the toxicity
  - Is not reversed with naloxone and may increase risk of seizures if naloxone given
- **Use extreme caution in patients with seizure disorder**
- **Use caution in patients with renal insufficiency**
- **Contraindicated with MAOI (monoamine oxidase inhibitors)—can cause serotonin syndrome or death**



# Codeine

- **60mg = 600 mg of aspirin**
- **Not appropriate for moderate to severe pain**
- **Usually more constipating**
- **Has more psychotomimetic effects**
- **Metabolized in the liver to morphine**
  - **Several metabolites**
  - **Metabolism is necessary for analgesia**
  - **Poor metabolizers may show absence of analgesia**
- **Reduced renal clearance in advanced renal failure**
  - **Reports of serious adverse effects in renal failure**

# Methadone—good news

- **Inexpensive**
- **Adverse effects similar to other opioids**
- **Rapid onset—30-60 minutes; duration 4-6 hrs; peak effect 2.5 hrs**
- **~ 80% bioavailability**
- **No active metabolites**
- **Long duration with continued use**
- **No ceiling dose other than side effects**
- **Has some SSRI and NMDA antagonist activity**
- **For opioid naïve patients → start at 2.5mg Q8H**
- **Excreted in feces—considered safe in renal insufficiency**

# Methadone—not so good news

- **Long half-life—15-60 hours-**
  - **Unpredictable**
  - **difficult to titrate**
  - **Difficult to convert from other opioids to methadone**
- **Duration initially is 3-6 hrs→8-12 hr with repeated dosing**
- **Varied inter-individual effects**
- **Efficacy is greater with repeated dosing**
- **Multiple drug-drug interactions that can induce or inhibit effect by other drug or be effected**
  - **Close observation is required**

# Dual-mechanism Analgesics

- **Tramadol—for mod to moderately severe pain**

- Weak mu-agonist and norepinephrine and serotonin reuptake inhibitory activity similar to TCAs
- Peak effect in ~ 2 hrs of 100mg dose
- Potency equivalent to codeine and five times less potent than morphine
- Ceiling effect
- Max dose is 400mg/24h
- Use with caution in pts w seizures or on SSRIs

- **Tapentadol – Nucynta**

- Agonist at mu and blocks reuptake of norepinephrine
- Schedule II drug
- Indicated for mod-severe pain
- Avoid combining with SSRIs

# Equianalgesic Dosing Guidelines

- **Equianalgesic means approximately the same pain relief**
- **The chart is a guideline. Titrate meds according to pt's response**
- **Chart is helpful when switching from one drug to another or when switching to another route**
- **Dosages are not necessarily starting doses**
- **Consider incomplete cross-tolerance**

<b>Drug</b>	<b>Oral Dose</b>	<b>IV Dose</b>	<b>Duration</b>
Morphine	30 mg	10 mg	3-5 hours
Fentanyl	Breakthrough only (OTFC)	100mcg (0.1mg) 100 mcg/h TD $\approx$ 4 mg/h IV MS; 1mcg/h TD $\approx$ 2 mg/24 h oral MS	0.5-1 hour
Hydromorphone	7.5 mg	1.5 mg	2-4 hours
Meperidine	300 mg NR	75-100 mg	2-4 hours
Codeine	200 mg NR	130 mg	3-4 hours
Methadone	---	---	---
Oxycodone	20-30 mg	-----	3-4 hours
Hydrocodone	30 mg	-----	3-4 hours
Nalbuphine	-----	10 mg	3-6 hours

# First-line Drugs in Chronic Pain

- gabapentin (Neurontin)—start w/100-300 mg/day Usual Effective Dose (UED) 300-3600 q8h
- pregabalin (Lyrica)—start with 100-150 mg/day; UED 150-600 q12h
- SNRI
  - Duloxetine (Cymbalta)—start w/ 30 mg/day; UED 60 mg q12h

## ADJUVANT ANALGESICS: MAJOR CLASSES

- **Anticonvulsants**
- **Antidepressants**
- **Psycho-stimulants**
- **Muscle relaxants**
- **Sedatives**

# Opioid Side Effects

- Nausea and vomiting
- Pruritus
- Urinary retention
- Mental status changes
- Sedation
- Respiratory depression

# Opioid Induced Constipation

- The hand that writes the prescription for an opioid and
- Fails to write the order for a laxative should be
- The hand that removes the impaction

# Balanced Analgesia

- **Inter-disciplinary approach**
  - **Medication management**
  - **Physical activity**
  - **Maximize nutritional contributions**
  - **Mental health**
  - **Support group**
  - **Spirituality**

# Non-Pharmacologic Interventions

- **Increase activity**
- **Individualize interventions**
  - **music**
  - **artwork**
  - **humor**
- **Address constipating effects of opioids**

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## To summarize:

- **Treat pain initially aggressively—**
  - **\*\*\*Titrate to Effect**
- **Adequate analgesia results in:**
  - **Early participation in activity**
  - **Prevention of complications**
  - **Decrease risk of chronic pain**
  - **Early return to individual level of functioning**
- **Use assessment tool specific to population**
- **Always combine modalities— opioids with nonopioids and pharmacologic with non-pharmacologic**

# Team

- **Purpose**
  - Keeping individual separated?
  - Safety?
  - Support? Change in functioning?
- **Respect** - has to be evidenced, consistent
  - Individuals
  - Health goals
  - Institutional goals
  - Societal expectations

# Team

- **Communication**
  - Verbal/written
  - One point
  - Frequency; emergency
- **Responsibilities**
  - Defined roles by training
  - Acquired roles by ability or habit
  - Guardianship/consent

# Course summary

- **Holistic view of patients**
- **Integrate context and communication**
- **Be creative in approaches**
- **Document strategies**
- **Keep raw data and observations clear from interpretations**

**Many thanks for your participation, comments, feedback and ongoing hard work!**

**This was the last in this series.**

resources and back issues can be found at  
Continuum of Care website:

<http://som.unm.edu/coc/Training/powerpointnew.html>