Pain Management

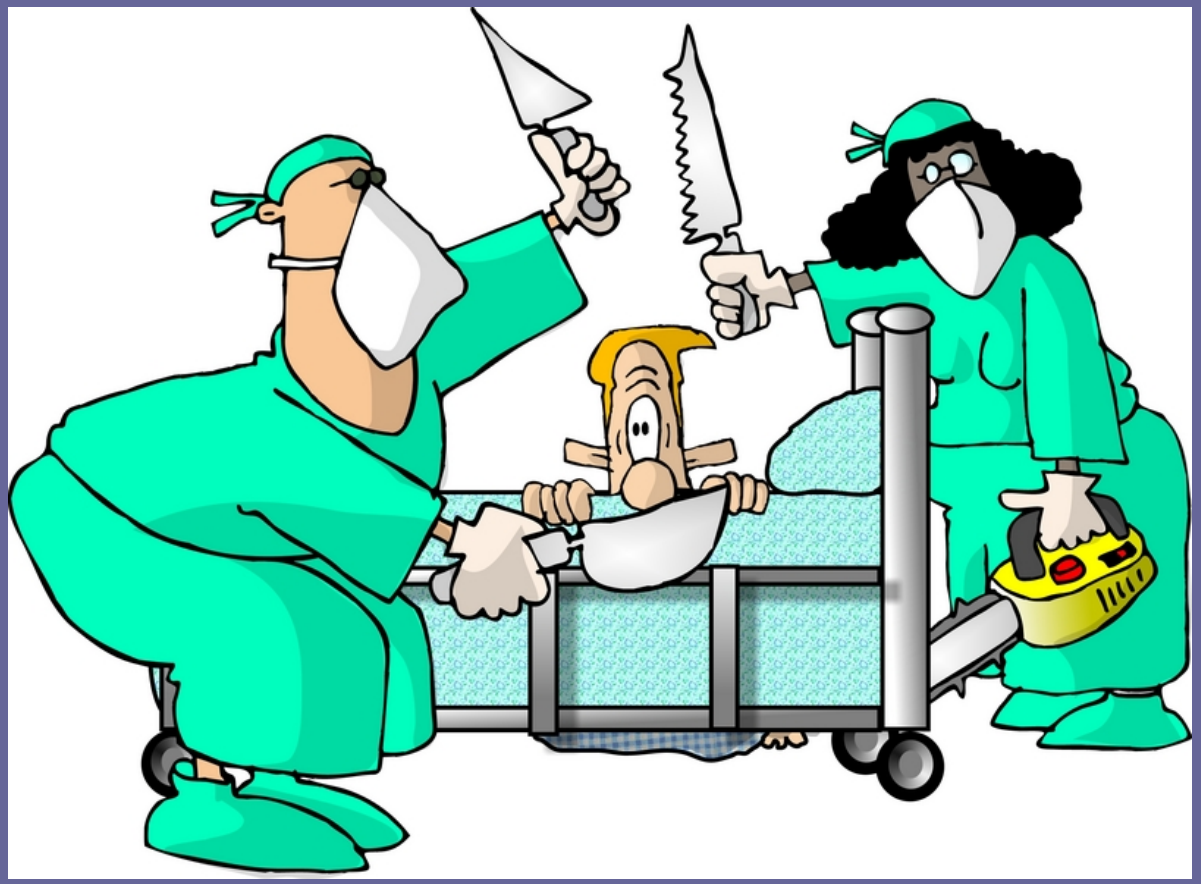
Definitions

- Pain: an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.

IASP, 1982

Your patient

- 64 year old male for right total knee arthroplasty
- PMH of HTN, GERD
- Hx of GA without complications



History

- NKDA
- Home meds: Lisinopril, Hydrocodone, Nexium
- Physical exam normal

Plan for Pain Management

- Pre-operative
- Intra-operative
- Post-operative

Why treat pain?

- Untreated pain increases anxiety and pain perception.
- Stress response is invoked by pain (and anxiety!).
  - Neuroendocrine response (ACTH, Epi, NE, glucagon, etc increased)
  - Results: Increased VO^2, CO^2 production, catabolic state
- The more pronounced the stress response, the higher the mortality.
- Animal models show that repeated pain during “infancy” causes alterations in the adult brain:
  - Altered pain sensitivity, anxiety, hyperactivity, impaired social skills, self-destructive behavior.

Metabolic Stress Response

- Complex, multifaceted behavioral, physiologic, and metabolic reaction to pain, anxiety, injury, surgery, etc.
- Results in increased adrenergic activity, energy expenditure, substrate turnover
- Segmental, supra segmental, and integrative components.

Importance of Perioperative Pain Management

- Prevention and effective relief of acute perioperative pain may:
  - Improve clinical outcomes
  - Decrease complications
  - Improve quality of life
  - Improve patient satisfaction

Jain S, Datta S. *Chest Surg Clin N Am*. 1997;7(4):773-799.

New Expectations for the Assessment and Management of Pain: JCAHO* Guidelines

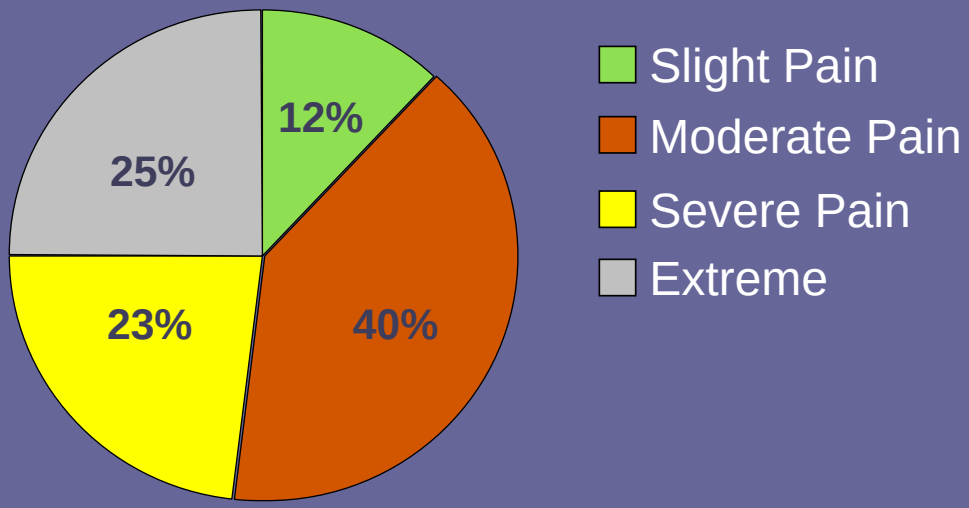
- JCAHO standards for physicians:
  - Recognize patients' rights to appropriate assessment and treatment of pain
  - Assure staff competency in:
    - Pain assessment
    - Pain management
  - Support appropriate use of effective pain medications

*Joint Commission on Accreditation of Healthcare Organizations
National Pharmaceutical Council. Pain: current understanding of assessment, management, and treatments. 2001:1-92. Note: This list of JCAHO standards is representative, not comprehensive.

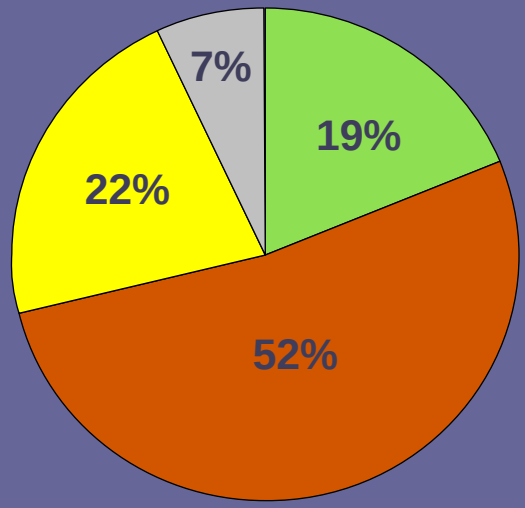
Postoperative Pain: Results from National Survey Suggest that Postoperative Pain Is Under Managed

Presence of pain and most intense pain experienced by inpatients

Pain Before Discharge



Pain After Discharge



Apfelbaum JL et al. *Anesth Analg.* 2003;97:534-540.

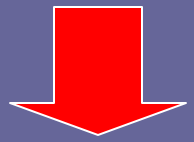
Pre-operative Pain Management

- Choices?

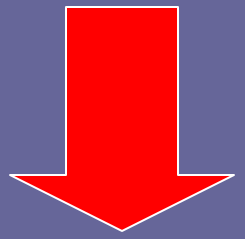
Sensitization:

Tissue Injury

Repetitive Stimulation of C-fibers



Progressive Increase in Action Potentials



Prolonged Increase in Spinal Cord Excitability

Opiates

- Ineffective at Pre-emptive analgesia
  - Tolerance
    - Vinik HR, Kissin I. Anesth Analg 1998
      - Rapid development of tolerance to analgesia during remifentanil infusion in humans.
    - Guignard et al. Anesthesiology 2000
      - Acute opioid tolerance: intraoperative remifentanil increases postoperative pain and morphine requirement.
    - Chia YT et al. Can J Anaesth 1999
      - Intraoperative high dose fentanyl induces postoperative fentanyl tolerance.

Anesth Analg 1998; 86:1307-11
Anesthesiology 2000 92(2):465-472
Can J Anaesth 1999;46:872-7

Opiates

- Ineffective as pre-emptive analgesia
  - "Opioids are generally not sufficient to provide an adequate blockade of spinal nocicpetive neurons to prevent central sensitization."

- Delayed Hyperalgesia ("wind-up")
  - Célèrier E et al. Anesthesiology 2000
    - Long-lasting hyperalgesia induced by fentanyl in rats: Preventive effect of ketamine.

Pharmacotherapy 2004;24(12):1714-1731
Anesthesiology 2000;93:409-17

NMDA-Antagonists

- Ketamine
  - Phencyclidine derivative
  - Mechanism of action
    - NMDA-Receptor Antagonist
    - Interacts with opiate-R, monoaminergic-R, and voltage sensitive calcium channels
  - Hepatic metabolism (P-450)
  - Analgesic
    - (0.2-0.5 mg/kg)
    - Central?
    - Without respiratory depression

Acetaminophen

- Mechanism of action uncertain
  - Peripheral
    - Decreased prostaglandin synthesis
    - Interference with NO pathways
  - Central
    - Modulation of descending pain pathways
    - Modulation of dynorphin release
- Excellent safety profile at doses of 1g Q 6 hours
- Toxicity (>4g/d)
  - Hepatotoxicity

NSAIDs

- *Advantages:*
  - Anti-inflammatory, analgesic, limited sedation, non-addicting, ±cheap, available OTC
- *Concerns:*
  - available OTC in multiple preps, GI effects, renal and hepatic toxicity, platelet effects, fluid retention

NSAIDS

- Ketorolac
  - Potent analgesic
  - Mild anti-inflammatory
  - Absence of ventilatory or cardiac depression
  - May cause excessive GI bleeding (limit course to 5d)
  - Meta-analysis
    - 36% reduction in opiate requirements
    - Ketorolac 10-30mg equivalent to Morphine 10-12 mg
    - No reduction in opiate related side effects

Pain Med 2001;2:336-51.

Pharmacologic Options

- Anti-inflammatory Agents: Nonspecific
  - Ketorolac
  - Naproxen
  - Ibuprofen
  - Diclofenac, Nabumetone
- Cox II specific agents
  - Celecoxib, Meloxicam

NSAIDS

- Effective over many surgical models
- Must continue regimen post-operatively
- Downsides
  - Paucity of IV administrations
  - Side Effects
    - Gastric Irritation
    - Platelet Dysfunction
      - Thromboxane production
      - Inhibits platelet aggregation through inhibition of prostaglandin synthesis
    - Renal toxicity if renal function dependent on Prostaglandins (CHF, hypovolemia, or hepatic cirrhosis)

NSAIDS

- Mechanism of Action
  - COX-1: constitutive
  - COX-2: inducible
- Effects (prevention of both central and peripheral sensitization)
  - Peripheral
    - Anti-inflammatory
    - Anti-nociceptive
  - Central
    - Anti-pyretic
    - Analgesic
- Adjuvant Therapy
  - Dose sparing effects
  - Fewer opiate related side effects

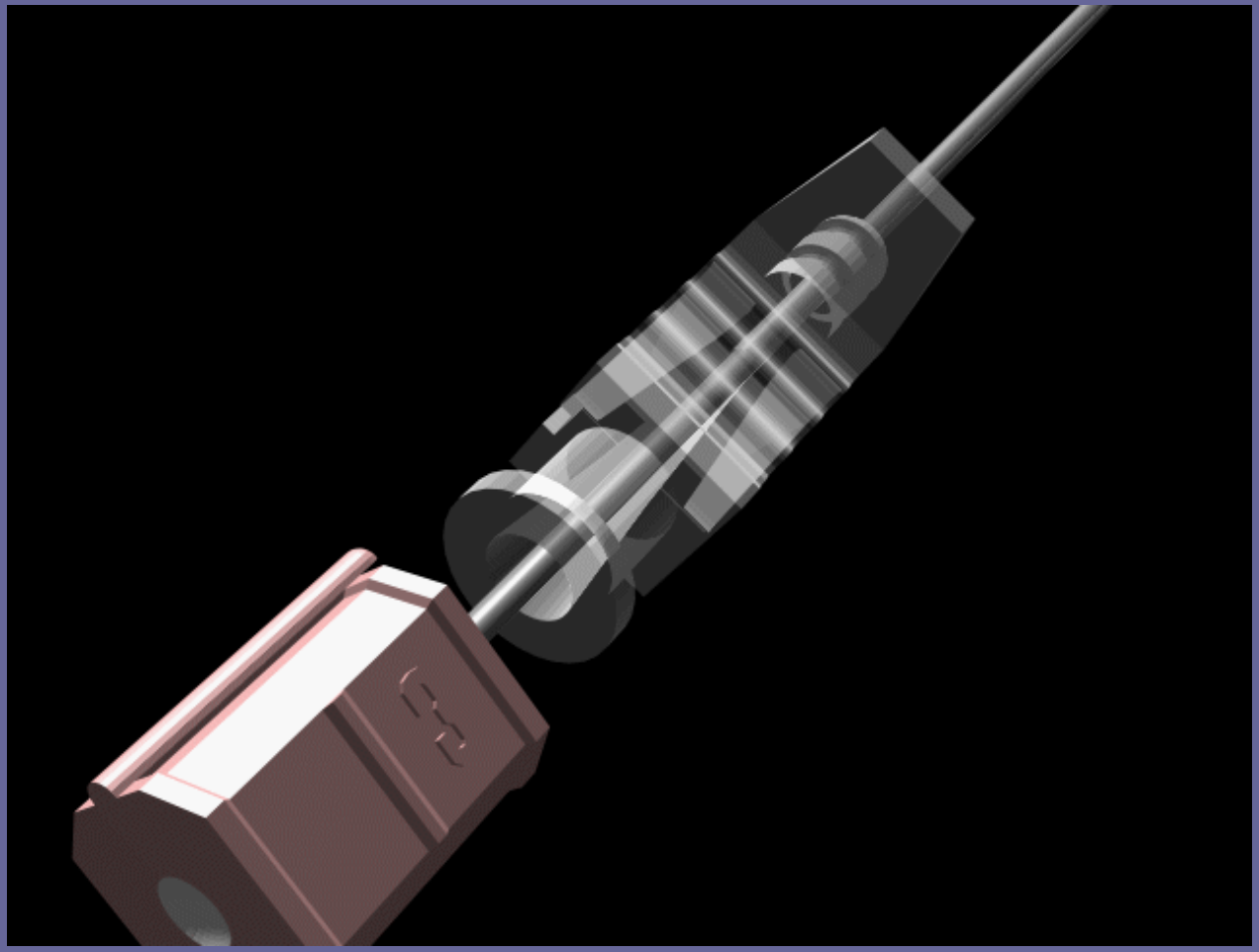
COX – 2 Inhibitor

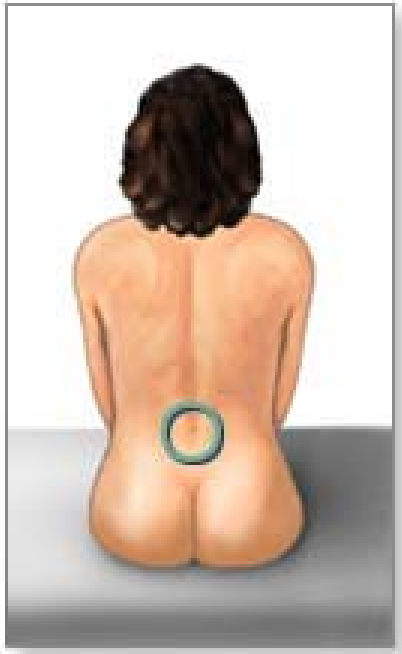
- Selective COX-2 Inhibition
  - Inhibition of prostaglandin production at sight of injury
  - Improved side effect profile
    - Decreased Gastro-intestinal side effects
    - Decreased bleeding complications
- Multiple studies
  - Analgesic efficacy
    - Rofecoxib 50 mg QD
    - Celecoxib 200 mg BID
  - Opiate sparing
  - Simplified dosing

Anticonvulsants

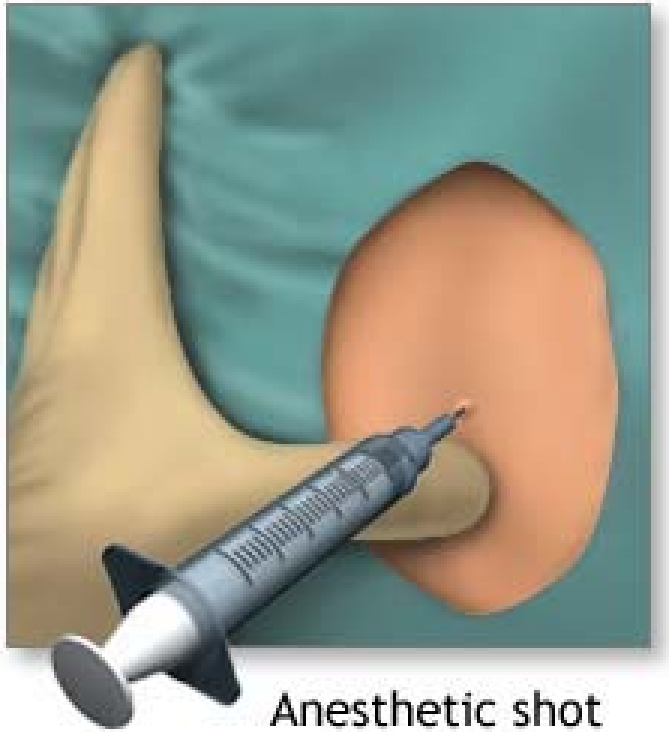
- Pro: Neuropathic pain: lancinating, burning
- Con: Ataxia, sedation, confusion (esp elderly)
- Drugs
  - Carbamazepine (Tegretol)
  - Gabapentin (Neurontin), Pregabolin (Lyrica)
  - Lamotrigine (Lamictal)
  - Topiramate (Topomax), Zonisamide (Zonegran)
  - Oxcarbazepine (Trileptal),
  - Clonazepam (Klonapin)**

Intra-operative Management



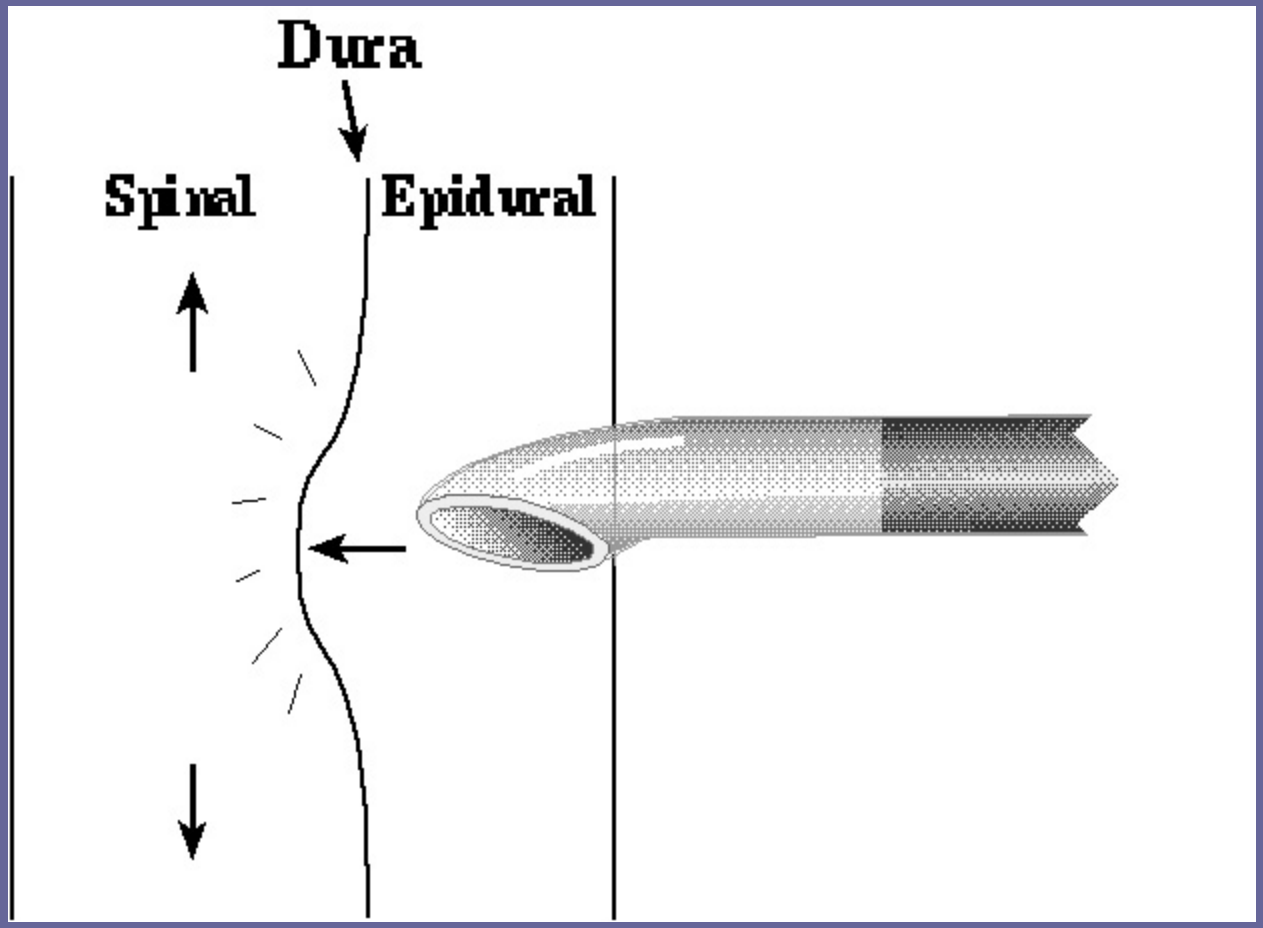


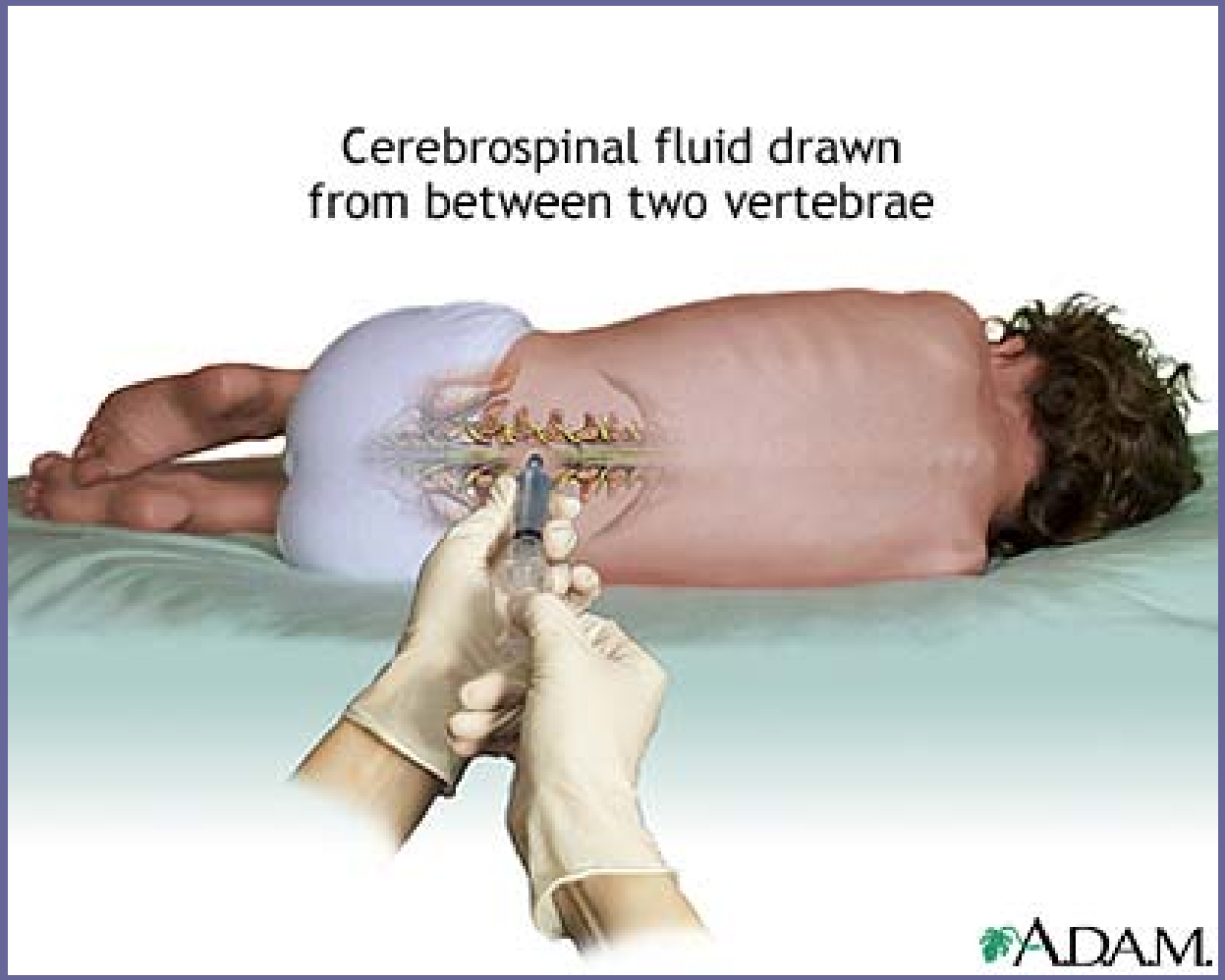
Injection site



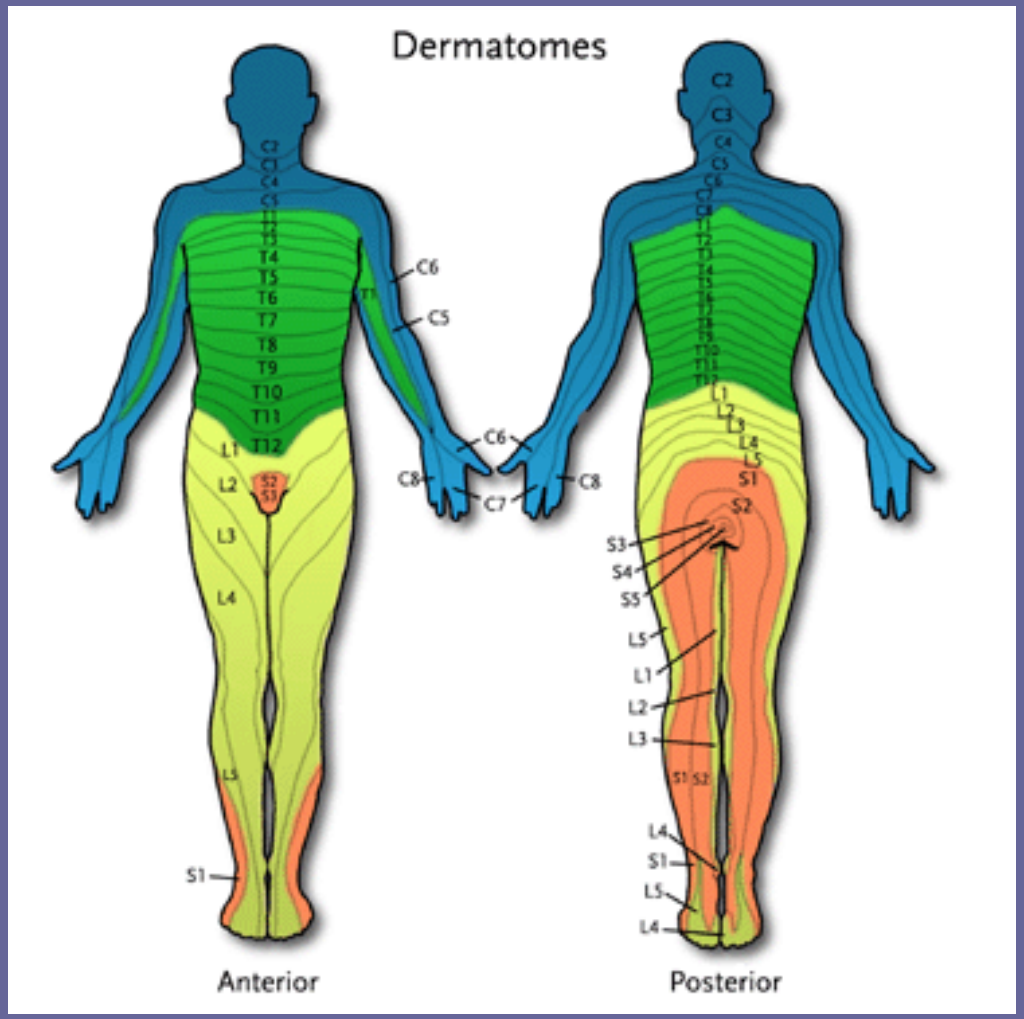
Anesthetic shot

A.D.A.M.

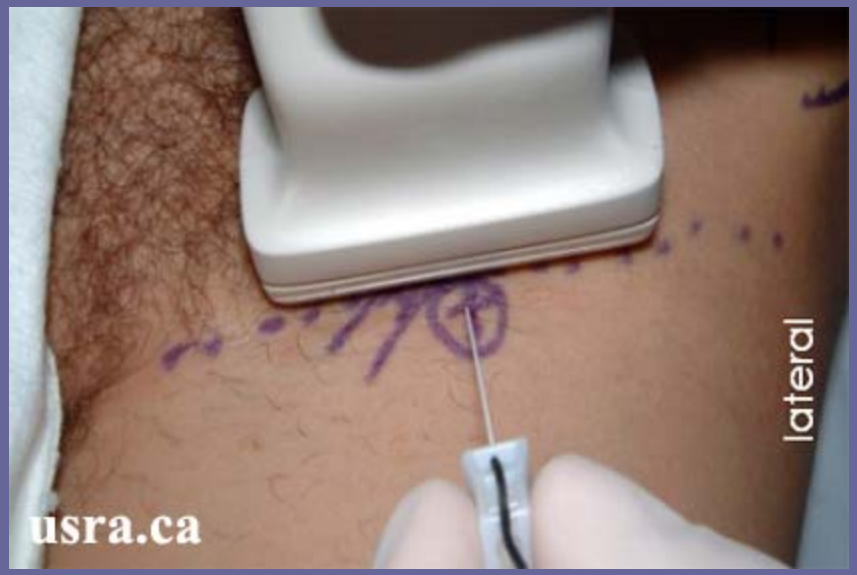

Dura
Spinal
Epidural

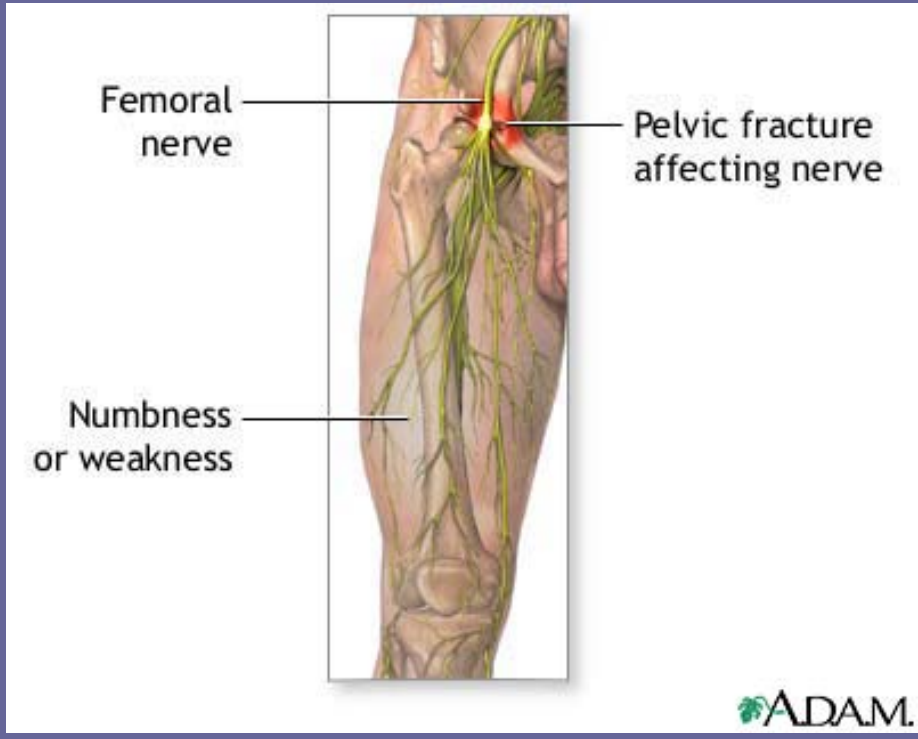


www.nlmnih.gov

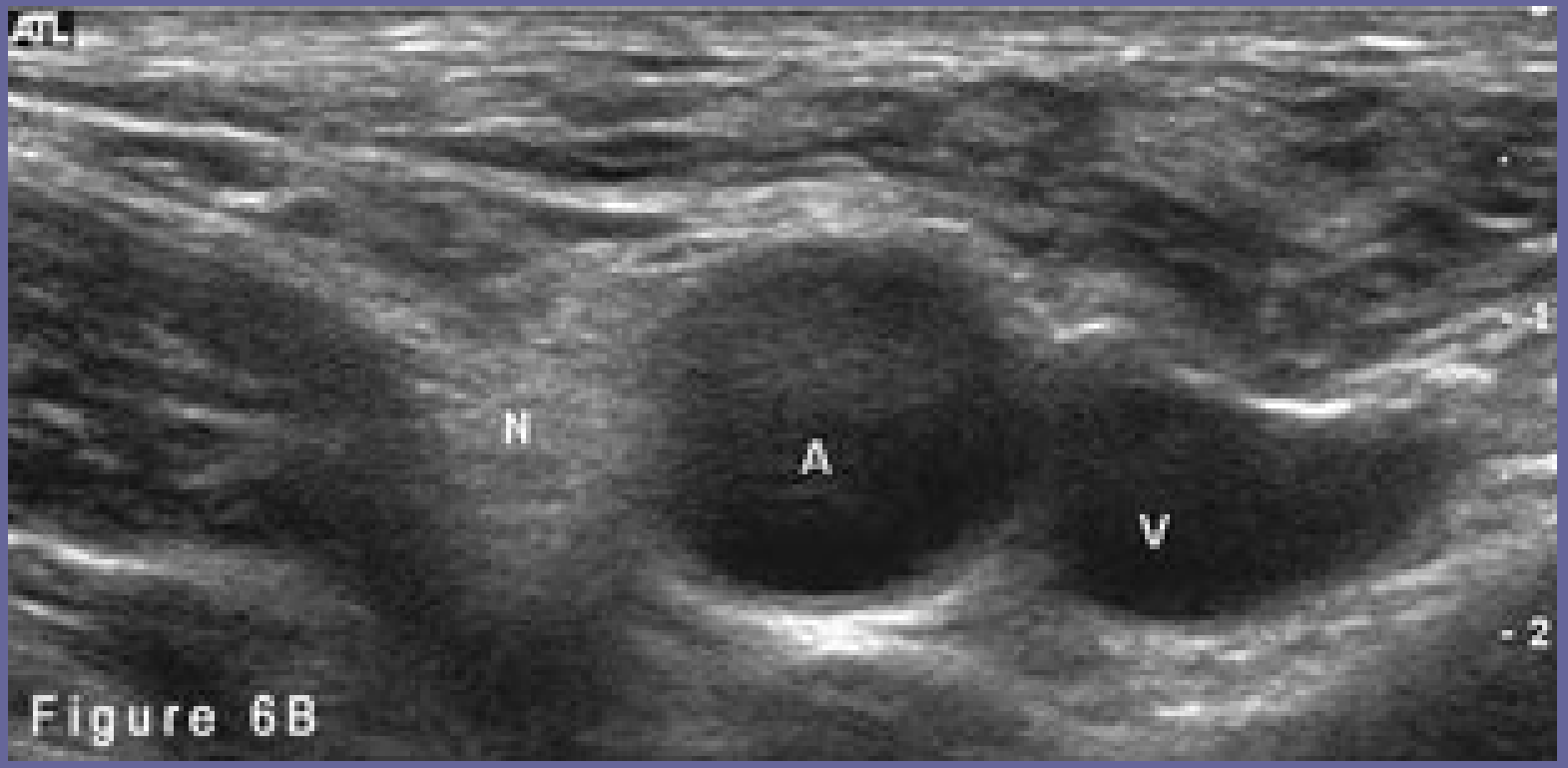


www.maturespine.com

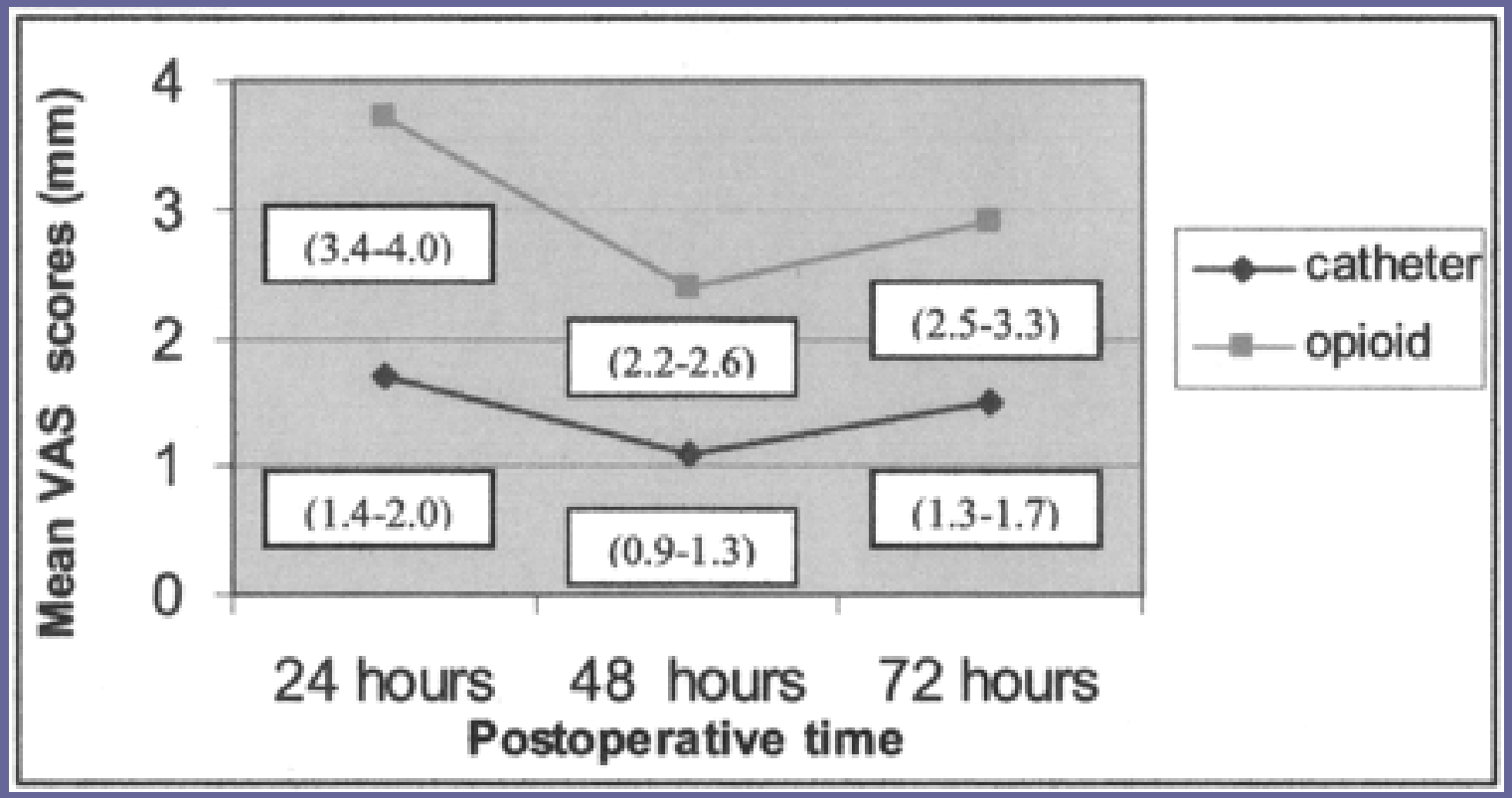

lateral
usra.ca


Femoral nerve
Pelvic fracture affecting nerve
Numbness or weakness
A.D.A.M.

Femoral Nerve Block

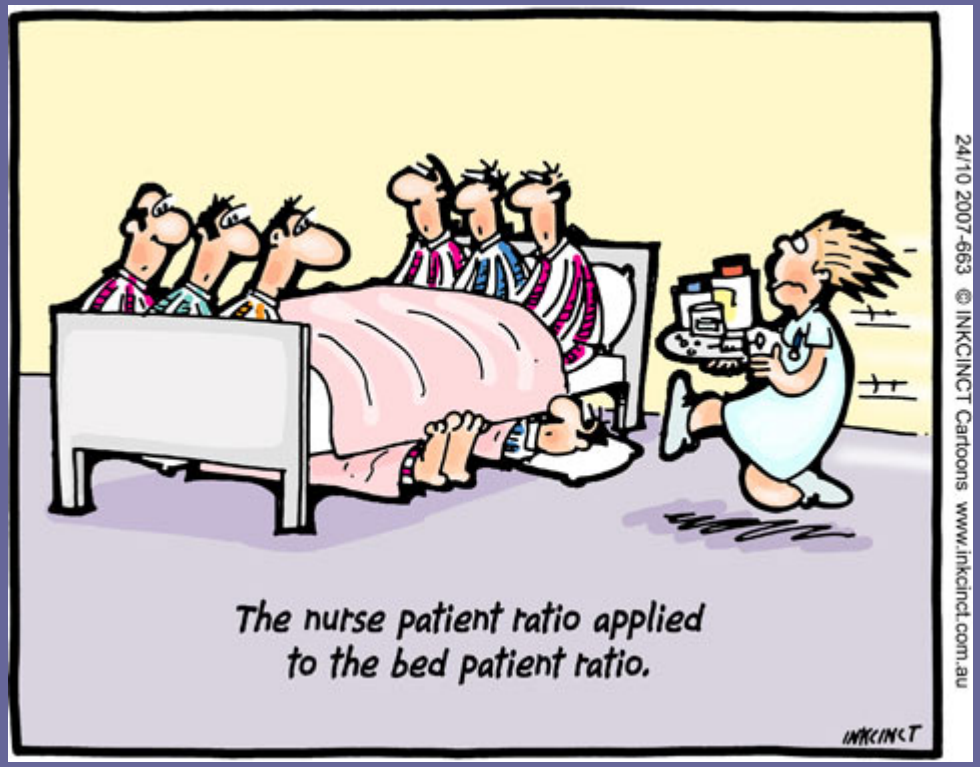


Post-operative VAS scores for nerve catheter versus opioid PCA



Swenson *et al*.

Post-Operative Management



NSAIDS

- Effective over many surgical models
- Must continue regimen post-operatively
- Downsides
  - Paucity of IV administrations
  - Side Effects
    - Gastric Irritation
    - Platelet Dysfunction
      - Thromboxane production
      - Inhibits platelet aggregation through inhibition of prostaglandin synthesis
    - Renal toxicity if renal function dependent on Prostaglandins (CHF, hypovolemia, or hepatic cirrhosis)

Opioids: The Alternative Buffet

How do opioids work?

- Remain the standard agent for pain management
- Nociceptive pain better blocked with opioids than neurpathic pain

Sites of Opioid Action

- Peripheral nerve endings
  - Stim of peripheral opioid receptors may block central transmission and release of inflammatory mediators (beta endorphin, proenkephalin A)
- Dorsal horn, spinal cord
  - Dynorphin, enkephalin rich
- Midbrain, brainstem, thalamus
  - Dynorphin, enkephalin rich,
  - Receive beta endorphin innervation from hypothalamus
- Limbic system, cortex
  - Emotional dimension of pain, rich in dynorphin, enkephalin, have beta endorphin input as well

Opiate Receptors

Receptor	Effect	Agonist	Antagonist
Mu 1	Analgesia Temperature control	Normorphine	Naloxone pentazocine
Mu 2	Supraspinal analgesia resp depression, constipation, GH release Euphoria, dependence	Morphine Sufentanil	Naloxone
Delta	Modulates mu Supraspinal analgesia Mediate euphoria, “brain reward”	Leu enkephalin B endorphin	Naloxone metenkephalin

Opiate Receptors, 2

Receptor	Effect	Agonist	Antagonist
Kappa	Spinal analgesia Sedation, miosis, resp depression Ataxia, locomotion	Dynorphin, MS Pentazocine Nalbuphine, butorphanol	naloxone
Sigma	Vasomotor and vent stimulation, dysphoria, hallucinations	Pentazocine Ketamine?, PCP Interact w/ D2 receptors	Naloxone haloperidol
Epsilon	Heat related anti-nociception	Beta endorphin	

Opioids Effects

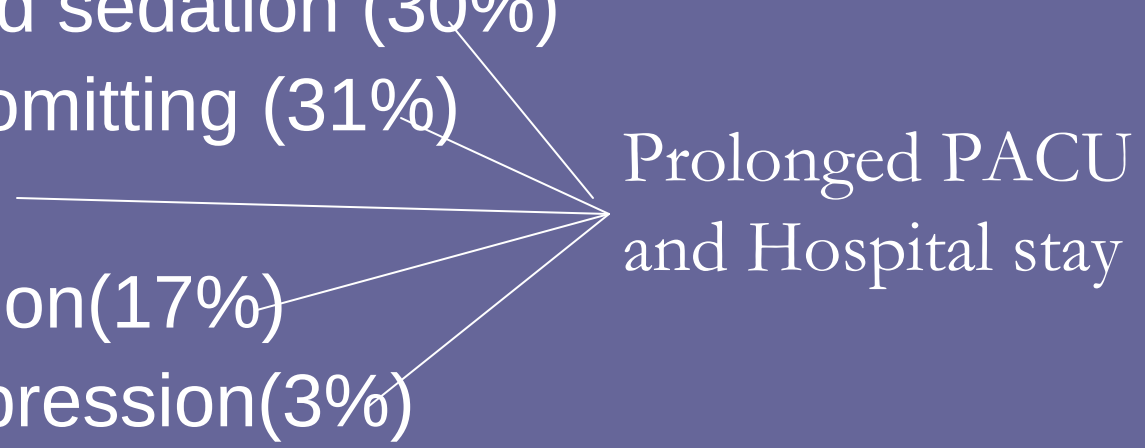
- Nausea, vomiting
- Ileus, constipation
- Pruritis
- Sedation, confusion
- Respiratory depression
- Bradycardia
- Cough respiration

Opioid Effects

- Tolerance
- Dependence
- Addiction

Opiates

- Effective Analgesics
- Variety of Administration Routes
- Adverse events with opiate usage
  - Drowsiness and sedation (30%)
  - Nausea and Vomitting (31%)
  - Pruiritis (18%)
  - Urinary Retention(17%)
  - Ventilatory Depression(3%)
- Tolerance



J Pin 2002;3:159-80

Morphine

- Prototypical opioid
- Slower onset (less lipid soluble)
- Causes histamine release
- Hepatic metab→Morphine 6 glucuronide, renally cleared
- Careful in renal patients
- IV, PO, epidural, spinal

Hydromorphone

- Congener of morphine
- Less accumulation in renal/hepatic insufficiency
- Faster onset than Morphine
- Shorter duration
- More potent than Morphine

Methadone

- T1/2 15-57 hours
- Synthetic opioid
- Extensive hepatic biotransformation
- BID to TID dosing usually
- Can have significant nausea associated
- Constipation

Fentanyl

- Synthetic, highly lipid soluble
- Fast onset, short duration
- IV, respiratory depression can be profound, but brief due to redistribution of drug
- Transcutaneous—stable drug level at 12-24 hr; IV, PO, Epidural, spinal

Meperedine

- Less potent than morphine
- Faster onset than morpine
- Shorter duration than morphine
- May actually cause tachycardia
- Active metabolite-normeperidine—CNS excitation, seizures

"We can give you enough medication to alleviate the pain but not enough to make it fun."