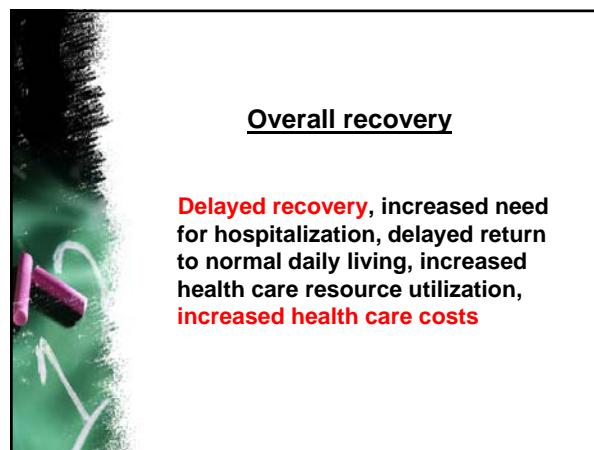


Immunologic
Impaired immune function, increased infection, tumor spread or recurrence

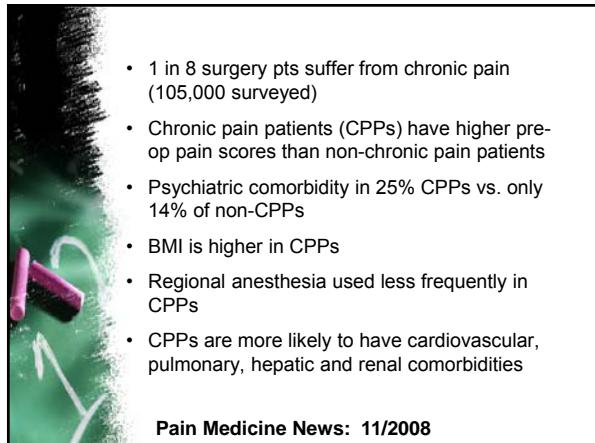
Muscular
Muscle weakness, limitation of movement, muscle atrophy, fatigue

Psychological
Anxiety, fear, anger, depression, reduced patient satisfaction



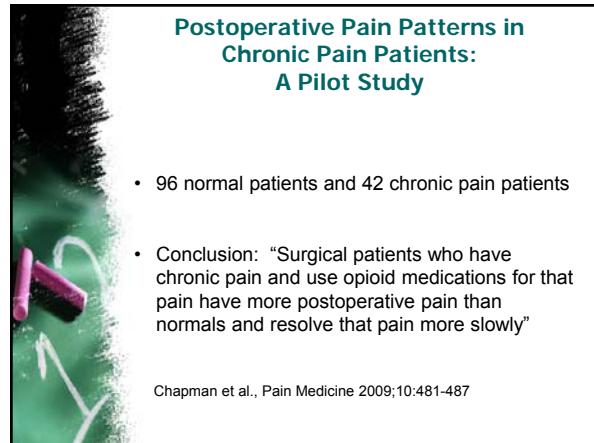
Overall recovery

Delayed recovery, increased need for hospitalization, delayed return to normal daily living, increased health care resource utilization, increased health care costs



- 1 in 8 surgery pts suffer from chronic pain (105,000 surveyed)
- Chronic pain patients (CPPs) have higher pre-op pain scores than non-chronic pain patients
- Psychiatric comorbidity in 25% CPPs vs. only 14% of non-CPPs
- BMI is higher in CPPs
- Regional anesthesia used less frequently in CPPs
- CPPs are more likely to have cardiovascular, pulmonary, hepatic and renal comorbidities

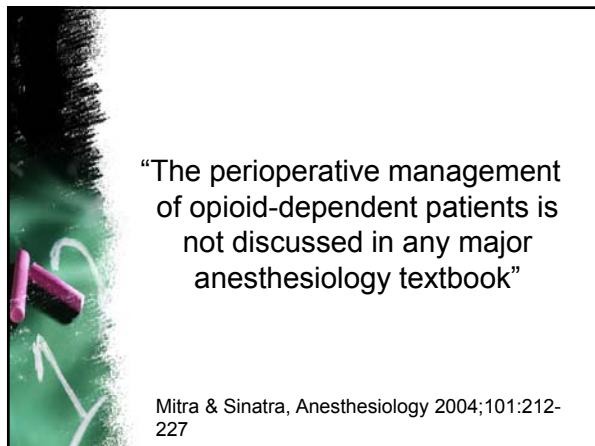
Pain Medicine News: 11/2008



Postoperative Pain Patterns in Chronic Pain Patients: A Pilot Study

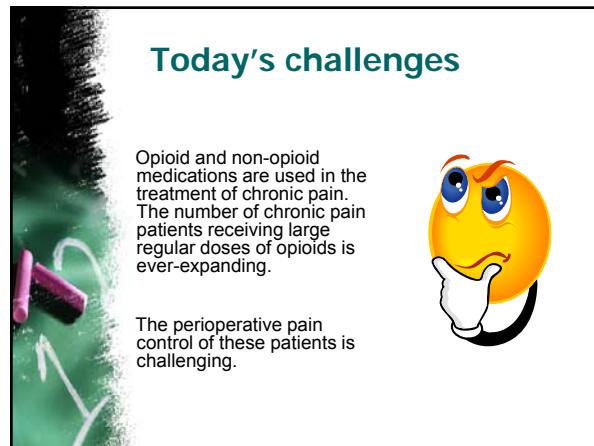
- 96 normal patients and 42 chronic pain patients
- Conclusion: "Surgical patients who have chronic pain and use opioid medications for that pain have more postoperative pain than normals and resolve that pain more slowly"

Chapman et al., Pain Medicine 2009;10:481-487



"The perioperative management of opioid-dependent patients is not discussed in any major anesthesiology textbook"

Mitra & Sinatra, Anesthesiology 2004;101:212-227

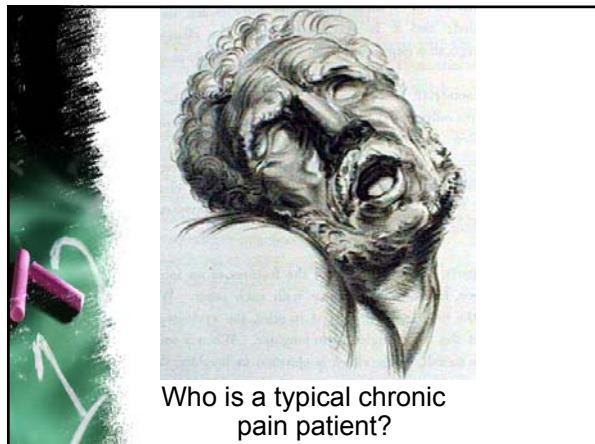


Today's challenges

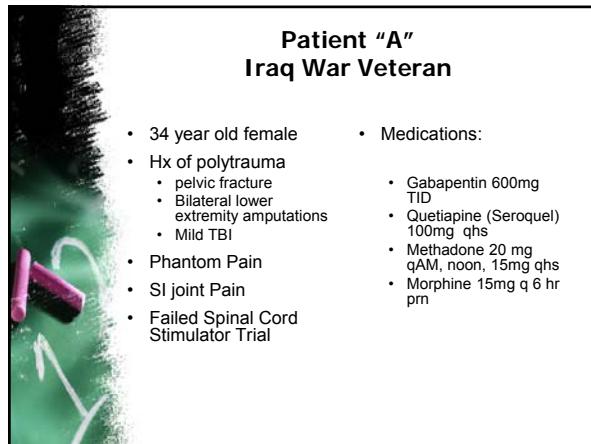
Opioid and non-opioid medications are used in the treatment of chronic pain. The number of chronic pain patients receiving large regular doses of opioids is ever-expanding.

The perioperative pain control of these patients is challenging.



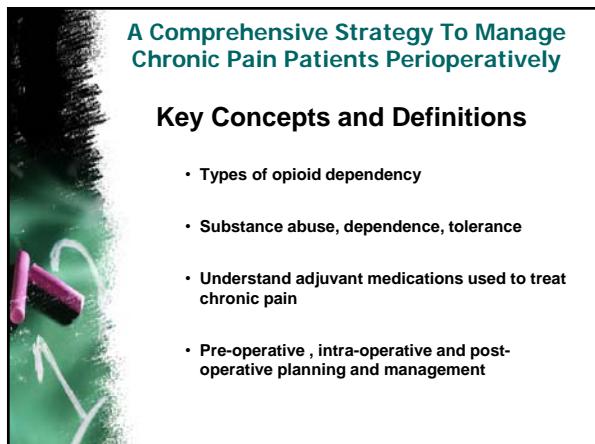


Who is a typical chronic pain patient?



Patient "A"
Iraq War Veteran

- 34 year old female
- Hx of polytrauma
 - pelvic fracture
 - Bilateral lower extremity amputations
 - Mild TBI
- Phantom Pain
- SI joint Pain
- Failed Spinal Cord Stimulator Trial
- Medications:
 - Gabapentin 600mg TID
 - Quetiapine (Seroquel) 100mg qhs
 - Methadone 20 mg qAM, noon, 15mg qhs pm
 - Morphine 15mg q 6 hr pm



A Comprehensive Strategy To Manage Chronic Pain Patients Perioperatively

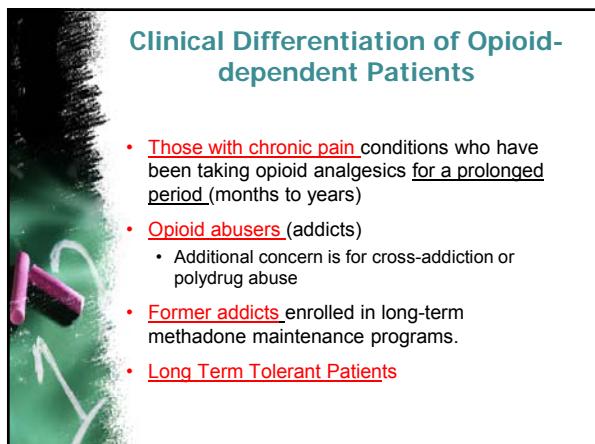
Key Concepts and Definitions

- Types of opioid dependency
- Substance abuse, dependence, tolerance
- Understand adjuvant medications used to treat chronic pain
- Pre-operative , intra-operative and post-operative planning and management



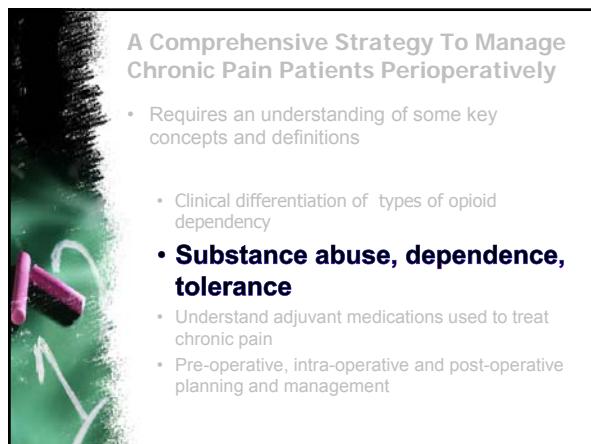
A Comprehensive Strategy To Manage Chronic Pain Patients Perioperatively Requires Knowledge of Key Concepts & Definitions

- **Clinical differentiation of types of opioid dependency**
 - Substance abuse, dependence, tolerance
 - Understand adjuvant medications used to treat chronic pain
 - Pre-operative, intra-operative and post-operative planning and management



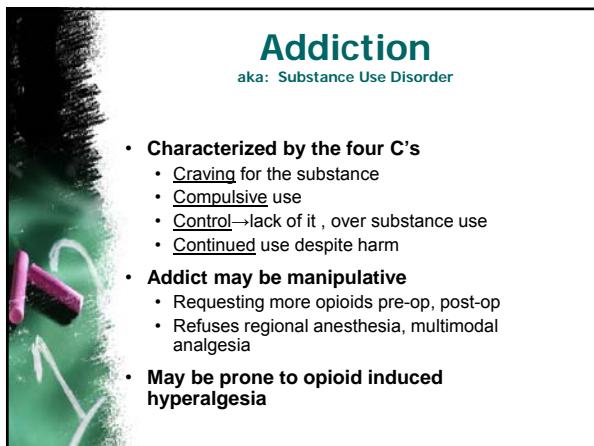
Clinical Differentiation of Opioid-dependent Patients

- Those with chronic pain conditions who have been taking opioid analgesics for a prolonged period (months to years)
- Opioid abusers (addicts)
 - Additional concern is for cross-addiction or polydrug abuse
- Former addicts enrolled in long-term methadone maintenance programs.
- Long Term Tolerant Patients



A Comprehensive Strategy To Manage Chronic Pain Patients Perioperatively

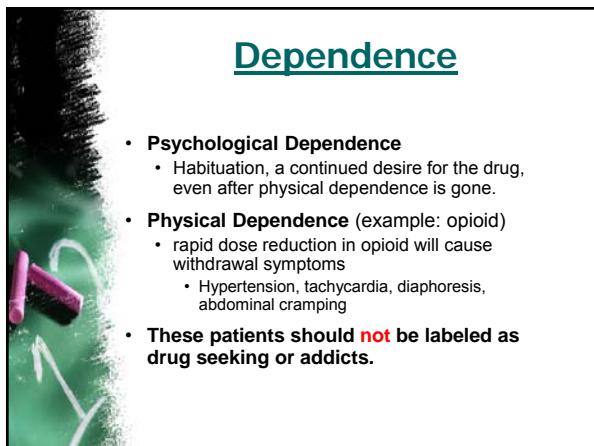
- Requires an understanding of some key concepts and definitions
- Clinical differentiation of types of opioid dependency
- **Substance abuse, dependence, tolerance**
 - Understand adjuvant medications used to treat chronic pain
 - Pre-operative, intra-operative and post-operative planning and management



Addiction

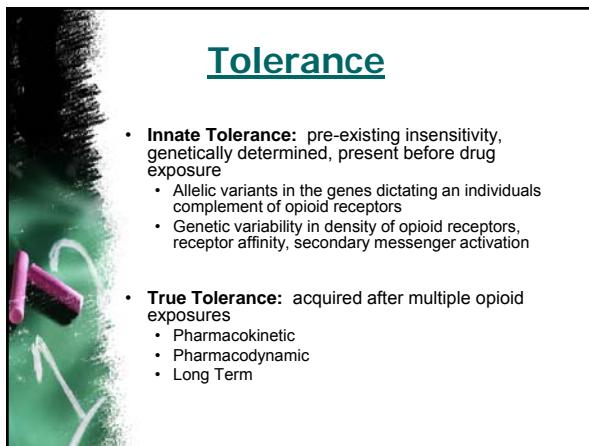
aka: Substance Use Disorder

- Characterized by the four C's
 - Craving for the substance
 - Compulsive use
 - Control→lack of it , over substance use
 - Continued use despite harm
- Addict may be manipulative
 - Requesting more opioids pre-op, post-op
 - Refuses regional anesthesia, multimodal analgesia
- May be prone to opioid induced hyperalgesia



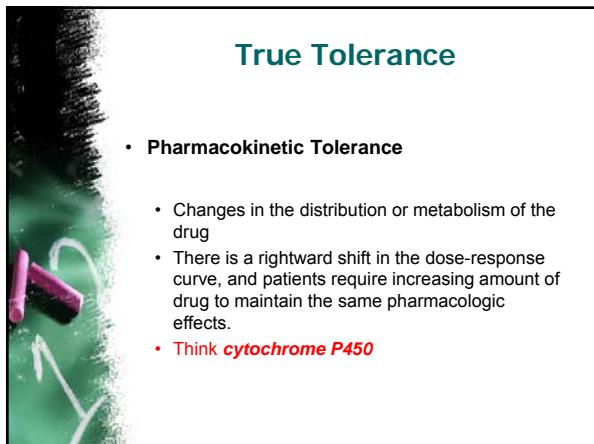
Dependence

- Psychological Dependence
 - Habituation, a continued desire for the drug, even after physical dependence is gone.
- Physical Dependence (example: opioid)
 - rapid dose reduction in opioid will cause withdrawal symptoms
 - Hypertension, tachycardia, diaphoresis, abdominal cramping
- These patients should **not** be labeled as drug seeking or addicts.



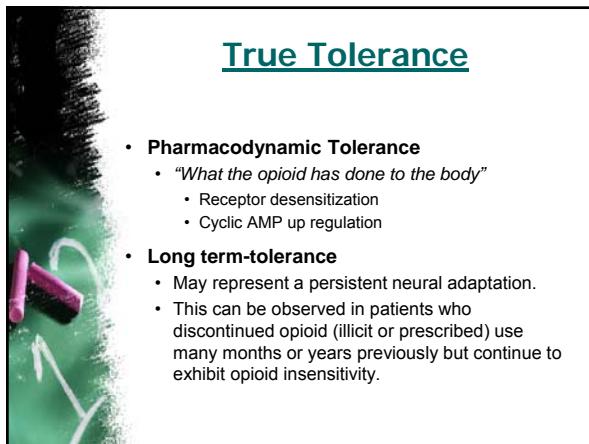
Tolerance

- Innate Tolerance: pre-existing insensitivity, genetically determined, present before drug exposure
 - Allelic variants in the genes dictating an individual's complement of opioid receptors
 - Genetic variability in density of opioid receptors, receptor affinity, secondary messenger activation
- True Tolerance: acquired after multiple opioid exposures
 - Pharmacokinetic
 - Pharmacodynamic
 - Long Term



True Tolerance

- Pharmacokinetic Tolerance
 - Changes in the distribution or metabolism of the drug
 - There is a rightward shift in the dose-response curve, and patients require increasing amount of drug to maintain the same pharmacologic effects.
 - Think *cytochrome P450*



True Tolerance

- Pharmacodynamic Tolerance
 - *"What the opioid has done to the body"*
 - Receptor desensitization
 - Cyclic AMP up regulation
- Long term-tolerance
 - May represent a persistent neural adaptation.
 - This can be observed in patients who discontinued opioid (illicit or prescribed) use many months or years previously but continue to exhibit opioid insensitivity.

A Comprehensive Strategy To Manage Chronic Pain Patients Perioperatively

- Requires an understanding of some key concepts and definitions
 - Clinical differentiation of types of opioid dependency
 - Substance abuse, dependence, tolerance
- Understand adjuvant medications used to treat chronic pain**
- Pre-operative, intra-operative and post-operative planning and management

Adjuvant Analgesics

- This is a diverse group of medications that were originally developed for a primary indication other than pain.
 - Antidepressants
 - Anticonvulsants
 - Alpha-2-adrenergic agonists
 - Corticosteroids
 - Local Anesthetics
 - NMDA antagonists
 - Cannabinoids
 - Bisphosphonates and Calcitonin
 - GABA agonists
 - Neuroimmunomodulatory agents

Antidepressants

- Tricyclics:** (eg, amitriptyline, nortriptyline)
 - Effective in neuropathic pain conditions.
 - Anesthetic implication: response to sympathomimetics remains complex and unpredictable.
- Serotonin and norepinephrine reuptake inhibitors (SNRIs):** (eg, duloxetine, venlafaxine)
 - modulate allodynia, effective for diabetic neuropathy and neuropathic pain in breast cancer.
 - Anesthetic implication: enhanced effects of sympathomimetics and CNS depressants, may impair platelet aggregation
- Selective serotonin reuptake inhibitors (SSRIs):** (eg, citalopram, paroxetine)
 - generally ineffective adjuvant analgesics
 - Used for depression

Anticonvulsants

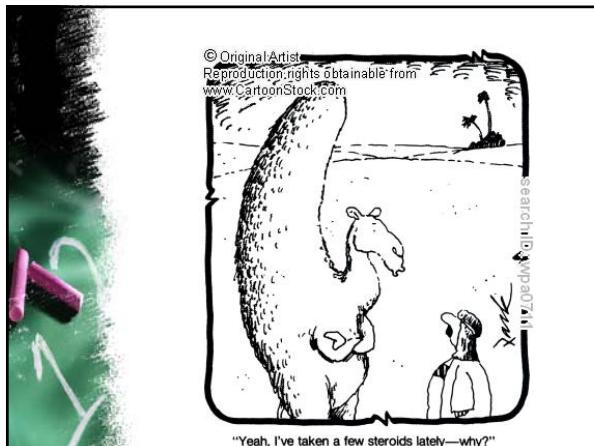
- Gabapentin and Pregabalin:**
 - first line therapy for neuropathic pain syndromes
- Carbamazepine and Oxcarbamazepine:**
 - trigeminal neuralgia
 - Carbamazepine can sig decrease plasma level of Methadone (enzyme CYP3A4, aka CP4502B6)
- Lamotrigine:**
 - carbamazepine resistant trigeminal neuralgia
- Newer Anticonvulsants:**
 - levetiracetam, zonisamide, tiagabine, topiramate all may be helpful in headache syndromes

Alpha-2-adrenergic Agonists

- Clonidine**
 - Binds to alpha-2-adrenergic receptors in the CNS and has a synergistic effect with opioids
 - Best intrathecally and epidurally
 - Can be used orally and transdermally for chronic pain
- Tizanidine**
 - manage spasticity
 - some usefulness in some painful states (neuropathic pain)

Corticosteroids

- Inflammatory neuropathic pain from peripheral nerve injuries.
- Have been used successfully to treat bone pain, pain from bowel obstruction, lymphedema, and headache associated with increased intracranial pressure.



Topical Agents

- Capsaicin, natural substance in hot chili peppers, activates the vanilloid neuronal membrane receptor
- Diclofenac patch
- Novel formulations



Local Anesthetics

- Analgesic properties at sub anesthetic doses.
- Indications:
 - Neuropathic pain
- Examples:
 - IV Lidocaine
 - Mexilitene (oral lidocaine)
 - Transdermal lidocaine (Lidocaine patch 5%)

Less Common Adjuvants

- **NMDA Antagonists**
 - Dextromethorphan, Ketamine
- **Cannabinoids**
 - Marinol
- **Bisphosphonates**
 - Pain reduction in bone metastases and Complex Regional Pain Syndrome
- **Calcitonin**
 - Pain reduction in bone metastases
- **GABA agonists**
 - Baclofen
- **Neuroimmunomodulatory Agents**
 - Thalidomide

Patient "A" Iraq War Veteran

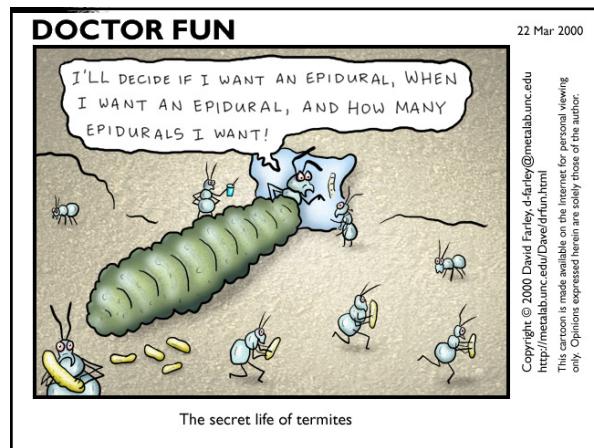
- 34 year old female
- Hx of polytrauma
 - pelvic fracture
 - Bilateral lower extremity amputations
 - Mild TBI
- Phantom Pain
- SI joint Pain
- Failed Spinal Cord Stimulator Trial
- Medications:
 - Gabapentin 600mg TID
 - Quetiapine (Seroquel) 100mg qhs
 - Methadone 20 mg qAM, noon, 15mg qhs
 - Morphine 15mg q 6 hr prn
- Planned Operation:
 - Bilateral Stump Revisions

Management Challenges

- Opioid Tolerant and Dependent
- Quetiapine
 - likely that this patient has PTSD from polytrauma in Iraq
- Acknowledge potential for increased postoperative pain

Management Plan Day of surgery

- Pre-op EKG (prolonged QT)
- Continue scheduled methadone
- Continue scheduled gabapentin
- Multimodal analgesia
 - Consider Celebrex (minimize inflammatory pain), or Acetaminophen
 - Regional Anesthesia (peripheral nerve block, epidural)
- Reassure patient regarding fears of adequate pain control



•Detour for methadone

For those on methadone....

- Risk of prolonged QTc for those on high dose methadone (generally >100mg/day)
- This could lead to development of torsade de pointes
- Conversion of Methadone to other opioids...is a complex conversion
- No universally safe conversion ratio exists

• Ann Intern Med, March 2009, 150 N.6 "QTc Interval Screening in Methadone Treatment"

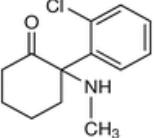
Management Plan Intra-Op

- Consider regional technique (peripheral nerve block, epidural , spinal)
- Surgeon can infiltrate surgical site with long acting local anesthetic before and after operation
- Administration of opioid to meet the following requirements: chronic, intraoperative surgical, anticipated postoperative
- Ketamine
- Allow for spontaneous breathing at end of case (if GETA), titrating opioid to RR of 12-14 breaths per minute and slightly miotic pupil

Now for a detour about Ketamine

Ketamine

- N-methyl-D-aspartate (NMDA) antagonist
- Used as an anesthetic – when given in high doses
- Produces a "dissociative" state
- Profound analgesia with sub anesthetic doses



Level 1 Evidence for Ketamine Analgesia

(Evidence from a systematic review (or meta-analysis) of all the relevant RCTs)

- Low-dose perioperative ketamine is "opioid sparing", "reduces PONV" and has "minimal" side effects.
- Ketamine is most effective as a "continuous low-dose" infusion for acute pain management.



IASP: Pain Clinical Updates, June 2007

Level 1 Evidence for Ketamine Analgesia

- Ketamine has "preventive" but not "pre-emptive" analgesic effects.
- Ketamine added to opioid PCA provides no additional analgesic benefit.



IASP: Pain Clinical Updates, June 2007

Level II Evidence for Ketamine Analgesia

(Evidence obtained from at least one properly designed RCT)

- Ketamine is most effective as an "antihyperalgesic," "antiallodynic," or "tolerance-protective" treatment.
- Ketamine is effective as a "rescue analgesic" for acute pain unresponsive to opioids.



IASP: Pain Clinical Updates, June 2007

Level II Evidence for Ketamine Analgesia

- Ketamine reduces acute wound hyperalgesia and allodynia.
- Ketamine may reduce the incidence of chronic post surgical pain following laparotomy, thoracotomy, and mastectomy.



IASP: Pain Clinical Updates, June 2007

Level II Evidence for Ketamine Analgesia

- Ketamine reduces lower limb ischemic rest pain, peripheral neuropathic pain, and spinal cord injury pain.
- Ketamine does not improve analgesia when used alone or in combination with local anesthetic for peripheral nerve blocks, intra-articular injection, or wound infiltration.



IASP: Pain Clinical Updates, June 2007

Level III Evidence for Ketamine Analgesia
(evidence obtained from nonrandomized controlled trials)

- Ketamine may reduce severe chronic phantom limb pain.
- Level IV (evidence from case series)
- Ketamine improves analgesia in opioid-tolerant patients.

IASP: Pain Clinical Updates, June 2007



Ketamine for Perioperative Pain Management

- Major (more painful-visceral) procedure:
 - Before Incision: 0.5mg/kg IV bolus
 - During Surgery: 0.5mg/kg/hr IV infusion OR 0.25mg/kg IV bolus q 30 min
 - If procedure ≥ 2 hr, stop 60 minutes before end of surgery
- Minor (less painful-hip) procedure:
 - Before Incision: 0.25 mg/kg IV bolus
 - During Surgery: 0.25 mg/kg/hr IV infusion OR 0.125mg/kg IV bolus q 30 min

Himmelseher, et al; Anesthesiology 2005, 102:211-20

Management Plan Post Op PACU

- Start IV PCA
- Continue applicable regional techniques
- Continue NSAIDs if possible (minimizing inflammatory pain) to augment opioid mediated analgesia
- Monitor for over sedation and withdrawal

PACU cont..

- Titrate opioids aggressively to achieve adequate pain control in PACU
- May continue Ketamine if started in OR, or institute Ketamine infusion if pain proves refractory to other measures
- Consider "rescue" regional technique for unrelieved pain

Post Op Transition Phase

- Resume maintenance doses of oral opioids and po adjuvants ASAP after surgery
- Transition from regional and parenteral techniques to oral opioids/adjuvants when possible

Chronic Pain Patient "B"

- 56 year old male
- Failed Back Surgery Syndrome
- Chronic Upper & Lower Back Pain, Left Leg Pain
- S/P Intrathecal Pump Placement
- Current Medications
 - Intrathecal: 1 mg/day morphine, & 300mcg/day Baclofen
 - Duloxetine (Cymbalta) 60mg BID
 - Eszopiclone (Lunesta) 2mg qhs
 - Lorazepam 0.5mg prn
 - Operation: Shoulder arthroplasty

Management Challenges

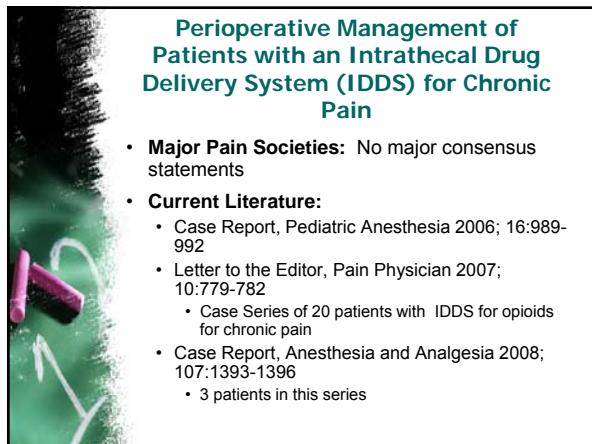
- Opioid Tolerant
- Implanted Intrathecal Pump
 - With opioid and baclofen
- Acknowledge potential for increased post operative pain

Management Plan Day of Surgery

- IDDS should be interrogated before surgery
- Continue intrathecal therapy
- Multimodal Analgesia
- Consider Regional Anesthesia
- Reassure patient regarding possible fears of pain control



• Detour for IDDS



Perioperative Management of Patients with an IDDS for Chronic Pain

Misconceptions:

- Pt's with an IDDS are more susceptible to respiratory depression/sedation with parenteral opioids
- There is no evidence to support this statement!

Further Misconceptions...

The IDDS may provide adequate pain control for the postop period.

IDDS is **only** providing the **baseline** narcotic requirement in these patients.

It is reasonable to then **continue** this during the perioperative period for their **baseline pain condition**.

Therefore:

Additional pain control will need to be provided via parenteral narcotics and potentially regional anesthesia.

Further Misconceptions....

IDDS infusion may be modified to provide acute pain control

- Programming and exchange of pump reservoir contents is a **complex** task requiring **experienced** personnel.
- Not all IDDS have complex programming capabilities, **eliminating the possibility of use as a titratable** postoperative pain modality.
- We use if only for baseline pain condition

Further Misconceptions...

- The reservoir or catheter may interfere with surgical access or regional anesthesia.
- An epidural for labor and for intraoperative and postoperative pain control have been successfully used in patients receiving intrathecal **Baclofen**.
- It is reasonable to extrapolate epidural analgesia could be successful with an IDDS delivering **opioid**.
- Fluoroscopic examination is a reliable way to locate the reservoir and to determine course of the intrathecal catheter.
- Other regional techniques (non-neuraxial) are encouraged in these patients when indicated.

Intra-Op Management Plan

- Consider regional technique (interscalene block)
- Administration of opioid to meet chronic, intraoperative and anticipated postoperative requirement
- Consider intraoperative Ketamine
- Allow for spontaneous breathing at end of case (if GETA), titrating opioid to RR of 12-14 and slightly miotic pupil

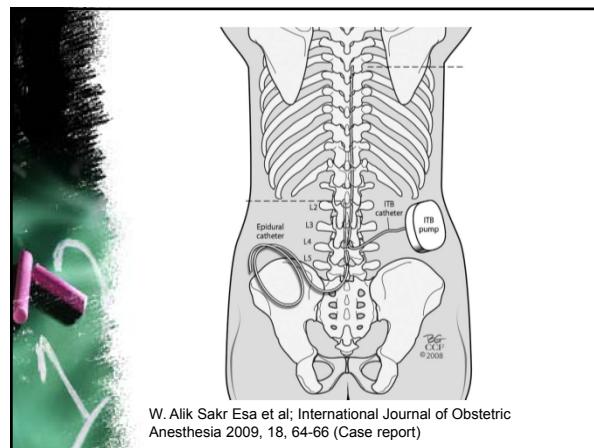
Management Plan PACU

- Start IV PCA
- Continue applicable regional techniques or offer rescue block if pain control inadequate
- Monitor for over sedation
- May continue Ketamine if started in OR, or institute Ketamine infusion if pain proves refractory to other measures

Pt with an intrathecal pump.....

Can an epidural be placed perioperatively?





Emerging Analgesics and Analgesic Technologies

- Catheter-free PCA
- Liposomes or nanoparticles will be used as transdermal drug carriers
- Iontophoresis, where serum levels can rise more rapidly than in transdermal systems.
- Sufentanil Nano Tab PCA system, an oral PCA system
- IV Acetaminophen (Ofirmev) filed with FDA in May 2009 for approval (already available in 80 countries)

For the average patient “joe or jane”

- Go to:
 - <http://www.postoppain.org/>