

# Stanford Acute Pain Management

## Resident Rotation Syllabus

**Version 2019-2020**

*Updated February 19, 2019*

<http://paincenter.stanford.edu>

### Table of Contents

PAIN MANAGEMENT FACULTY .....	2
GOALS AND OBJECTIVES .....	2
ADVERSE EFFECTS OF PERIOPERATIVE PAIN .....	5
OPIOIDS .....	7
NEURAXIAL ANALGESIA .....	15
REGIONAL ANESTHESIA AND PERIPHERAL NERVE CATHETERS.....	23
ADJUVANTS .....	30
OPIATE TOLERANT PATIENTS .....	40
CANCER PAIN .....	37
ACUPUNCTURE AND PAIN MANAGEMENT .....	41

## **PAIN MANAGEMENT FACULTY**

- Sean Mackey MD, PhD, Chief, Division of Pain Management, Professor
- Anuj Aggarwal MD, Clinical Instructor
- Meredith Barad MD, Clinical Associate Professor
- Ian Carroll MD, Clinical Assistant Professor
- Stephen Coleman MD, Clinical Assistant Professor
- Beth Darnall PhD, Clinical Professor
- Ryan Derby, Clinical Assistant Professor
- Pamela Flood MD, Professor
- Alpana Gowda MD, Clinical Assistant Professor
- Jennifer Hah MD, Assistant Professor
- Michele Jehenson DDS, Clinical Associate Professor
- Joshua Kirz PhD, Clinical Associate Professor
- Jiang-Ti Kong MD, Clinical Instructor
- Michael Leong MD, Clinical Associate Professor
- Chinwe Nwaneshiudu MD, Clinical Instructor
- Heather Poupore-King PhD, Clinical Assistant Professor
- Xiang Qian MD, Clinical Associate Professor
- Vafi Salmasi MD, Clinical Instructor
- Peter Schmidt MD, Clinical Instructor
- Vanila Singh MD, Clinical Associate Professor
- Kristen Slater PsyD, Clinical Instructor
- Vivianne Tawfik MD, PhD, Assistant Professor
- Natacha Telusca MD, Clinical Instructor
- Kale Wedemeyer MD, Clinical Instructor

## **GOALS AND OBJECTIVES**

*Sean Mackey, MD, PhD*

The inpatient rotation occurs over a one month period. It includes the postoperative pain service, cancer pain service, and acute consultative service throughout the hospital. The role of consultant physician is emphasized with the appropriate communication and follow-up with the primary service.

### **PATIENT CARE**

Goal: To coordinate the care of individuals suffering from chronic and acute pain in an inpatient setting and to develop the ability to function independently as a consulting physician.

Objectives: Upon completing this rotation, residents should understand

- How to provide primary care for patients admitted directly to the Med-Surg Unit

- How to manage the continuum of acute postoperative pain by providing preoperative consultation, intraoperative suggestions and postoperative care, including the use of patient- controlled analgesia, spinal medication delivery and regional anesthesia techniques
- How to perform a comprehensive musculoskeletal examination with emphasis on both structure and function as it applies to diagnosing acute and chronic pain problems
- How to assess for psychiatric and psychological comorbidities (e.g., chemical dependency issues, somatoform disorders, mood disturbances, personality disorders, etc.) in an inpatient setting
- How to create and implement complex treatment plans across a variety of disciplines in an inpatient setting
- The common obstacles that often interfere with successful implementation of treatment plans and how to overcome them in an inpatient setting

## MEDICAL KNOWLEDGE

Goal: To acquire a comprehensive understanding of the essential basic and applied medical and social sciences as they relate to management of acute and chronic pain conditions in an inpatient setting.

Objectives: Upon completing this rotation, residents should understand

- The anatomy, physiology, and pharmacology of pain transmission and modulation
- The role of opiate and adjunctive medications in providing an environment for faster postoperative recovery
- The role of surgical and interventional treatment modalities for various pain conditions
- The role of functional, vocational, and psychological treatment modalities for various pain conditions
- The use of various strategies and techniques as a means of reducing the impact of pain on a patient's life while concurrently improving functional capacity and quality of life

## PRACTICE-BASED LEARNING & IMPROVEMENT

Goal: To be able to perform self-assessments; retrieve, understand, and apply scientific evidence related to the practice of pain medicine; and make meaningful contributions to the education of others.

Objectives: Upon completing this rotation, residents should be able to

- Identify their personal strengths and weaknesses and how this affects their practice
- Incorporate feedback from performance evaluations into daily practice
- Utilize hospital and university information technology systems to optimize learning
- Actively contribute to the education of patients, families, students, and other health professionals

## INTERPERSONAL & COMMUNICATION SKILLS

Goal: To be able to demonstrate strong interpersonal and communication (verbal and written) skills that result in effective exchange of information with patients, families, and other health professionals.

Objectives: Upon completing this rotation, residents should be able to

- Provide appropriate consultative recommendations to the various medical and surgical teams in the hospital for management of acute, chronic, cancer, and trauma care
- Communicate effectively with patients, family members, and the general public across broad socio-economic and cultural domains
- Work collaboratively with other physicians and health professionals from other disciplines
- Maintain appropriate, timely, and accurate medical records

## PROFESSIONALISM

Goal: To strictly adhere to ethical principles in all aspects of practice.

Objectives: Upon completing this rotation, residents should be able to

- Demonstrate compassion and respect for patients, families, and other health care professionals
- Have a pervasive sense of personal integrity
- Demonstrate sensitivity to individuals of diverse socio-economic and cultural backgrounds

## SYSTEMS-BASED PRACTICE

Goal: To understand how the practice of pain medicine is a part of a larger context of health care organization and to be able to utilize resources from the larger system to optimize patient care.

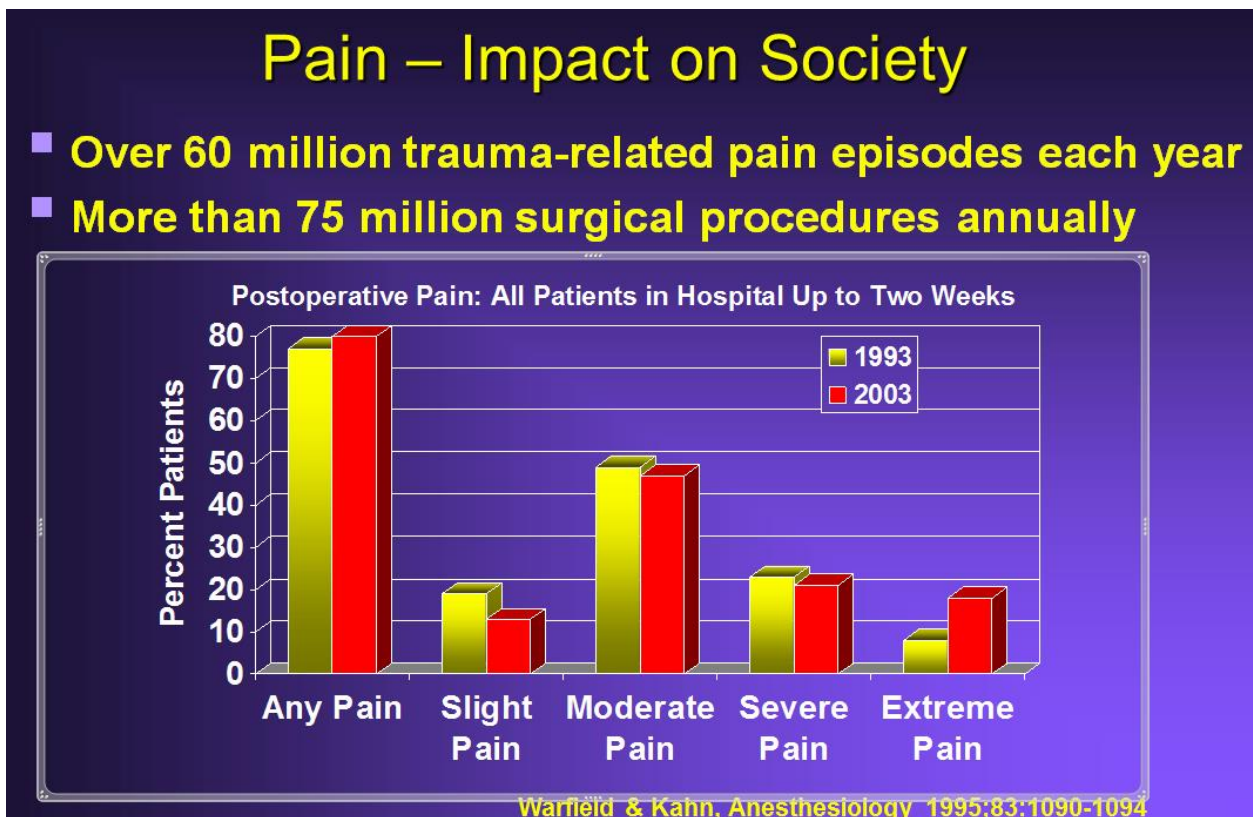
Objectives: Upon completing this rotation, residents should be able to

- Be proficient with cost analysis and cost containment as it relates to patient care
- Consistently employ quality assurance and improvement techniques in professional work
- Work collaboratively with others to improve health care procedures and systems to positively impact patient care

# **ADVERSE EFFECTS OF PERIOPERATIVE PAIN**

*Stephen D Coleman, MD*

Peri-operative pain affects multiple organ systems and may impact the development of chronic pain. Intra operative anesthesia, regional and general, make suitable operating conditions and mitigates many of the ill effects of intra-operative stimulus. During the transition from intra operative anesthesia to post operative care the effects of intra-operative anesthesia dissipate frequently resulting in pain. Postoperative pain activates the sympathetic nervous system producing a stress response which in turn may adversely affect multiple organ systems. In addition to physiologic effects of postoperative pain, patient quality of life measures, patient satisfaction are impacted as well as play a role in the development of chronic pain. Further, there is an ethical responsibility to address acute pain.



## **CARDIOVASCULAR**

Acute postoperative pain may result in an increased heart rate, angina, dysrhythmias, and congestive heart failure. Further, acute stress response enhances perioperative hypercoagulability increasing the likelihood of coronary thrombosis.

## **COAGULATION**

Postoperative patients have increased coagulation factors, enhanced platelet activity, reduced coagulation inhibitors, and reduction of fibrinolysis. Postoperative patients, particularly if they are experiencing pain, may have reduced physical activity in the setting of hypercoagulability, thus, leading to deep vein thrombosis, arterial thrombosis and coronary artery thrombosis.

## PULMONARY

Pulmonary compromise is most severe after upper abdominal procedures. FEV-1 decreased by 60% compared to preoperative levels. Pain can also influence respiratory mechanics resulting in rapid, shallow breathing increasing the work of breathing. Patients may also experience postoperative diaphragm dysfunction. Deep breathing appears efficacious in reducing postoperative pulmonary complications.

## GASTROINTESTINAL

Postoperative pain is thought to inhibit intestinal motility by way of spinal reflex. In addition, activation of sympathetic system may reduce intestinal motility.

## STRESS RESPONSE

Stress response induces changes in neuroendocrine hormones and local tissue cytokines and prostaglandins. Some of the effects of stress response include tachycardia, hypotension, fever, hypercoagulability, ileus, reduced immune function, sodium and water retention, and increased blood glucose levels. A hypermetabolic catabolic state results in negative nitrogen balance and increased oxygen consumption. This response can adversely affect healing as well as additional organ dysfunction.

## Physical Function

Acute post operative will reduce patient's ability to participate in physical therapy resulting in delay in reestablishing function. If prolonged there may be substantial loss of physical function which may be difficult to overcome.

## Chronic Pain

Development of chronic pain after surgical procedures varies by the type of surgery and is relatively common. The incidence of chronic postoperative pain after leg amputation is 30%-80%, thoracotomy 22%-67% and breast surgery 11%-57. Although many factors may increase the risk of developing chronic postoperative pain, multiple publications associate poorly managed postoperative pain with the development of chronic pain.

## REFERENCES:

Warner D. Preventing Postoperative Pulmonary Complications. *Anesthesiology* 2000;92:1467-72.

Wu C, Naqibuddin M, Rowlingson A, Lietman S, Jermyn R, Fleisher L. *The Effect of Pain on Health-Related Quality of Life in the Immediate Postoperative Period.* *Anesth Analg*, 2003;97:1078-85.

Warner D. *Preventing Postoperative Pulmonary Complications.* *Anesthesiology*, 2000;92:1467-72.

Miller RD. (2015) *Miller's Anesthesia*. Eight Edition. Elsevier

Thomazeau J, Rouquette A, Martinez V. Predictive Factors of Chronic Post-Surgical Pain at 6 Months Following Knee Replacement: Influence of Postoperative Pain Trajectory and Genetics. *Pain Physician* 2016; 19:E729-E741.

Aasvang E, Gmaehle E, Hansen JB. Predictive Risk Factors for Persistent Postthoriotomy Pain. *Anesthesiology* 2010; 112:957-69.

Gan TJ. Poorly controlled postoperative pain: prevalence, consequences, and prevention. *Journal of Pain Research*; 2017;10:2287–2298

H. Beloeil, L. Sulpice. Perioperative Pain and its Consequences: *Journal of Visceral Surgery* 2016; 153:S15-S18.

Desborough JP. The Stress Response to Trauma and Surgery. *Br J Anaesth* 2000;85:109-117.

Hans JG, Aduckathil S, Van Wijck, AJ. Pain Intensity on the First Day after Surgery. *Anesthesiology* 2013;118:934-44.

## QUESTIONS

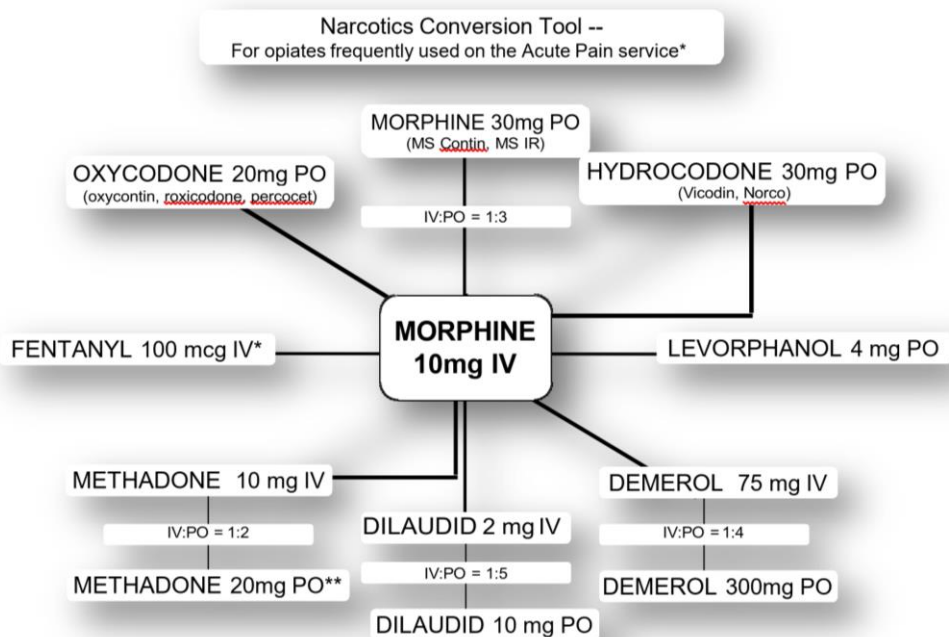
1. As an anesthesiologist what options are available to address postoperative pain pre-operatively, intraoperatively and postoperatively?
2. Besides pain scores what additional information is helpful in assessing post operative pain?
3. What are two long-term consequences of poorly managed acute postoperative pain?

## **OPIOIDS**

*Anuj Aggarwal, MD; Meredith Barad, MD*

Opiate Conversion:

1. Evaluate total opiate usage over the past 24-48 hours.
2. Convert all IV medications to morphine IV (see chart below).
3. Convert morphine from IV to PO, 1:3 respectively.
4. Convert from morphine PO to desired PO meds (see chart below).
  - a. 50% of total to be given as a long acting oral medication
  - b. 50% given as short acting on a prn basis for breakthrough pain
5. Contextualize dosing to the sensitivity of your patient.



\*This chart does not replace clinical decision-making. Use caution when dosing for elderly patients or patients with severe hepatic or renal disease.

\*\*Methadone IV:PO ratio of 1:1 does not hold at higher doses (>100mg IV).

## NEURAXIAL OPIATES

**10:1:0.1**: IV: Epidural : Intrathecal – most applicable for hydrophilic opioids such as morphine and dilaudid, fentanyl being lipophilic largely considered 1:1:1

Opioid	Relative Lipid Solubility	Dose	Onset (min)	Peak (min)	Duration (hrs)	Infusion Rate
Morphine	1	2-5mg	15-30	60-90	4-24	0.3-0.9mg/hr
Fentanyl	600	50-100 µg	5-10	10-20	1-3	25-50 µg/hr
Sufentanil	1,200	20-50 µg	5-15	20-30	2-6	10-25 µg/hr
Hydromorphone	1.5	0.75-1.5mg	10-15	20-30	6-18	0.1-0.2mg/hr

## SIDE EFFECTS

### CENTRAL:

- Respiratory depression: reduction of sensitivity to pCO<sub>2</sub> in the respiratory centers of the brain. At risk: opiate naïve, extremes of age, pre-existing respiratory disease, dramatic decrease in pain with maintained opiate dose. Delta and kappa agonists may cause less respiratory depression than mu agonists.
- Cough suppression: inhibitory effects of opiates in the brain stem nuclei of the cough reflex pathway.
- Nausea, vomiting: activation of the chemoreceptor trigger zone in the area postrema of the medulla.
- Sedation and cognitive impairment
- Hallucinations/delirium
- Rigidity, myoclonus, seizures: most commonly seen in use of morphine, meperidine and tramadol due to build up of metabolites.
- Pruritis: more commonly associated with neuraxial opiates, thought to be due to  $\mu$  receptor activation at the dorsal horn of the medulla.
- Hyperalgesia
- Bradycardia, vasodilatation with high doses
- Reward, Euphoria: nucleus accumbens

### PERIPHERAL:

- Pupil constriction: opiate action on oculomotor nucleus
- Constipation: maintained contraction of smooth muscle reducing gut motility and decreased secretion in gut, and increased sphincter tone
- Urinary retention: increased bladder and sphincter tone resulting in urgency and retention
- Pruritis: systemic histamine release from mast cells

### TREATMENT OF SIDE EFFECTS: NAUSEA/VOMITING

- Metoclopramide 10-20 mg IV/PO q3h or q4h or q6h
- Promethazine
  - 6.25 -12.5 IV
  - or 12.5-25 mg PO/PR q4-6h
- Ondansetron 4 mg IV

### CONSTIPATION

- Docusate 250 mg PO bid
- Milk of Magnesia 30 ml PO bid
- Lactulose 30 ml PO bid
- Senna 1-4 tabs PO daily
- Bisacodyl
  - 5-10 mg PO or 10 mg PR q day
- Phosphate enema prn
- Magnesium citrate 300 ml PO prn

## PRURITUS (COMMONLY RESOLVES IN 1-2 DAYS)

- Diphenhydramine 25 mg IV/PO q6h – will often sedate patients but not treat opioid receptor mediated pruritis
- Hydroxyzine 25 mg PO/IM q6h
- Nalbuphine

## OVERDOSE:

- Naloxone: For respiratory rate <6/MIN or for somnolence/sedation:
  - o **0.04 MG IV push. May repeat once.**
- For APNEA or if UNAROUSABLE;
  - o **0.2 – 0.4 MG IV push. May repeat once.**

**\*\*STICK AROUND**, the 1/2 life of naloxone is shorter than that of opioids, a repeat dose of naloxone may be necessary.

## IMPORTANT NOTES

### MORPHINE:

- Extensive first pass metabolism with resultant variable bioavailability (10- 45%)
- Glucuronidation of morphine leads to two major metabolites:
  1. Morphine-3-glucuronide – causes adverse effects
  2. Morphine-6-glucuronine – more potent than morphine
  3. The ratio between the two is difficult to predict, metabolites can build up in patients with renal failure
- Short acting tablets are difficult to find

### METHADONE:

- Excellent oral bioavailability (60-95%)
- Lack of active metabolites
- NMDA antagonist
- Serotonin reuptake inhibitor
- Hepatic and renal impairment do not influence methadone clearance significantly
- Steady state plasma concentration takes 5-10 days (variable half –life of 8-80 hours)
- For chronic pain conversion ratio can range from 1:4- 1:16

### FENTANYL:

- Use caution with transdermal dosing especially in acute settings. (excellent conversion chart on UptoDate). Generally contraindicated for acute pain and utilized for chronic pain in terminal illness.
- Takes 12-24 hours to reach peak plasma concentration and a residual depot remains in subcutaneous tissue for 24 hours after removal of patch.

## BUPRENORPHINE:

- Partial  $\mu$  agonist, weak  $\delta$  agonist,  $\kappa$  antagonist
- Give sublingually due to high first pass metabolism
- Max dose 32mg/day
- Available in transdermal in sublingual forms
- Currently, transdermal is not available in the Stanford formulary and would need to be provided by patients
- Perioperative management of buprenorphine remains controversial, most national guidelines recommend discontinuation of buprenorphine in the perioperative period due to fears regarding pain control given the high affinity of buprenorphine for opioid receptors and its partial agonist activity limiting the ability to overdrive with other opioid medications. At Stanford, we have adopted a policy of buprenorphine continuation (detailed at the end of the chapter)

## MEPERIDINE

- Has anti-cholinergic effects
- Normeperidine – metabolite – causes agitation, tremors, myoclonus, generalized seizures

## TYPES OF OPIOIDS

- Pure  $\mu$  agonist: morphine, fentanyl, oxycodone, hydromorphone, methadone
- Partial  $\mu$  agonist: buprenorphine, tramadol
- Pure antagonists: naltrexone, naloxone
- $\kappa$  agonist/  $\mu$  antagonist: butorphanol, pentazocine, nalbuphine
- 

## WITHDRAWAL

- Psychomotor arousal
  - Irritability, restlessness, pacing, sleeplessness
- Autonomic arousal
  - Mydriasis, yawning, sweating, diarrhea, lacrimation, rhinorrhea, mild tachycardia and hypertension
- Pain: muscle aching, joint pain, stomach cramping

## DEFINITIONS

1. Tolerance: the need for increasing doses to maintain a defined pharmacodynamic effect.
2. Physical dependence: the occurrence of withdrawal symptoms after the abrupt discontinuation of a drug or the administration of an antagonist.
3. Addiction (psychological dependence): A behavioral pattern of compulsive drug use resulting in physical, psychological and social harm.
4. Pseudoaddiction: Behavior perceived by the healthcare professional as addiction, but an iatrogenic syndrome of abnormal behavior developing as a direct consequence of

inadequate pain management.

#### THE 4 A'S:

Assessed in all patients on opiates:

1. Analgesia
2. Activities of Daily Living (Functionality)
3. Adverse effects
4. Aberrent drug taking (addiction related outcomes)

#### PERIOPERATIVE MANAGEMENT OF BUPRENORPHINE

Considerable controversy exists regarding the perioperative management of buprenorphine and many national guidelines, and test answers, call for the discontinuation of buprenorphine preoperatively to prevent difficulty with pain control due to the partial agonism of opioid receptors and the high affinity of buprenorphine for opioid receptors, leading to theoretically difficulty in overdriving buprenorphine and achieving increased opioid receptor activity for postoperative pain control.

However, many patients are on buprenorphine for both opioid addiction/misuse as well as chronic pain. To reintroduce buprenorphine after surgery requires the patient stop all opioids and be in withdrawal prior to reinduction of buprenorphine. In a patient with acute on chronic pain, history of opioid misuse/addiction, and new prescriptions of opioids at home, this can be a challenging time and has been associated with relapse of opioid misuse/abuse, heroin use, overdose, and death.

At Stanford, we have adopted a policy of buprenorphine maintenance prior to surgery, with a goal to reduce higher doses (>10mg/day) down to <10mg/day and the summary is included below. If there are more questions in regards to buprenorphine policy at Stanford, questions can be directed to Anuj Aggarwal at [akaggarw@stanford.edu](mailto:akaggarw@stanford.edu).

#### **Preoperative**

Patients on ≤10mg Buprenorphine/day, Buprenorphine Patch, or Buprenorphine Implant

- Should be continued on buprenorphine; buprenorphine prescriber should be made aware of upcoming surgery
- Documentation of buprenorphine in preoperative anesthesia note
- Pain consult via preop order set
- Patients on buprenorphine patch should bring supply to hospital (hospital formulary has Suboxone™ and Subutex™)
- Patients should continue buprenorphine; may discontinue up 24 hours before if necessary (ie patch would need to be replaced the evening before surgery and then would be removed upon arrival in the preop check in)

Patients on >10mg Buprenorphine/day

- Should be continued on buprenorphine; buprenorphine prescriber should be made aware of upcoming surgery
- If scheduled for surgery with anticipated high degree of post-surgical pain, consider taper to 8mg/day dose in conjunction with buprenorphine provider at least 72 hours prior to surgery; may warrant delay in surgery if elective
- Documentation of buprenorphine in preoperative anesthesia note

### **Day of Surgery**

- All patients should take buprenorphine day of surgery, patients with BuTrans ® patch will have to remove per Stanford policy, will need to be reapplied in the PACU/ICU
- Recommend patients receive acetaminophen PO + gabapentin/pregabalin + NSAID in the preoperative area
- Regional anesthesia or neuraxial anesthesia should be employed if possible; if not, all patients should receive ketamine infusion +/- lidocaine infusion

### **Postoperative**

- All patients will be followed by the Acute Pain Service in the postoperative period for multimodal management (PCA with IV hydromorphone +/- ketamine infusion +/- lidocaine infusion in addition to other non-opioid analgesics).
- If patients cannot take the sublingual form of buprenorphine in the postoperative period, buprenorphine should be converted to IV formulation\*.
- Patients should be continued on home dose of buprenorphine (patch or sublingual); higher home doses should be divided into q6h or q8h dosing with consideration of a supplemental PRN dose\*\*
- Discharge patient on home dose of buprenorphine with one week supply of PO opioid for acute pain needs; patient should have follow up with buprenorphine provider at the time of discharge.

\* IV and sublingual buprenorphine have a similar duration of action (6-9 hours) with different peak and onset of action (5 min onset/5 min peak and 15-45 min onset/0.5-3.5 hours peak for single dose and 1-2 hour peak for multiple dose respectively for IV and sublingual). Despite decreased bioavailability (29% compared to estimated 100% for IV for sublingual), morphine equivalence in the literature is reported as the same for IV and sublingual buprenorphine. As such, decreased doses of IV should be titrated in under physician guidance until optimal dosing found.

\* Successful case reports of 2mg buprenorphine sublingual as q6 to q4 hour PRN dosing; totals with standing buprenorphine dose reaching as high as 72mg/day without adverse outcomes but adequate analgesia.

### **REFERENCES**

Morgan GE, Mikhail MS. (1996) Clinical Anesthesiology. Stamford, CT: Appleton & Lange.

McMahon S, Koltzenburg M, eds. (2006) Wall and Melzack's Textbook of Pain 5<sup>th</sup> Ed. London, UK: Elsevier Limited.

# NEURAXIAL

## ANALGESIA

*Stephanie Jones, MD (Vivianne Tawfik, MD, PhD)*

A large component of perioperative acute pain management is the maintenance of neuraxial analgesia. Every institution has different practices in regards to specific infusions. **Here at Stanford, the typical practice is to run a basal epidural infusion of bupivacaine .125% with Dilaudid, and additional PCEA Fentanyl for patient controlled analgesia.**

During your time on the acute pain service, you will typically receive patients from the PACU that have been started on epidural infusions. The infusions are usually initiated by the PACU resident. At times, due to scheduling issues (ex. late case out of the OR), the acute pain service may be responsible for initiating the postoperative epidural infusions.

Although the OR teams are typically the ones placing the epidurals, occasionally the acute pain service may be consulted for initial epidural placement. Typical scenarios which require the acute pain team to place epidurals include - the surgical service desires an epidural prior to the morning of service (typically the CV service), thoracic epidural placement for pain control in multiple rib fractures, or epidural blood patch placement for post-dural puncture headaches. For the most part, however, the primary role of the acute pain service is to manage the epidurals once they come out of the OR. Because of this it is wise to recognize the typical infusions used at Stanford.

### EPIDURAL INFUSIONS

- Local anesthetic infusion
  - Bupivacaine 0.125% at 2-8 ml/hr
  - Rarely, if patient's hemodynamics tolerate, and inadequate density of the block, may increase up to 0.25% concentration
  - In some cases when epidural is not providing adequate analgesia can consider switching to epidural lidocaine infusion 3-6 ml/hr to start- this will provide systemic levels and therefore "rescue" an epidural that may not be in the exact ideal position. This also means that **q8hrs lidocaine blood levels need to be ordered.**
- Opioid infusion concentrations
  - Hydromorphone 0.05 mg/ml
  - If allergy to hydromorphone, consider Morphine 0.15 mg/ml
- Opioid maintenance options
  - Continuous hydromorphone (0.2 mg/hr) or morphine infusion, with PCEA fentanyl
  - –or- Intermittent bolus (q12 hours) of hydromorphone or morphine, plus PCEA fentanyl prn

### TIPS ON ADJUSTING INFUSION RATES

For mid to low thoracic epidurals (approximately T6-T8 levels), we typically run the basal infusion of 1/8% Bupivacaine at 6 ml per hour. From there, one may adjust upwards or downwards accordingly. For those patients with limited comorbidities, one may choose to run a baseline Dilaudid infusion at 0.2 mg per hour. For the frail, elderly, or those patients with significant comorbidities, the typical practice is to limit the epidural Dilaudid to 0.2 mg every 12 hours as bolus dosing. Baseline Fentanyl PCEA dosing is typically 10 mcg every 15 minutes for opioid naïve, frail, or elderly patients; one may easily titrate up the Fentanyl to 15 – 25 mcg every 10 minutes as tolerated.

For lower thoracic to high lumbar epidurals (approximately T10 – L1 levels), we typically run the basal infusion at 8 – 10 ml per hour, and adjust upwards or downwards accordingly. Of course, epidural

management is dependent on each individual patient case, and sometimes requires multiple adjustments until the appropriate regimen is found.

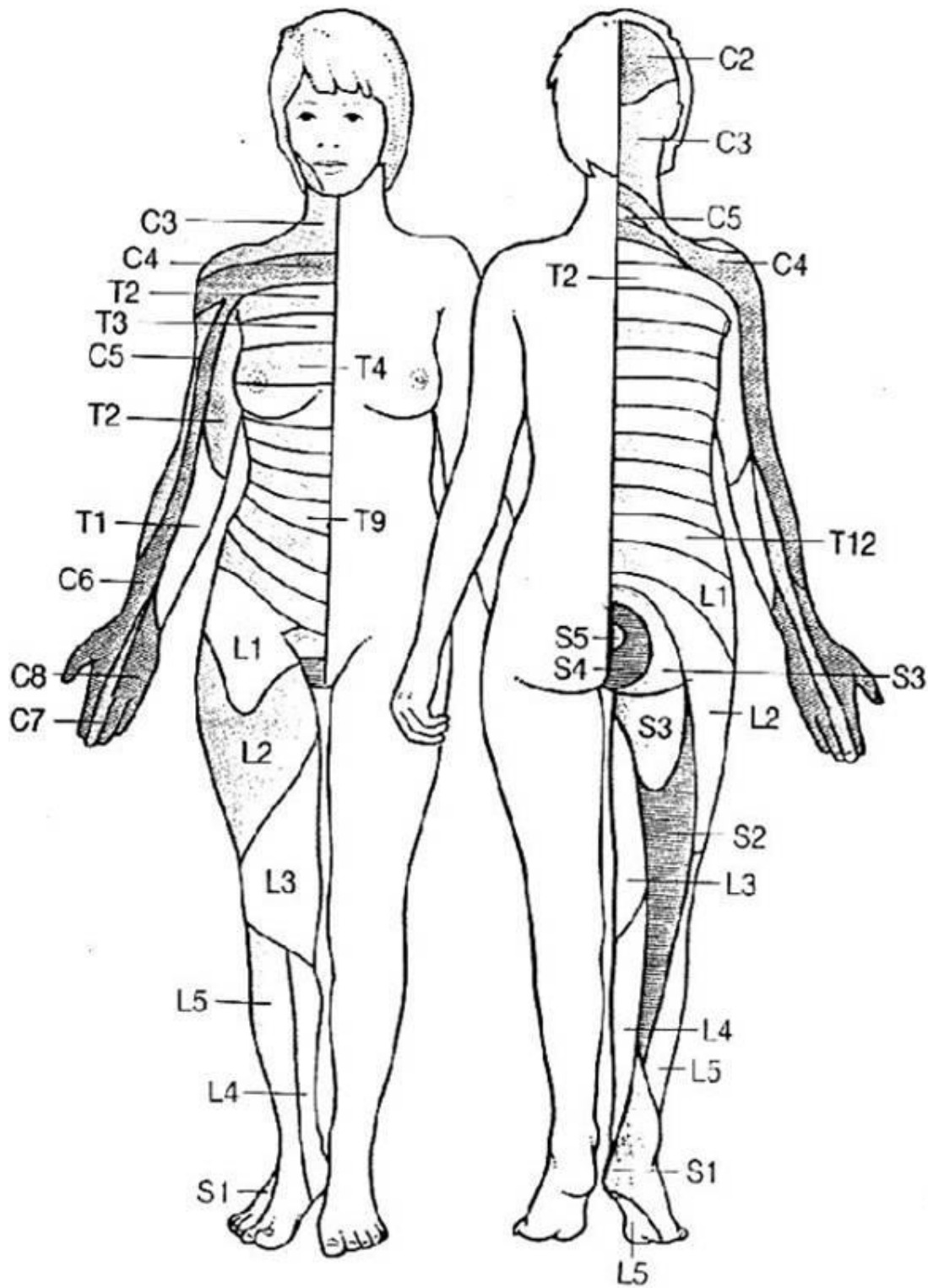
## INITIAL EVALUATION OF THE PATIENT WITH AN EPIDURAL CATHETER

1. When getting sign-out from the PACU resident (or sometimes the OR team who placed the catheter), find out the pertinent information regarding the catheter placement.
  - What level was the catheter placed? How deep was loss of resistance, and how deep was the catheter threaded and secured? Was it a difficult placement? Was there a recognized dural puncture? Was it used during the case for analgesia?
2. Examine the patient
  - Assess the vitals – is the patient hypotensive, tachycardic, altered? All of these disturbances can possibly be attributed to the effects of the epidural infusion
  - Assess the block – it is typically a good idea to assess the patient's baseline block (one can use ice or sometimes an alcohol prep if ice is unavailable to assess temperature sensitivity)
  - Assess baseline neurologic exam – where is the sensory level, note strength examination, is the block unilateral? Does the patient complain of weakness or dense numbness?
  - Examine the epidural site – an occlusive dressing should be intact; the area over the insertion site should be visible through the transparent dressing – a small amount of blood is typically okay and associated with the initial placement; active bleeding should be assessed; a small amount of leakage is also acceptable, large amounts of leakage should also be assessed; palpate over the insertion site for tenderness, evaluate for erythema, warmth or other signs of infection (initially postoperative it would be highly unlikely the patient would have signs of infection)

### i. HOW TO DETERMINE EPIDURAL SENSORY LEVEL

1. use alcohol prep (or ice wrapped in glove) – touch patient on upper chest to establish baseline temperature sensitivity (cold vs wet)
2. touch patient above the knee and compare to baseline (bilateral)
3. work cephalad, testing thighs, hips, abdomen, ascending torso (bilateral)
4. repeatedly confirm each dermatome against baseline “cold vs wet” (“is it more or less here? What about here?” etc...)
5. the point at which the sensation is equivalent, is the patient's sensory level (ie T4 – T10 – change in sensation at the level of the nipples to the belly button bilaterally)
6. may not be symmetric
7. can be confounded if patient has baseline neurologic deficits (ie. Baseline decreased sensation on abdominal wall due to previous surgical incisions)
8. it is a good idea to get a baseline sensory level on all patients postoperatively, however, on daily rounds if the patient has no complaints and no weakness/dense numbness/etc – some advocate there is no need to continue to test the level if the patient has adequate pain relief – some attendings may want daily assessment, so clarify!

## DERMATOMES FOR SENSORY LEVEL TESTING



## Evaluate for Side Effects

- Hypotension - Although this often is not solely attributable to the epidural infusion, it is usually a wise idea to **reduce the rate of the epidural local anesthetic infusion** until the etiology of hypotension can be determined. The patient may require a fluid bolus, but this is best discussed with the primary team prior to bolusing fluids (some surgical specialties, such as Thoracic surgery with large pulmonary resection patients, are extremely conservative with perioperative fluid therapy, and may in fact rather the epidural be discontinued, or manage the patient with pressors prior to bolusing fluids). It is a good idea to carry ephedrine and phenylephrine with you during your time on acute pain to address any immediate blood pressure disturbances directly attributable to sympathectomy with the epidural infusions. At times, the epidural infusion may need to be completely held until the etiology of hypotension is addressed.
- Pruritus – one of the most common side effects associated with epidural opioids is pruritus; we typically give Benadryl PRN pruritus (although limited efficacy), or Nubain (an opioid agonist/antagonist) – the antagonist effect of Nubain is usually enough to reduce the opioid-induced pruritus without inducing withdrawal or reducing analgesia; one should be cautious with Nubain dosing so as not to have too much opioid antagonism (and precipitate withdrawal)
- Nausea – epidural opioids are also associated with the side effect of nausea; zofran is a first-line agent for nausea; phenergan is less ideal secondary to sedating effects, but in some may be more efficacious; one may consider topical Scopolamine patch, but one should be cautious using Scopolamine in the elderly secondary to sedating effects; the basal Dilaudid infusion may need to be reduced if the patient has persistent nausea despite pharmacologic treatment
- Progressive neurologic changes – an epidural is expected to “block” the sensory dermatomes and motor output at least a few levels above and below the insertion site but if there is ever any question or concern about **new onset weakness, too dense a block, too high a block, too low a block, anything that worries the patient, RN, team or you, just stop the bupivacaine infusion and re-evaluate sensation and strength with a neuro exam one hour later**. The block should be receding by then and if it isn't you need to escalate your concerns to the pain fellow and/or pain attending for possible MRI evaluation and rule out of epidural hematoma.

### 3. Initial troubleshooting

- Patient with poor pain control
  - i. Examine the catheter and insertion point
    1. hematoma, erythema, fluid collection?
    2. is the catheter still secured at the reported depth, migration?
  - ii. Evaluate the sensory level – if inadequate for surgical coverage...
    1. bolus the catheter
      - a. it is a wise idea to always carry emergency drugs ephedrine and phenylephrine while on the acute service, in the case of sympathectomy/hypotension with epidural bolusing
      - b. always aspirate the catheter prior to bolusing! Evaluate for CSF or blood on aspiration
      - c. bolus the catheter with 3-5 ml of 1% lidocaine (it is fast-acting and will quickly allow one to assess if the catheter is indeed in the epidural space); for higher thoracic catheters and elderly patients, start with only 3 ml aliquots and monitor blood pressure closely – higher catheters are more prone to sympathectomy
      - d. recheck sensory level every 5 minutes; can bolus up to about 10 ml total (cautious with blood pressure/sympathectomy) – if patient still has no block after 10 ml of 1% lidocaine, the epidural is most likely inadequate for perioperative analgesia, and the decision must then be made for

- replacement vs conversion to PCA
  - e. unilateral block – position the patient lateral decubitus with the deficient side down (if tolerated depending on surgery); then bolus the catheter as above; if still unilateral, consider pulling the catheter back in a sterile manner by 1-2 cm, as it may have migrated unilaterally
  - f. if the block improves s/p bolus, but recedes over time, increase the basal rate of the infusion by 2 ml/hour or consider **PCEA fentanyl + local anesthetic boluses**
  - g. if despite all efforts the block is insufficient for perioperative analgesia, consider replacement of the catheter vs PCA (discuss with attending and patient)
4. Daily rounds on epidural catheters
- Generally, catheters remain for 5 days postoperative (but this is highly variable depending on the surgical service involved; for thoracotomies, it is wise to leave the catheter as long as the patient has a chest tube in place; always keep track of daily temperatures, WBC counts (to monitor for signs of infection))
  - **Visualize and palpate insertion site daily! Look for signs of infection (tenderness to palpation, erythema, drainage)**
  - Daily documentation of side effects and respective treatment
    - i. N/v, itching, constipation, weakness, dense numbness, shortness of breath, somnolence
  - Anticoagulation
    - i. Hold morning dose of Heparin/Lovenox prior to catheter discontinuation
    - ii. INR >1.4 – precludes manipulation of the catheter due to risk of epidural hematoma  
**\*epidural hematoma** is one of the most devastating risks associated with epidural analgesia/anesthesia – bleeding into a confined space leads to progressive, often painless, compression of neural structures and potentially permanent neurologic sequelae! If you are ever concerned, this must be immediately evaluated with MRI, and emergent neurosurgical evaluation for decompression
    - iii. An INR >1.2 should be discussed with fellow/attending
    - iv. Prior to discontinuation of catheter with INR of 1.4 – reconfirm lab value, administration of FFP, neurochecks, postpone catheter discontinuation if INR trending down
5. Spinal anesthesia
- spinals are followed for 24 hours by the acute team
  - neuraxial morphine can have effects up to 24 hours later! Always concern for delayed respiratory depression, especially if patient is receiving concurrent IV opioids
  - this type of respiratory depression is centrally mediated, and associated with older age, obesity, OSA, and concurrent respiratory depressants (ie benzodiazepines)
  - when examining the patient the morning after surgery - document strength, sensory exam, side effects, spinal insertion site for tenderness, erythema, drainage
  - we do not manage these patient's postoperative pain unless specifically requested of the primary team – usually our role is just to monitor for any adverse sequelae associated with the spinal in the first 24 hours, and then sign-off

# **SPECIFICS REGARDING SIGN-OUT, RESPONSIBILITIES, AND ICU PATIENTS**

## **EPIDURAL GUIDELINES - QUICK START GUIDE**

### **OR DIRECT TO ICU - BEFORE 5 PM**

1. Bypass PACU resident.
  2. Always call report to pain fellow (#46836) or on-call pain resident.
  3. Pain Service will place orders and try to be at bedside for evaluation and initiation of epidural.
  4. Pain Service will communicate with ICU team before starting local or opioid.
- (Spectral phone numbers for ICU Services: CVICU #42829, MICU #48820 SICU #53234)

### **OR DIRECT TO ICU - AFTER 5 PM**

1. Bypass PACU resident
  2. Always call report to on-call pain resident.
  3. OR team will evaluate epidural and place orders for Dilaudid/fentanyl, if no local (Use order set # 616: IP PAI EPIDURAL ANALGESIA POSTOP).
  4. OR team will evaluate epidural and place orders for bupivacaine as well if infusion has been initiated in OR and hemodynamics are stable. (Use order set # 616: IP PAI EPIDURAL ANALGESIA POSTOP).
  5. Pain will come to ICU and evaluate epidural and do orders if OR team unable to evaluate patient at hand-off (intubated, unstable then becomes stable later on at night).
  6. Consider holding bupivacaine after 11 PM if patient at risk for hypotension.
  7. Pain Service will communicate with ICU team before starting local or opioid.
- (Spectral phone numbers for ICU Services: CVICU #42829, MICU #48820 SICU #53234)

### **OR TO PACU/FLOOR - BEFORE 5 PM**

1. Call PACU resident for report and orders.
2. PACU resident evaluates epidurals before sending to floor.
3. PACU resident gives report/signoff to Pain Service at 5 PM.

### **OR TO PACU/FLOOR - AFTER 5 PM**

1. Try to call PACU resident before 5 PM for report and orders.
2. If PACU resident gone, OR team will place orders and contact on-call Pain resident for report.
3. OR team evaluates epidural before sending patient to floor.
4. If OR team unable to evaluate epidural, on-call Pain resident will evaluate epidural before starting medications on floor. As OR call resident is in-house overnight, this should be rare.

### **OR TO ASC PACU - AFTER 5 PM**

1. OR team will attempt to write orders and evaluate epidural. Call acute pain service for report.
2. Acute pain service will write orders and evaluate epidural if OR team not available.

### **GENERAL COMMENTS REGARDING EPIDURAL MANAGEMENT IN PACU:**

- Place orders early so medications are available when patient arrives in PACU/ICU.
- Give report to PACU resident (before 5 PM) or Pain Service (after 5 PM) so patient is not lost to rounding. COMMUNICATE IMPORTANT INFORMATION.
- Although we work closely with PACU residents during the day, patients in the PACU remain under the care and supervision of the primary OR attending. The Pain Service does not assume care

until the patient arrives to the ICU or floor.

- We do not evaluate, write orders, or take calls on non-Stanford epidurals (ie. PAMF), unless specifically consulted.
- **Communicate directly with on-call surgery team** if there is problem, such as hypotension when local anesthetic already turned off. Provide direct physician-to-physician communication, especially when problems or unanticipated events occur.

LINK TO ON-CALL ACUTE PAIN TEAM:

[HTTP://ETHER.STANFORD.EDU/SECURE/CALL\\_SCHEDULE.HTML](HTTP://ETHER.STANFORD.EDU/SECURE/CALL_SCHEDULE.HTML)

PACU MAIN DESK: 3.6661

## EPIDURAL GUIDELINES - DETAILS

### ICU

The OR team will always call the pain team (#46836 day, acute resident on call pager at night) directly to give report on the patient. If the patient is expected to be extubated and tolerating epidural local anesthetic and opioids, this should occur in a timely fashion so that orders can be completed and medications available on arrival to ICU. The pain resident should attempt to be at bedside when patient comes to the ICU, and finalize the orders based on patient physiology and analgesic requirements. This includes evaluating if the epidural is functioning and replacing as necessary. Initiation of epidurals by pain resident should always include a conversation with the ICU on-call team, even at night (CVICU

#42829, MICU #48820, SICU #53234) to discuss sympathectomy and opioid effects.

--- If it is late at night, and the patient will be on Dilaudid and fentanyl only, a phone report to the on-call acute pain resident is sufficient. OR team evaluates epidural and completes orders.

--- If it is late at night, and the patient has already been on local infusion in the OR and is stable to continue, a phone report to the on-call acute pain resident is sufficient. OR team evaluates epidural and completes orders.

--- If it is late at night and the patient will require local anesthetic, but epidural can't be tested and initiated by OR team immediately, on-call acute pain resident comes to ICU to evaluate and initiate epidural when appropriate.

After 11 PM, epidural local anesthetic will on most occasions be held until AM.

Management of any physiological instability should be coordinated with the CVICU/MICU/SICU resident covering that patient, and acute pain resident is expected to come in and evaluate patient when necessary. Communication is key.

### PACU/FLOOR

Before 5 PM, the OR team calls PACU resident for report and orders. This includes cases getting out after 5 PM with known catheters. PACU resident completes basic, safe orders to ensure epidural medications are available in PACU when patient arrives.

The PACU resident evaluates all epidurals and catheters before releasing them to the floor. Any questions regarding appropriate dosing are communicated to acute pain team. Any non-working catheter gets replaced by:

1. OR team if available and wish to do it
2. PACU resident with pain fellow/attending supervision

### 3. Acute pain team.

After 5 PM, if communication occurred with PACU resident, catheter should be evaluated by OR team and orders reviewed to ensure they are compatible with patient physiology. Any concerns should be communicated to acute pain resident on-call.

PACU resident is expected to report all patients and patient concerns to the acute pain resident on call prior to leaving hospital.

After 5 PM, if PACU resident has not been involved in case, the OR team will place orders in a timely fashion to ensure epidural medications are available in PACU when patient arrives. OR team will evaluate epidural catheter and confirm orders are physiologically appropriate. OR team is expected to call the acute pain resident for giving report on patient, as this patient would otherwise be missed for

rounds the next day. Epidural placement has to be communicated to PACU resident or acute pain resident to make the rounding list.

If OR team is unable to evaluate and initiate catheter, the acute pain resident is expected to come in and do this prior to patient going to the floor.

This should prevent any epidurals from being unknown by the acute pain resident on call. This ensures only anesthesiologists initiate, evaluate, and write orders, and can be maintained regardless of what service is covering the patient.

#### NON-STANFORD ANESTHESIOLOGY EPIDURALS (PAMF ETC...)

We do not manage these catheters. We do not evaluate the patient, take overnight calls, or place orders. The exception is the very rare case in which the primary team surgeon formally consults the pain fellow. However, you are an anesthesiologist and physician first. If there are acute patient safety issues, act appropriately.

If there is conflict at night with surgeons or nurses on patients with epidural catheters, **communicate directly with the on call surgeon**. Don't play phone tag with the RN in the middle. For example, if a patient is hypotensive and the local anesthetic is already turned off, explain to the surgeon that the epidural is no longer the source of hypotension. Often the primary team thinks the acute team was unresponsive overnight to hypotensive patients because they see the epidural still hooked up when they round in the morning, when, in fact, the local was turned off immediately and only Dilaudid and fentanyl PCEA remains.

Although we are happy to assist with management of patients in the PACU on request, our service is not conjoined with the PACU. PACU is a separate rotation and a separate service. We generally assume care once the patient arrives in the ICU or on the floor.

# **REGIONAL ANESTHESIA AND PERIPHERAL NERVE CATHETERS**

*Ryan Derby, MD*

## **GENERAL OVERVIEW**

Regional anesthesia and nerve blocks are utilized for pain management and are an important part of opioid sparing multimodal analgesic strategies. Peripheral nerve catheters (PNC) are a way of providing continuous regional anesthesia that lasts as long as the PNC is in place and are used when it is anticipated that a patient will have moderate to severe pain beyond the duration of a single injection of local anesthetic.

Peripheral nerve catheters are a key part of several surgical clinical pathways including total knee arthroplasty (TKA), total shoulder arthroplasty (TSA), TRAM flap for breast reconstruction, as well as many ERAS protocols. They are routinely placed for other surgeries including orthopedic, plastic, oncologic, trauma, thoracic, cardiac, and breast surgeries. On occasion, perineural catheters are placed for non-operative indications such as limb ischemia, chronic pain syndromes such as CRPS, or in anticipation for surgery such as for hip fractures.

A continuous nerve block consists of:

1. A pump
2. A catheter
3. Infusion of local anesthetic

While on the APS you will be asked to manage and troubleshoot PNCs, however you may also be asked to evaluate a patient who has had a “single shot” injection with persistent pain or concerns for complication. You may also be asked to evaluate a patient for appropriateness of having a nerve block performed. This overview will cover the basics of PNCs.

## **COMMON LOCATIONS OF CATHETERS**

- The most commonly placed catheters used at Stanford include:
  - Adductor canal catheters (ACC) placed mid-thigh for TKA and surgeries involving the medial aspect of the leg below the knee;
  - Femoral nerve catheters for hip fractures;
  - Sciatic nerve catheters (popliteal fossa or more proximal at gluteal/sub-gluteal areas) for surgery below the knee;
  - Brachial plexus catheters (supraclavicular, interscalene, infraclavicular) for surgery involving the upper extremity including TSA;
  - Paravertebral catheters (unilateral or bilateral) for cardiac and thoracic surgeries including VATS;
  - Transverse Abdominus Plane (TAP) catheters placed for abdominal procedures such as hernia repairs, laparoscopies, TAH/BSO, and TRAM flaps. These are often utilized when an epidural is not indicated or cannot be placed;
  - Erector Spinae Plane (ESP) catheters placed for chest wall surgeries and rib fractures

when an epidural cannot be placed.

## METHOD OF PLACEMENT

Peripheral nerve catheters are typically placed using ultrasound guidance with or without nerve stimulation. Correct catheter placement is often confirmed at the time of placement and checked prior to surgery. However, catheters can become dislodged or migrate through normal patient movement or when transferring to and from the operating table.

As a general framework, perineural catheters either target specific nerves (interscalene, ACC, sciatic, etc.) or larger compartments (i.e. TAP, ESP, PVB) in which the nerves of interest are found. This is important because catheters placed in compartments often need larger volumes of infusate whereas catheters targeting specific nerves are placed very close to the nerve and require much less volume and precise placement to be effective.

The catheters are secured with an occlusive dressing and a STATLock device to prevent dislodgement. The “white butterfly” securing device is not always placed at the site of insertion and instead is intended to be out of the surgical field. Dermabond is frequently used at the insertion site to secure the catheter in place and help prevent dislodgement. An antimicrobial Biopatch is typically placed over the insertion site as well.

## ORDERS

The orders for the catheter are placed by the PACU resident. Any issues pertaining to the catheter will be relayed by the Regional Team to the PACU resident or directly to the pain team. It is important to communicate with the Regional Team and the PACU resident with any questions regarding orders so that patients receive the intended infusion in a timely manner.

While there are several parameters that can be altered using the Nimbus pumps, the essential elements of an order for a PNC include:

1. Local anesthetic type and concentration;
2. Basal continuous rate;
3. Demand dose;
4. Demand lock out time (LO);
5. Automatic bolus volume
6. Automatic bolus time interval (LO).

Examples of standard settings for most common catheters include\*:

Block	Local**	Basal Rate***	Demand Bolus/LO	Auto-bolus/LO
Adductor, interscalene, popliteal, infraclav	Ropivacaine 0.2%	5 ml/hr	5ml q30 min	n/a
TAP/QL	Ropivacaine 0.2%	0 ml/hr	10 ml q60 min	5 ml q30 min
PVB/ESP	Ropivacaine 0.2%	0 ml/hr	10 ml q60 min	5 ml q30 min

\*These programs are susceptible to change. When in doubt, please check with the individual or team that placed the catheter.

\*\*Ropivacaine can be substituted with bupivacaine. Both are long acting local anesthetics with a better differential blockade than lidocaine.

\*\*\*You will also be asked to manage catheters that are part of study protocols which may be managed by either the regional team, APS, or the surgical team. Please ensure that you are aware of the study protocol before making any changes to these catheters.

## TROUBLESHOOTING CATHETERS

There are several possible reasons why a patient may experience pain in the setting of a PNC and it is important to consider the patient as a whole when you are asked to evaluate a catheter. While this is not an exhaustive list, things to consider when examining a patient include:

1. Dislodged catheter (also called “migration”);
2. Well-functioning catheter but pain is in nerve distribution not covered by block;
3. Pump malfunction or incorrect programming;
4. Catheter obstruction (ie closed clamp);
5. Infusate problem;
6. Block complication such as expanding hematoma or nerve injury resulting in pain;
7. Surgical explanations such as overly tight dressing, compartment syndrome, etc.

If a patient has pain and you are called to assess them, you should:

1. EXAMINE THE PATIENT;
2. Obtain thorough history of when pain started, quality, timing, exacerbating and alleviating factors;
3. Identify the exact area of the patient’s pain using ice to test for sensation loss if needed;
4. Review the surgical note to determine exactly what was done to the patient;
5. Review the patient’s past medical history to determine chronic pain or opioid use;
6. Review the PNC procedure note to determine which block was performed, whether there were any difficulties or complications, and what local anesthetics were initially injected;
7. Inspect the PNC insertion site and dressing to look for dislodgement;
8. Inspect the PNC tubing to ensure there are no obstructions or closed clamps;
9. Inspect the pump to ensure that it is running and using the appropriate pump settings;
10. Review other pain medications that patient has available to them as well as whether they have been using the PNC demand button.

It is important to first make sure that the catheter is really not working before pulling it. If there is any uncertainty that it is working then ensure patient has other pain medications immediately available to them. At this point, options for management include:

1. Replace catheter;
2. Discontinue catheter – best if you are certain catheter is dislodged;
3. Increase settings (ie demand bolus, basal rate, etc.)
4. Bolus catheter with stronger local anesthetic to see if you can achieve coverage;

5. Interrogate catheter with ultrasound to determine if PNC is still in proper place;
6. Change infusate to lidocaine in order to achieve an analgesic plasma level.

It is best to involve your attending, fellow, and Regional Team in any decisions you make.

Important note, while bolusing a catheter with a stronger local anesthetic is an easy way to demonstrate that a PNC is working, it should be done with caution as it may complicate any replacement by exposing the patient to toxic doses of local anesthetic or partially anesthetizing the nerves. This might mask a paresthesia and thereby increase risk of nerve injury if a procedure is performed around these nerves.

## REPLACEMENT OF CATHETERS

If you decide that replacement of the catheter is warranted, contact the Regional Team immediately as they can help assist with or perform the block.

Next, consent patient for replacement of the block using the APS or Regional attending's name as the performing physician.

Replacement of PNC's can occur either on the floor or in the pre-op block bay depending on space and logistics. When the patient is in the appropriate location, place ASA monitors, oxygen and acquire sedation if needed.

There are two ultrasound machines (ASC and Main OR) which can be brought to the floor. Alternatively, the patient can be brought to the PACU for the block replacement. Please check with the Regional Team prior to using any ultrasound machines.

After a block is placed, the patient will need to be monitored for at least 30 minutes by you or a nurse for local anesthetic systemic toxicity (LAST) and complications from sedation or the block.

## LOCAL ANESTHETICS: BRIEF OVERVIEW

The main mechanism of action of local anesthetics (LAs) is by blocking intracellular sodium channels. Binding at this site ultimately blocks sodium movement through the channel thus preventing membrane depolarization and blocking the nerve action potential. Nociceptive nerves fibers (A delta - fast sharp pain, C – slow throbbing pain) are more susceptible to LA blockade than larger motor nerve fibers (A alpha). In general, pain and autonomic nerves are blocked before those for temperature and light touch, followed by proprioception, deep pressure and lastly motor function.

### *Physicochemical Properties:*

All LAs have similar structural components - a lipophilic and hydrophilic end connected by an amide or ester linkage, which determines their site of metabolism (liver and plasma respectively). Local anesthetics are weak bases with pKa between 7.5 and 9. Thus, at a normal physiologic pH of 7.4, the protonated or ionized form of LAs is favored in extravascular environments.

*Speed of Onset:* To reach its intracellular site of action, the neutral form of the molecule must traverse the cell membrane whereupon the ionized form then binds the sodium channel. In general, the lower the pKa of a LA (closer to physiologic pH), the more the balance is shifted to the neutral form and the faster the onset.

*Potency:* Local anesthetic potency is related to hydrophobicity. Local anesthetics that are more hydrophobic penetrate the lipid cell membrane and reach the intracellular site of action more easily.

*Duration of effect:* Duration of a local anesthetic is multifactorial but is related to protein binding. Local anesthetics bind readily to albumin and alpha-1 glycoprotein. Highly bound drugs will stay bound to the site of action and have a longer duration.

Block outcomes and characteristics are highly dependent on which LA is chosen, the volume and concentration used. The concentration of a LA also has significant effect on block outcomes. As LAs must pass through multiple fascial and fibrous layers of the epi-, peri-, and endoneurium as well as the cell membrane itself, a diffusion gradient is necessary for block onset. Increasing drug concentration thus can hasten onset. Increasing concentration will also allow for a greater effect on the larger myelinated motor fibers allowing for motor blockade in addition to a dense sensory block. Increased concentration similarly increases block duration as it will take a longer time for local blood flow to clear more LA. It is imperative however to consider the maximum allowable dose as one increases drug concentration, especially for high volume blocks or when performing multiple blocks in smaller patients as toxic plasma levels can quickly be reached.

Local Anesthetic	pKa	Maximum Dose plain/epi (mg/kg)	Onset (min)	Duration (hr)	Concentrations (%)
Lidocaine	7.7	4.5/7	5-10	0.5-1.5	1-2
Mepivacaine	7.6	5/7	5-10	1-2	1.5
Bupivacaine	8.1	2.5/7	10-30	4-10+	0.125, 0.25, 0.5
Ropivacaine	8.2	3/4	10-30	4-8	0.2, 0.5
Chloroprocaine	8.7	10/15	1-2	0.5-1.5	3

## LOCAL ANESTHETIC SYSTEMIC TOXICITY

Local anesthetics have systemic effects which can be toxic and even lethal when plasma concentrations exceed the therapeutic range. Although doses causing local anesthetic systemic toxicity (LAST) have been described, it is important to note that similar toxic effects can be caused by a small dose injected directly intravascularly. Thus, one should always strive to use the minimum amount of LA necessary to achieve a successful block in order to minimize the risk of LAST.

### *Signs and Symptoms:*

At toxic doses LAs have an excitatory effect in the central nervous system (CNS) by blocking inhibitory pathways manifests as clonus, visual disturbances, tinnitus, perioral numbness or paresthesia, generalized anxiety, agitation or disinhibition. Patients often express feelings of impending doom. Untreated, these symptoms can progress to seizure, respiratory arrest and death. Cardiovascular (CV) symptoms generally follow CNS symptoms as the cardiovascular system is more resistant to the effects of LAs. Symptoms include cardiac arrhythmias (brady and tachy-arrhythmias), hypotension and cardiovascular arrest.

### *LA Absorption:*

Toxicity is related to systemic absorption and ultimately, plasma concentration of LA. Absorption is related to the site of injection with the greatest plasma concentrations achieved by direct intravascular injection. Absorption by site of injection from greatest to least is as follows:

intercostal > caudal > epidural > brachial plexus > femoral/sciatic > subcutaneous > intraarticular > spinal.

Treatment of LAST (per ASRA guidelines):

AMERICAN SOCIETY OF REGIONAL ANESTHESIA AND PAIN MEDICINE

## CHECKLIST FOR TREATMENT OF LOCAL ANESTHETIC SYSTEMIC TOXICITY (LAST)

**The Pharmacologic Treatment of LAST is Different from Other Cardiac Arrest Scenarios**

- ❖ **Reduce** individual **epinephrine** boluses to  $\leq 1$  mcg/kg
- ❖ **Avoid** vasopressin, calcium channel blockers, beta blockers, or other local anesthetics
- Stop injecting local anesthetic
- Get help
  - Consider lipid emulsion therapy at the first sign of a serious LAST event
  - Call for the LAST Rescue Kit
  - Alert the nearest cardiopulmonary bypass team - resuscitation may be prolonged
- Airway management
  - Ventilate with 100% oxygen / avoid hyperventilation / advanced airway device if necessary
- Control seizures
  - Benzodiazepines preferred
  - **Avoid** large doses of **propofol**, especially in hemodynamically unstable patients
- Treat hypotension and bradycardia – **If pulseless, start CPR**

Lipid Emulsion 20%	
(Precise volume and flow rate are not crucial)	
Greater than 70 kg patient	Less than 70 kg patient
<b>Bolus 100 mL Lipid Emulsion 20%</b> rapidly over 2-3 minutes	<b>Bolus 1.5 mL/kg Lipid Emulsion 20%</b> rapidly over 2-3 minutes
• Lipid emulsion infusion 200-250 mL over 15-20 minutes	• Lipid emulsion infusion ~0.25 mL/kg/min (ideal body weight)
<b>If patient remains unstable:</b>	
• Re-bolus once or twice at the same dose and double infusion rate; be aware of dosing limit (12mL/kg)	
• Total volume of lipid emulsion can approach 1 L in a prolonged resuscitation (e.g., > 30 minutes)	

- Continue monitoring
  - At least 4-6 hours after a cardiovascular event
  - Or, at least 2 hours after a limited CNS event
- Do not exceed 12 mL/kg lipid emulsion (particularly important in the small adult or child)
  - Much smaller doses are typically needed for LAST treatment
- See reverse side of this checklist for further details



## OTHER BLOCK CONCERNS

### *Paravertebral Catheters (PVBs):*

The catheter can be placed unilaterally or bilaterally. If unilateral then less likely to have hypotension. Concerns regarding infection, bleeding, pneumothorax need to be considered. More commonly being done for VATS, Breast Mastectomies, and occasionally thoracotomies.

### *Hip Fracture Protocol:*

Stanford's hip fracture protocol was put in place to reduce the significant morbidity and mortality of patients who arrive in the ED with a hip fracture who are usually elderly and with other comorbidities. The protocol activates several services including orthopedic surgery, internal medicine, radiology, and anesthesiology in an attempt to expedite the safe transition of the patient to the operating room. The Acute Pain Service is not a formal component of the care of these patients until the catheter has been placed by the Regional Anesthesia service. However, the acute pain resident is often the first point of contact when the ED activates the hip fracture protocol and is also responsible for placing the nerve block after hours.

Upon diagnosis of a hip fracture, ortho/ED calls the BLOCK pager. During the day, the Regional Anesthesia team will place the block. The responsibility switches to the night APS resident after hand-off in the evening. It is expected that the APS night float resident will coordinate performing the block with the on-call Regional Anesthesia attending.

### *Patients Discharged Home with PNC:*

1. Review discharge instructions pamphlet (Continuous Nerve Block Catheter Instructions) and zip inside pump bag. These are available in PACU to right of PACU resident in the drawer.
2. CALL REGIONAL RESIDENT TO LET THEM KNOW PT IS BEING DISCHARGED WITH A PUMP. A regional resident will call them at home to follow up.
3. Depending on the desired length of time you wish the patient to have the PNC, you may need to refill the infusate.
4. Note: Patient must be reliable and be able to communicate over the phone with the Regional resident. If any questions with language barrier, talk to the regional team before sending pt home with PNC. The pt cannot have infection, catheter site must be inspected (site not red, catheter secure), pt must be willing to remove own catheter

### *Common Phone Calls from Outpatients:*

"My blocked extremity feels numb?"

- This is usually a result of the block and often occurs when patients' expectations are different than reality.
- If this persists after pulling the catheter, usually we watch and wait for a day or two to gauge progression. If it is resolving, it most likely will continue to get better. If it is worsening, the regional service would like to know for any possible interventions.

"How long can I keep my catheter in?"

- The catheter should only be kept in for 2-3 days. There could be exceptions to this. The local anesthetic will usually run-out during this time frame however. The risk of keeping the catheter in longer may result in increased risk of infection.

“How do I pull my catheter out?”

- The catheter comes out very easily. You can make the analogy to pulling off a Band-Aid. Remove the adhesive tape and apply slow gentle traction to the catheter until it is removed.
- If the catheter feels stuck, the patient may need to pull harder. Do not cut the catheter. If still having trouble, then present to OSC during normal business hours for assistance.
- It may be helpful for the subset of patients with a bolus mechanism in place to press the button 1-2x before catheter removal.

“How do I cover pain after catheter is removed?”

- Recommend coverage with prn medications first. If pain remains uncontrolled, escalate to a multimodal regimen. Hold off on NSAIDs unless already prescribed by surgeon (usually Celebrex) or ok'd by surgical team. Caution dosage amounts and duration of therapy with NSAID's, Tylenol, and opioids based on patient history.

“I feel <any of the following symptoms: hearing is changing, perioral numbness, metallic taste, agitated, palpitations, seizure>”

- These may be early signs of local anesthetic systemic toxicity. Discontinue the pump. If symptoms severe, consider presentation to emergency department.

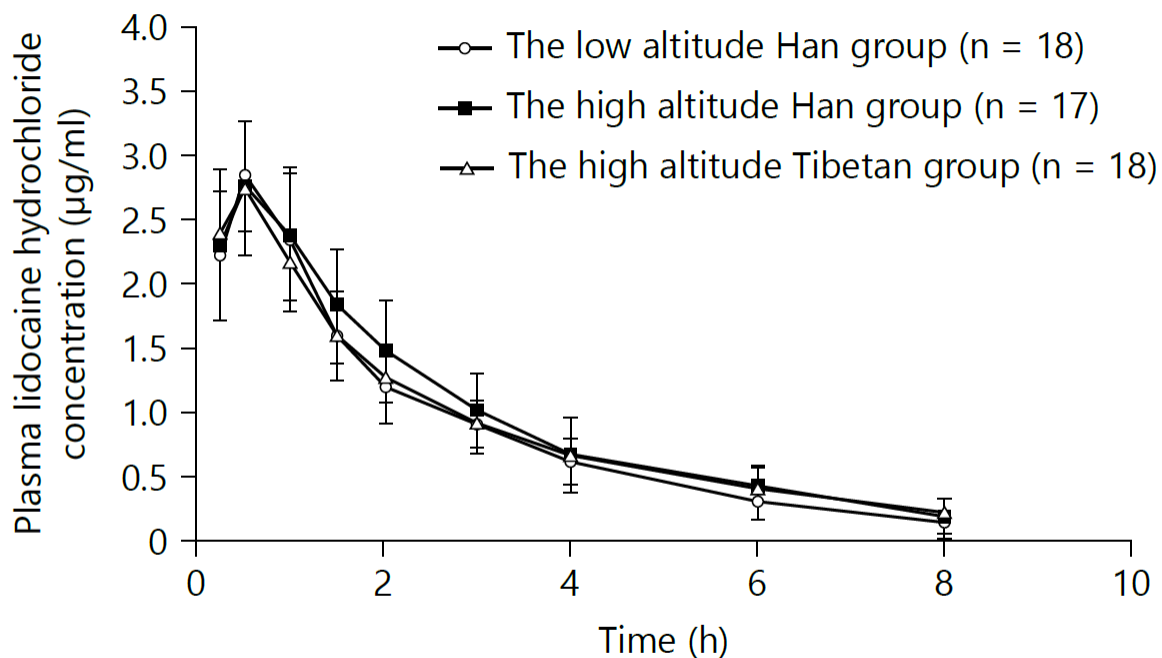
## **ADJUVANTS**

*Einar Ottestad, MD and Pamela Flood, MD MA*

### **IV LIDOCAINE**

- Amide-type local anesthetic and Antiarrhythmic Agent, Class Ib
- Mechanism of Action: Blocks both the initiation and conduction of nerve impulses by decreasing the neuronal membrane's permeability to sodium ions
- Adverse reaction:
  - Cardiovascular: Arrhythmia, bradycardia, arterial spasms, cardiovascular collapse, heart block, hypotension, sinus node suppression,
  - Central nervous system: Agitation, disorientation, dizziness, drowsiness, euphoria, hallucinations, lethargy, seizure, slurred speech, somnolence
  - Otic: Tinnitus
  - Gastrointestinal: Metallic taste, nausea, vomiting, perioral numbness
  - Respiratory: respiratory depression or arrest
- Pharmacodynamics/kinetics:
  - Single bolus dose:
  - Onset of action: 45-90 seconds
  - Duration: 10-20 minutes

- Metabolism: 90% hepatic; active metabolites monoethylglycinexylidide (MEGX) and glycinexylidide (GX) can accumulate and may cause CNS toxicity
- Half-life elimination: Biphasic: Prolonged with congestive heart failure, liver disease, shock, severe renal disease; Initial: 7-30 minutes;
- Terminal: 1.5-2 hours
- 50% decrement in about 2 hours
- Excretion: Urine (<10% as unchanged drug, ~90% as metabolites)
- Dosing:
  - IV bolus: 0.75-1 mg/kg over 5-10 minutes. Patient likely to have tinnitus/perioral numbness/sedation which quickly resolves
  - IV infusion: Start 1 mg/kg/hr ~70 mg/hr. Titrate up or down 10-15% depending on plasma level
- Monitoring: Check plasma lidocaine levels q8 hours
  - Therapeutic: 2.5-5.0 mcg/mL (SI: 6-21  $\mu\text{mol/L}$ )
  - Potentially toxic: >6 mcg/mL (SI: >26  $\mu\text{mol/L}$ )
  - Toxic: >9 mcg/mL (SI: >38  $\mu\text{mol/L}$ )

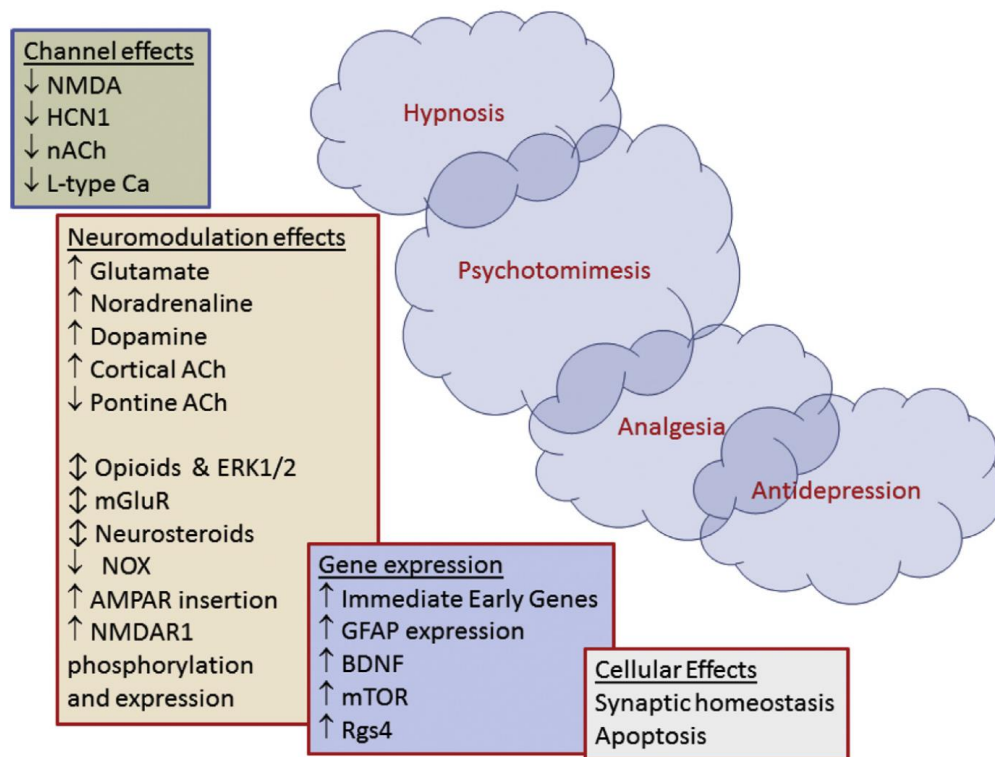


Pharmacology 2016;97:107–113

## KETAMINE

- Dissociative anesthetic
- Mechanism of Action:
  - Hypnosis: Produces a cataleptic-like state in which the patient is dissociated from the surrounding environment by direct action on the cortex and limbic system. Hypnotic effect due to blockade of NMDA and HCN1 receptors.
  - Analgesic effect multifactorial (and controversial) involving cholinergic, aminergic and direct effect on delta opioid receptor that augments mu-opioid function. Reduces opioid tolerance.
  - Autonomic: Endogenous catecholamine release (epinephrine, norepinephrine) maintain blood pressure and heart rate. Reduces polysynaptic spinal reflexes.
  - Antidepressant anti OCD activity: long lasting effect after hours of low dose treatment (0.5 -1 mg/kg/hr) that lasts weeks. Associated with synaptic remodeling and dendritic sprouting.

*J. Sleigh et al. / Trends in Anaesthesia and Critical Care 4 (2014) 76–81*



- Adverse reaction:
  - Cardiovascular: Arrhythmia, bradycardia, hyper-/hypotension, pulse rate increased
  - Ocular: Diplopia, intraocular pressure increased, nystagmus
  - Central nervous system: CSF pressure increased, confusion, delirium, dreamlike state, excitement, hallucinations, irrational behavior, vivid imagery
  - Neuromuscular & skeletal: Skeletal muscle tone enhanced (tonic-clonic movements)
  - Increased neuronal apoptosis and behavioral deficits in young animal models (including primates) with anesthetic dosing more than 3 hours.
- Pharmacodynamics/kinetics:

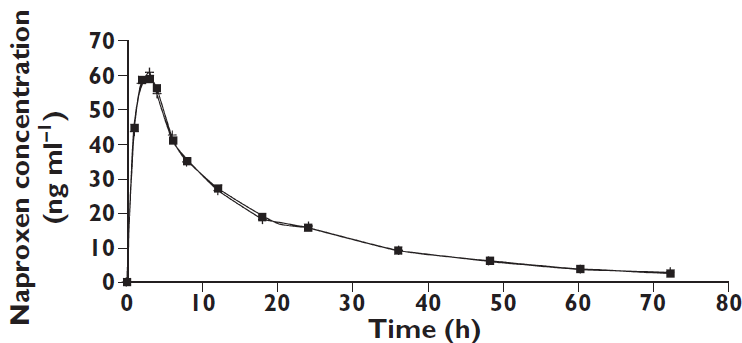
- Onset of action: IV: 30 seconds
- Oral: 10-30 minutes
- Duration: IV 5-10 minutes
- Oral: 40-50 minutes
- Metabolism: Hepatic via hydroxylation and N-demethylation; the metabolite norketamine is 33% as potent as parent compound
- Half-life elimination: Alpha: 10-15 minutes; Beta: 2.5 hours
- Excretion: Primarily urine
- Bioavailability oral: 20-25 %
- Analgesic concentration 200 ng/ml
- Dosing:
  - Oral: 20-30 mg q1-2 hours then titrate to efficacy or adverse reaction
  - IV: 10-20 mg/hr titrated to efficacy and side effects

## NSAIDS

- Anti-inflammatory, antipyretic, analgesic
- Mechanism of Action: Reversibly inhibits cyclooxygenase-1 and 2 (COX-1 and 2) enzymes, which result in decreased formation of prostaglandin precursors
- Adverse reaction:
  - Cardiovascular: Edema (1% to 3%), MI
  - Renal: Urea increased (7%), renal impairment (6%), creatinine increased (3%), urine output decreased (3%)
  - Gastrointestinal: Gastric ulcer, GI bleed, nausea, liver failure 3/1million patients
  - Hematologic: Inhibition of platelet aggregation
- Pharmacodynamics/kinetics:
- COX Non-selective Safety:
  - no difference between celecoxib, ibuprofen and naproxen in risk of MI or stroke, GI and renal events were lower with celecoxib. (Precision Trial: N engl j med 375;26 nejm.org December 29, 2016)
- Ibuprofen
  - Onset of action: Analgesic: 30-60 minutes; Anti-inflammatory: ≤7 days
  - Duration: 4-6 hours
  - Metabolism: Hepatic via oxidation
  - Half-life elimination: 2-4 hours
  - Excretion: Urine (80% as metabolites; 1% as unchanged drug); some feces
- Naproxen:
  - Onset of action: Analgesic: PO.: 1 hour
  - Duration: Analgesic: 50% decrement 10 hours, can be dosed bid
  - Metabolism: Hepatic
  - Half-life elimination: 12-17 hours; prolonged 30% to 50% in elderly; up to 19 hours in renal impairment

Br J Clin Pharmacol / <b>78</b> :4 / 877–885 / 877
--

- Excretion: Renal 66-92% conjugated, 3% feces



- Ketorolac:
  - Onset of action: Analgesic: I.M.: ~10 minutes
  - Duration: Analgesic: 6-8 hours
  - Metabolism: Hepatic
  - Half-life elimination: 2-6 hours; prolonged 30% to 50% in elderly; up to 19 hours in renal impairment
  - Excretion: Urine (92%, ~60% as unchanged drug); feces 1%
- Celecoxib COX2 selective
  - Onset of action: Analgesic: I.M.: ~10 minutes
  - Duration: Analgesic: 6-8 hours
  - Metabolism: Hepatic, 2x increase in Cmax in elderly; no dosing change renal impairment
  - Half-life elimination: 8-12 hours;
  - Excretion: Urine (92%, ~60% as unchanged drug); feces ~6%
- Dosing:
  - Ibuprofen 400-800 mg PO TID
  - Naproxen 500 mg bid
  - Ketorolac 15 mg IV q6 hours; max 5 days
  - Celecoxib 200-400 mg q 6 hrs

## ANTICONVULSANT ADJUVANTS (MEMBRANE STABILIZERS)

*Stephen Coleman, MD and Pamela Flood, MD MA*

There is good evidence that certain anticonvulsants exhibit analgesic action in neuropathic pain as a result of reduced neuronal excitability. Individual mechanisms differ, gabapentin modulates neuronal calcium channels, and carbamazepine, oxcarbazepine and lamotrigine act to block sodium channels, and topiramate blocks both.

*See for meta-analysis on pregnancy and breastfeeding: Veroniki et al. Comparative safety of antiepileptic drugs for neurological development in children exposed during pregnancy and breast feeding: a systematic review and network meta-analysis. BMJ Open. 2017 Jul 20;7(7):e017248*

*See Breastfeeding Handbook for Physicians, 2nd Edition: Edited by Richard J. Schanler, Nancy F. Krebs, and Sharon B. Mass. Chapter 12*

Drugs for migraine prophylaxis that are the best choices during breastfeeding are amitriptyline, gabapentin,

metoprolol, nortriptyline, propranolol, sertraline, and valproic acid. Initial Therapy for Acute Migraine Headache The initial therapy for acute migraine headache may range from nonpharmacologic measures, such as rest, darkened room, and a wet cloth to the forehead, to some of the newest drugs. The use of acetaminophen and nonsteroidal anti-inflammatory drugs is acceptable during lactation because most are weak acids and highly protein bound, although short-acting drugs (eg, ibuprofen) are preferred while nursing a newborn. Products that contain a combination of acetaminophen with caffeine are considered safe during lactation

- **Analgesic Adjuvants**

## GABAPENTIN

- Mechanism of Action: Binds with high affinity to  $\alpha 2\delta$  subunit of  $Ca^{+}$  channel. Not GABA receptor, "Membrane stabilizer"
  - Adverse reaction:
    - sedation,
    - rare peripheral edema
    - weight gain with long term dosing
  - Pharmacodynamics/kinetics:
    - Bioavailability 30 to 60 % dose dependent, 60% for dosage of 900 mg/day, 33% for dosage of 3600 mg/day. Not metabolized, majority excreted in urine. Absorbed in duodenum with saturable absorption not more than 1200 mg can be absorbed at once.
    - Clinical Efficacy: HIV-associated neuropathy, Postherpetic Neuralgia, Pain associated with Gullain- Barre Syndrome, Cancer related neuropathic pain, Diabetic neuropathy, CRPS, fibromyalgia, perioperative pain, reduction of opioid utilization
  - Breast feeding: Infant concentration 6-12% of maternal, no adverse effects observed
  - Pregnancy: see figure below
- See: Nir R-R, Nahman-Averbuch H, Moont R, et al. Preoperative preemptive drug administration for acute postoperative pain: a systematic review and meta-analysis. Eur J Pain 2016;20:1025–43.  
Reimers A. New antiepileptic drugs and women. Seizure. 2014 Sep;23(8):585-91.

## PREGABALIN

Pharmacology: High bioavailability, predictable pharmacokinetics (unlike gabapentin), not metabolized and is excreted in the urine.

Clinical Efficacy: Diabetic neuropathy, post-herpetic neuralgia, fibromyalgia, central neuropathic pain, general anxiety.

See: Eipe N, Penning J, Yazdi F, Mallick R, Turner L, Ahmadzai N, Ansari MT. Perioperative use of pregabalin for acute pain-a systematic review and meta-analysis. Pain. 2015 Jul;156(7):1284-300.

Safety: Dizziness, sedation, otherwise well tolerated.

Membrane Stabilizer	Mechanism	Side Effects
---------------------	-----------	--------------

Carbamazepine (Tegretol)	Na channel blockage	Sedation, dizziness, gait abnormalities, hematologic changes, weight gain, rash
Oxycarbazepine Trileptal	Na channel blockage	Hyponatremia, somnolence, dizziness
Topiramate	Na channel blockage, potentiate GABA	Sedation, kidney stones, glaucoma,
Gabapentin (Neurontin)	Block L-type voltage-dependent Ca channel	Dizziness, sedation, weight gain
Lamotrigine (Lamictal)	Stabilize slow Na channel: suppress release of glutamate from presynaptic neurons	Rash, dizziness, somnolence, Stevens-Johnson syndrome
Pregabalin (Lyrica)	Binding to the alpha-2 delta subunit of voltage-gated Ca channels.	Dizziness, sedation

## LAMOTRIGINE

Pharmacology: Bioavailability 98%, renal clearance.

Clinical Efficacy: Pain in incomplete spinal cord injury, central post-stroke pain, HIV-associated neuropathy, diabetic neuropathy

Safety: Rash, Stevens-Johnson syndrome occurs more frequently with rapid titration. Recommend slow titration 4 to 6 weeks. Discontinue at first sign of rash.

## CARBAMAZEPINE

Pharmacology: bioavailability 70-80%; 98% liver metabolism CYP3A4, causes autoinduction of metabolism, has active metabolite.

Clinical Efficacy: Trigeminal Neuralgia effective compared to placebo in multiple studies with up to 77 patients treated with drug. Many of the studies were performed in the 1960's and 1970's. Diabetic Neuropathy-effective compared to placebo in older studies however there are fewer and smaller studies than for trigeminal neuralgia.

Safety: Rare agranulocytosis, aplastic anemia, impairment of liver function and hyponatremia, and rash in up to 10% of patients,

Recommend: Check drug blood levels and CBC every 2 to 4 months

## OXYCARBAZEPINE

Pharmacology: Bioavailability 95%, liver metabolism, has active metabolite

Clinical Efficacy: Trigeminal Neuralgia, Diabetic Neuropathy. Efficacy seems similar to Carbamazepine with fewer side effects.

Safety: Compared to Carbamazepine less likely to cause CNS and hematologic side effects. Hyponatremia may occur, typically in first 3 months of treatment, rash 3% of patients.

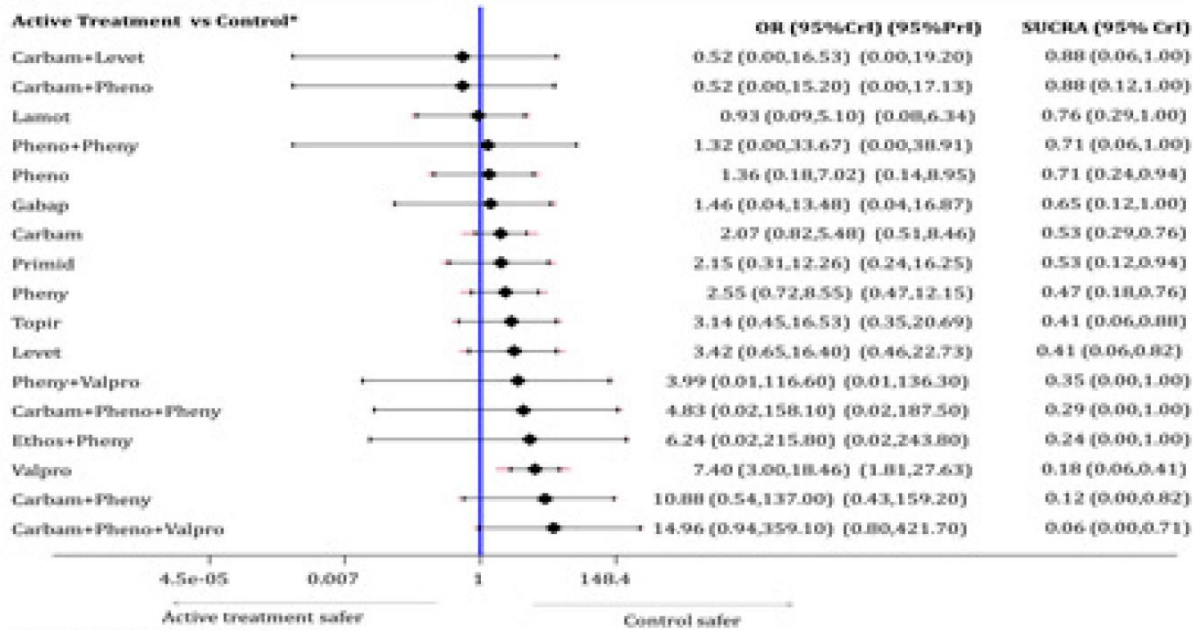
Recommendation: Monitor Sodium levels during initiation of medication

Use During Pregnancy: Avoid oxcarbazepine (OR 13.51, CrI 1.28 to 221.40) risk of autism and psychomotor delay when added to valproate

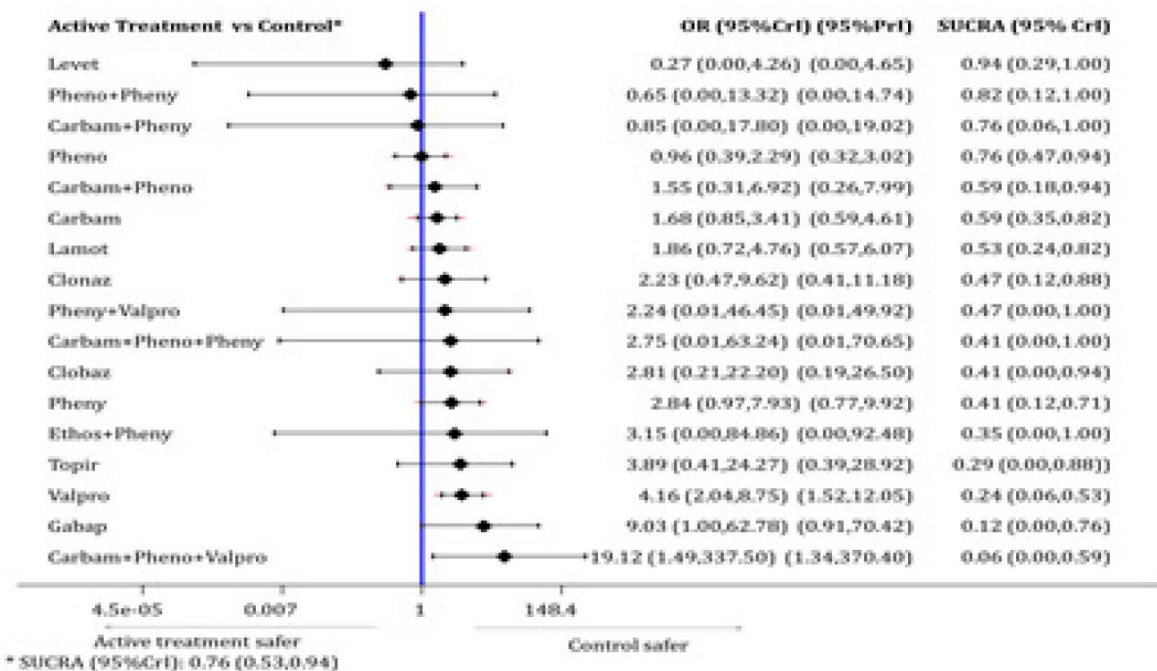
## TOPIRAMATE

Pharmacology: Bioavailability 85%, Metabolism hydroxylation and hydrolysis resulting in inactive metabolites. Renal clearance.

### a. Cognitive Developmental Delay



### c. Psychomotor developmental delay



AED	NAAPR	UK Epilepsy and Pregnancy Register	EURAP
	<i>n</i> = 4899	<i>n</i> = 3607	<i>n</i> = 4540
	Hernandez-Diaz <i>et al.</i> [2012]	Morrow <i>et al.</i> [2006]	Tomson <i>et al.</i> [2011]
	<b>MCM 3 months after birth</b>	<b>MCM 6 weeks after birth</b>	<b>MCM 12 months after birth</b>
	% (95% CI) (n)	% (95% CI) (n)	% (95% CI) (n); dose
Lamotrigine	2% (1.4–2.8) (31)	3.2% (2.1–4.9) (21)	2.0% (1.19–3.24) (17); <300 mg /day 4.5% (2.77–6.87) (20); ≥300 mg/day
Levetiracetam	2.4% (1.2–4.3) (11)	0% (0.0–14.9) (0)	–
Carbamazepine	3% (2.1–4.2) (31)	2.2% (1.4–3.4) (20)	3.4% (1.11–7.71) (5); <400 mg/day 5.3% (4.07–6.89) (56); ≥400 mg/day to <1000 mg/day 8.7% (5.24–13.39) (18); ≥1000 mg/day
Phenytoin	2.9% (1.5–5.0) (12)	3.7% (1.3–10.2) (3)	–
Valproic acid	9.3% (6.4–13.0) (30)	6.2% (4.6–8.2) (44)	5.6% (3.60–8.17) (24); <700 mg/day 10.4% (7.83–13.50) (50); ≥700 mg/day to <1500 mg/day 24.2% (16.19–33.89) (24); ≥1500 mg/day
Topiramate	4.2% (2.4–6.8) (15)	7.1% (2.0–22.6) (2)	–
Oxcarbazepine	2.2% (0.6–5.5) (4)	–	–
Gabapentin	0.7% (0.02–3.8) (1)	3.2% (0.6–16.2) (1)	–
Zonisamide	0% (0.0–3.3) (0)	–	–
Clonazepam	3.1% (0.4–10.8) (2)	–	–
Phenobarbital	5.5% (2.8–9.7) (11)	–	5.4% (2.51–10.04) (9); <150 mg/day 13.7% (5.70–26.26) (7); ≥150 mg/day
Unexposed	1.1% (0.37–2.6) (5)	3.5% (1.8–6.8) (8)	–
CI, confidence interval; EURAP, International Registry of Antiepileptic Drugs and Pregnancy; NAAPR, North American Antiepileptic Drug Pregnancy Registry.			

Clinical Efficacy: Migraine prophylaxis, Diabetic Neuropathy efficacy in randomized double-blinded study

Safety: Withdrawal symptoms with abrupt discontinuation

## QUESTIONS:

1. What are the some of the differences between gabapentin and pregabalin.
2. Are there advantages to using oxycarbazepine over carbamazepine?
3. You have just started a patient on lamotrigine for painful diabetic neuropathy. At the next visit you notice a diffuse macular erythematous rash on her back. She was not aware of the rash until you mention it. She reports the pain in her legs is much better. What should you do?

## **OPIATE TOLERANT PATIENTS**

*Jennifer Hah, MD*

*Ian Carroll, MD, MS*

*Sean Mackey, MD, PhD*

See:

Carroll I, Angst M, Clark J. *Management of Perioperative Pain in Patients Chronically Consuming Opioids*. *Regional Anesthesia and Pain Medicine*, 2004;29(6):576-591 [PDF](#)

VICODIN IS THE MOST FREQUENTLY PRESCRIBED DRUG IN THE UNITED STATES (100 MILLION RX PER YEAR ...there are only 300 million people)

- Opioids are second only to NSAIDS in terms of prescription frequency for chronic pain
- Impact of chronic opioid therapy on postoperative pain:
  - preoperative opioid use predicts poorer pain control and increased analgesic requirements in the postoperative period
  - even consumption of a modest daily opioid dose makes postoperative pain management more difficult
- Difficulty with postoperative pain control may hint to opioid analgesic / heroin abuse
  - opioid daily dose of abusers/addicts is many times the 40 to 50 mg daily oral morphine equivalent used by the chronically opioid consuming patient for pain control
  - opioid abusers/ addicts often have co-existing psychiatric diseases
  - inadequate pain control is more likely in abusers/addicts secondary to tempered opiate use by healthcare providers
- Causes for increased post-operative pain and opioid consumption in patients chronically using opioids

- Opioid-induced hyperalgesia: state of facilitated nociceptive signaling, chronic opioid administration leads to compensatory neurobiological changes facilitating nociception—little data in humans about this occurring
- Opioid tolerance- little data in humans, controversy regarding rate and extent of development

## OPTIMIZING PERIOPERATIVE OPIOID USE

- Preoperative
  - Discussion of the following:
    - Precise opioid use (dose, opioid type, *illicit use* etc.) (Obtain name/ phone number of prescribing provider, pharmacy where prescription filled can help clarify dose, note opioid use history and side effects with previous opioids)
    - Potential for increased postoperative pain
    - Patient's fears and expectations related to pain management
    - Effective management strategies after previous procedures
    - Postoperative management options/appropriate regional techniques for complementing opioid analgesia
    - Postoperative pain management plan
  - Caution with high-dose methadone (>100mg/day) for QT prolongation and arrhythmias, also exacerbated by other QT-interval prolonging meds and metabolic conditions, check EKG
  - If the patient has an implanted infusion device continue usual dosage of opioid.
  - Initiation of appropriate preoperative medications:
    - Continuation of preoperative opioid regimen on day of surgery (prevent withdrawal, falling behind on opioid requirement)
    - Consideration of acetaminophen 1,000 mg 1 to 2 hours before surgery
  - Consideration of a COX-2 inhibitor (celecoxib) 1 to 2 hours before surgery- caution with hypovolemia, decreased renal function- can precipitate ARF, risk of MI
  - Consider gabapentin before surgery (30 minutes to 3 hours)- please refer to **Anesthesia and Pain Service Protocol For Primary Total Hip and Knee Arthroplasty** on <http://ether.stanford.edu/> under policies and protocols
- Intraoperative
  - Administration of opioids to meet the following requirements:
    - Chronic
    - Intraoperative surgical

- Anticipated postoperative
- Titration of long-acting opiate to respiratory rate of 14 to 16 if possible in spontaneously ventilating patient
- Consider methadone 5-10mg IV if patient did not receive usual dose of long- acting opioid on day of surgery
- Administration of adjuvant medications:
  - Ketamine 0.5 mg/kg IV bolus followed by 4 mcg/kg/min infusion
  - Ketorolac 15 mg IV (if NSAID or COX-2 not started preoperatively)
  - Acetaminophen 1,000 mg PR if not started preoperatively
- Institution of appropriate regional technique:
  - Continuous techniques preferable
  - Wound lavage or local infiltration with local anesthetic if other technique not possible
- Avoid placing warming blankets or other warming device over or near transdermal fentanyl patches.
- Postoperative (acute phase)
  - Titration of opioids, adjuvant medications, and regional techniques to patient comfort:
  - Expect postoperative opiate requirements to be up to 2 to 4 times the dose required in an opioid naive person. Remember that no individual's requirements can be predicted with confidence.
  - Titrate opioids aggressively to achieve adequate pain control in the postoperative care unit.
  - Start opioid PCA:
    - If oral route is available, replace normal oral opioids and use PCA for breakthrough pain. Expect PCA intermittent boluses to be higher (typically starting at 2mg q 10min, and increasing the mg amount from there—not infrequently increased to 3 mg q 10 or 4 mg q10. DO NOT REDUCE LOCKOUT INTERVAL.)
    - If oral route is unavailable, consider basal rate for PCA, be extra cautious with basal rate and only use the basal rate to replace the patient's normal daily preoperative dose. Use the intermittent bolus function to allow the patient to titrate the opioids to their needs. **Both** Attending physician and Fellow need to OK the basal rate before afternoon signout. If after signout, page the fellow and attending. Don't start a basal rate overnight without this check. Basal rates are among the most dangerous things we do, and opioid tolerant patients are at twice the baseline risk of respiratory depression or over-sedation (up to 40%).
  - In patients undergoing a regional technique, plan to administer at least half of the preoperative opiate requirement systemically *to avoid withdrawal*.

- Continue applicable regional techniques. Consider use of high-potency opioids such as fentanyl/sufentanil in place of morphine for epidural management. The recommendation is to start with either hydromorphone or morphine. (Partial opioid agonists- buprenorphine/ nalbuphine used to treat opioid SEs such as pruritis may precipitate abrupt opioid withdrawal in this population)
- Continue acetaminophen 1,000 mg every 6 hours, and/or continue acetaminophen, NSAID, or COX-2 inhibitor for several days with attention to renal function and risk of bleeding. Take care to not exceed 4gm per day of acetaminophen, and even less in patients who abuse alcohol or have hepatic dysfunction.
- Continue oral ketamine if started in OR (typical starting dose 20-40 mg po q 2hours prn severe breakthrough pain and increasing from there). Oral ketamine may be given on the regular post-surgical floors at Stanford Hospital. Consider ketamine infusion with continued severe acute pain refractory to other measures. Ketamine can only be prescribed by the Pain Service or Palliative Care Service. If we initiate ketamine, we have to stay with the patient until we discontinue it. (IV ketamine infusion requires ICU admission, (or occasionally admission to BMT or Oncology floor with palliative cases), check with nursing supervisor (61767) for all floor locations regarding infusion policies)
- -Other adjuvants: As a reminder gabapentin is the recommended front line agent prior to initiating treatment with ketamine, alpha-2 agonists (dexmedetomidine, clonidine)
- Monitoring for oversedation and opioid withdrawal:
  - Chronically opioid-consuming patients are at higher risk for respiratory depression than are opioid naive patients and must be monitored appropriately with regular evaluation of sedation and oxygen saturation. There is controversy among experts about whether postoperative oxygen administration and monitoring of oxygen saturations actually increases risks to patients by masking hypoventilation (and elevated CO<sub>2</sub>) until it has progressed significantly. (Remember hypoventilating patients on O<sub>2</sub> will have normal oxygen saturation until PaCO<sub>2</sub> is very high). Nonetheless, we administer O<sub>2</sub> and monitor O<sub>2</sub> sat in order to decrease the severity of consequences of hypoventilation and to possibly detect it earlier. Note signs of hypoventilation are often not sedation until very late stage (e.g. CO<sub>2</sub> narcosis). Early signs of the hypoventilating patient include tachycardia, hypertension, sweating, mild delirium, and agitation—all signs of increased sympathetic outflow. On several occasions we have been called for a near respiratory arrest on a patient who we had seen just 30 minutes earlier. In these cases patients did not appear somnolent when we saw them but did seem “off”. They answered questions incorrectly, made inappropriate comments, and seems generally like they were “sun-downing”. When you see this behavior be suspicious: think diminished cerebral function and check is there adequate perfusion (HR and BP)? Is there adequate oxygenation (eg. aspiration, pneumonia, ARDS, PE)? Is there adequate ventilation (eg. narcotized)? Is there adequate glucose (diabetics that are NPO)?
- Post-operative (transition phase)
  - Transition from regional and parenteral techniques to oral opioids/adjuvants:
  - Use the opioid requirements during the first 24 to 48 hours to determine daily oral opioid

dose.

- Deliver half of estimated oral requirement as a long-acting formulation.
- Allow PRN use of short-acting opioid every 3 hours in sufficient quantity to provide the remaining required opioid dose.
- Consider continuing acetaminophen, NSAID, or COX-2 inhibitor during transition phase.
- Plan taper from postoperative opioid doses toward preoperative doses and discuss with patient or care provider. (*Usually can be accomplished over 2-4 weeks*) Determine need for specialty follow-up if regimen is particularly complex.

## EMPIRICAL GUIDELINES FOR OPIOID ROTATION

(from PG Fine, RK Portenoy, *A Clinical Guide to Opioid Analgesia*. (Vendome Group, 2007)

Note: Evidence for efficacy of opioid rotation is not high and opioid rotation is especially dangerous in patients on chronic opioids where the appropriate conversion is always a matter of guesswork based on individual differences. Avoid opioid rotation if you can. Involve fellow and attending in decision. Also note that opioid rotation can be disruptive when the patient returns to PCP prescribing the opioids. Residents should contact physician who prescribes opiates as outpatient when considering changes in baseline opioid regimen to facilitate transition of care. (For example, conversion of patient previously taking Suboxone to methadone post-operatively.)

1. Use equianalgesic table to calculate dose of the new opioid roughly equivalent to current opioid dose.
2. Determine clinically relevant starting point:
  - a. If switching to opioid other than methadone or fentanyl, decrease equianalgesic dose by 25-50%
  - b. If switching to methadone, reduce the equianalgesic dose by 75-90%
  - c. If switching to transdermal fentanyl, do not reduce the equianalgesic dose.
3. Consider further dose adjustments on the basis of medical condition and pain
  - a. If pt is elderly or has significant organ failure, consider further dose reduction
  - b. If pt has severe pain, consider less dose reduction
4. With "rescue dose" calculate 5-15% of total daily dose and administer at an appropriate interval. Reassess and titrate new opioids to therapeutic response and SEs

## OPIOID ANALGESICS STARTING ORAL DOSE COMMONLY USED FOR SEVERE PAIN

(adopted from American Pain Society, Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain Sixth Ed. (APS, Illinois, 2008))

	<b>Equianalgesic Dose (mg)</b>		<b>Starting Oral Dose</b>		
<b>Name</b>	<b>Oral</b>	<b>IV</b>	<b>Adults (mg)</b>	<b>Comments</b>	<b>Precautions &amp; Contradictions</b>
Morphine	30	10	15-30	Controlled release MS Contin and OramorphSR release drug over 8-12 hrs. Kadian and Avinza last 12-24 hrs.	
Hydromorphone (Dilaudid)	7.5	1.5	4-8	Slightly shorter duration than morphine.	
Fentanyl	-	0.1	-		
Oxycodone	20	-	10-20		
Methadone	See below				
Levorphanol (Levo-Dromoran)	4 acute	2 acute	2-4	Long plasma half-life (12-16 hours, may be as long as 90-120 hours after 1 wk of dosing.	Accumulated on days 2-3. Use with caution in elderly.
Oxymorphone (Numorphan)	10	1	5-10	Controlled release preparation (Opana) releases drug over 12 hours. 5mg rectal suppository ~ 5 mg parenteral morphine	Like parenteral morphine

Meperidine (Demerol)	Not recom mende d				
Nalbupine (Nubain)	-	10	-	Not scheduled under Controlled Substances Act.	May precipitate withdrawal in opioid dependent patients
Butorphanol (Stadol)	-	2	-	Like nalbuphine. Available in nasal spray.	
Pentazocine (Talwin)	50	30	-		
Buprenorphine (Buprenex)	-	0.4	-	Lower abuse liability. SL tablet now available plain and with naloxone for opioid-dependent patient management. Tablets not approved as analgesics.	May precipitate withdrawal in narcotic-dependent patients; not readily reversed by naloxone; avoid in labor.

## GUIDELINES FOR METHADONE ADMINISTRATION

1. Stop morphine or other opioids
2. Give methadone at fixed intervals (every 8 hours)
3. If total morphine equivalent dose per day is <90 mg (oral), methadone dose ratio of 1:4 (methadone to morphine) is used. Divide methadone dose by 3 and administer every 8 hours.
4. If total morphine dose per day is 90-300mg (oral), methadone dose ratio of 1:8 (methadone to morphine) is used.
5. If total morphine dose per day is >300mg (oral), methadone dose ratio of 1:12 (methadone to morphine) is used.
6. Pts on q 8 hour schedule may have 10% of daily methadone dose for breakthrough pain.

Methadone should be used cautiously in the perioperative period. It can easily lead to dose stacking and subsequent respiratory depression. Do not start the first dose of methadone in the evening. Treat the above conversion of other opioids to methadone as only a guideline. It is highly uncommon to ever need to start a patient on methadone at doses larger than 20mg BID. Much more typical is starting 5-10mg BID.

## CONVERSION OF ORAL MORPHINE TO TRANSDERMAL FENTANYL

<b>Oral Morphine (mg/day)</b>	<b>Transdermal Fentanyl (mg/day)</b>	<b>Transdermal Fentanyl (mcg/hr)</b>
30-90	0.6	25
91-150	1.2	50
151-210	1.8	75
211-270	2.4	100
271-330	3.0	125
331-390	3.6	150
391-450	4.2	175
451-510	4.8	200
511-570	5.4	225
571-630	6.0	250
631-690	6.6	275
691-750	7.2	300
For each additional 60mg/day	+0.6	+25

### REFERENCES:

Carroll IR, Angst MS, Clark JD. Management of Perioperative Pain in Patients Chronically Consuming Opioids. Regional Anesthesia and Pain Medicine. 2004;29: 576-591.

Rozen D, Grass GW. Perioperative and Intraoperative Pain and Anesthetic Care of the Chronic Pain and Cancer Pain Patient Receiving Chronic Opioid Therapy. Pain Practice. 2005;5: 18-32.

# **CANCER PAIN**

## WORLD HEALTH ORGANIZATION (WHO) 3-STEP ANALGESIC LADDER

*Xiang Qian, MD, PhD, Theresa Mallick-Searle, NP*

The WHO 3 step guidelines for cancer pain treatment were originally published in 1986. The guidelines recommend prompt oral administration of drugs ("by the mouth") when pain occurs.

**If** the patient has mild pain, the pain can be treated with non-opioid drugs such as acetaminophen or aspirin with or without "adjuvants" such as non-steroidal anti-inflammatory drugs (NSAIDs) including COX-2 inhibitors.

**If** complete pain relief is not achieved or disease progression necessitates more aggressive treatment, a weak opioid such as codeine, dihydrocodeine or tramadol is added to the existing non-opioid regime.

**If** above therapy becomes insufficient, a weak opioid is replaced by a strong opioid, such as morphine, diamorphine, fentanyl, buprenorphine, oxymorphone, oxycodone, or hydromorphone, while continuing the non-opioid therapy, escalating opioid dose until the patient is pain free or at the maximum possible relief without intolerable side effects.

**Of note:** if the initial presentation is severe pain, this stepping process should be **skipped** and a strong opioid should be started immediately in combination with a non-opioid analgesic

**In summary**, if cancer pain occurs, there should be prompt oral administration of drugs in the following order: non-opiates; then, as necessary, mild opiates; then stronger opiates such as morphine, until patient is "free" of pain. To calm fears and anxiety, additional drugs, "adjuvants", should be used.

To maintain freedom from pain, drugs should be given "**by the clock**", that is q2-6hr, rather than "on demand".

This WHO three-step approach of administering the right drug in the right dose at the right time is inexpensive and 80-90% effective.

### **Keys to remember:**

1. The Oral route is preferred for all steps of pain ladder (however, parenteral therapy may be required in cases of refractory pain or inability to take P.O.)
2. Cancer pain is continuous.
3. Analgesics should be scheduled at regular intervals as opposed to on a PRN basis.
4. Adjuvant drug therapy is used to decrease the anxiety and fear associated with chronic pain. These adjuvants can include antidepressants, anticonvulsants, etc.

The Principles of the WHO Analgesic Ladder include:

- Using analgesics in adequate doses.
- Titration for the individual patient.
- Administration on a strictly regular basis to prevent pain not pro re nata (PRN), as pain occurs.
- Developing a management plan for breakthrough pain.
- Using oral route whenever possible.
- Review and reassess analgesic requirements
- Keep it simple.

### **Step1: MILD PAIN**

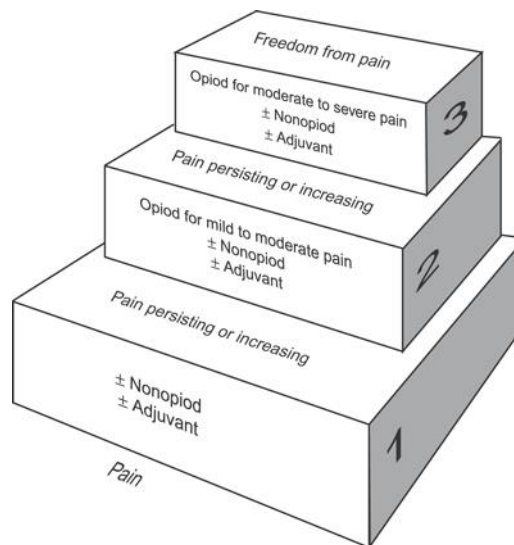
Non-opiate (Tylenol, NSAIDS) +/- Adjuvants (anticonvulsants, antidepressants, corticosteroids, disphosphonates (bisphosphonate), anxiolytics)

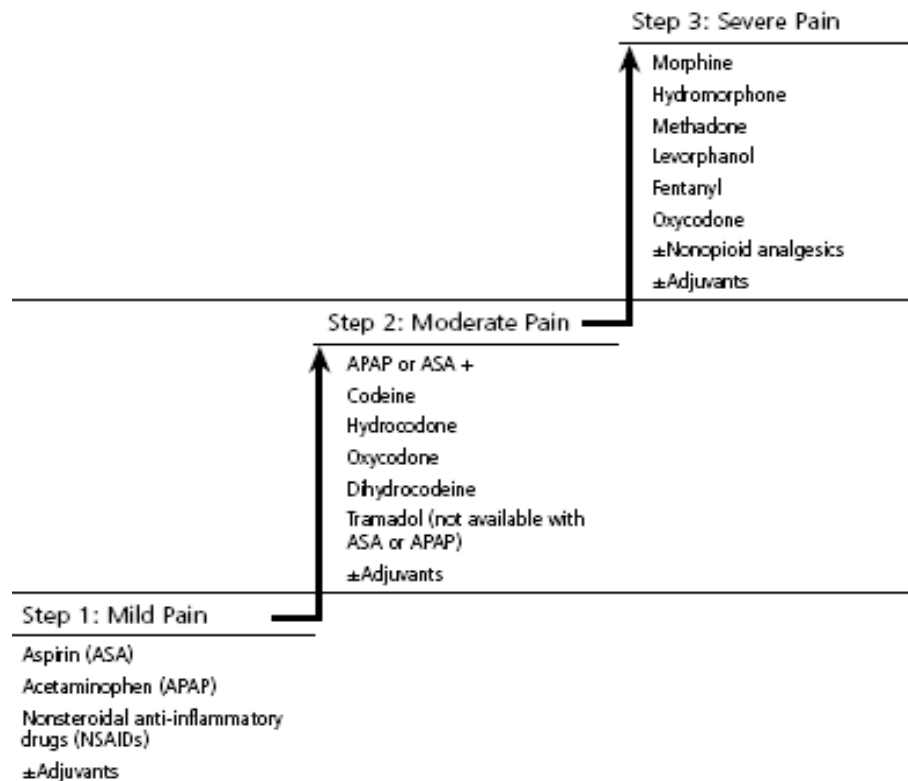
### **Step 2: MILD TO MODERATE PAIN**

Opiate/weaker (long & short acting formulations; po, IM, IV) +/- Non-opiate +/- Adjuvants

### **Step 3: MODERATE TO SEVERE PAIN**

Opiate/stronger +/- Non-opiate +/- Adjuvants





#### QUESTIONS

1. Identify four causes of cancer-related pain.
2. Describe the WHO analgesic ladder.
3. According to the WHO analgesic ladder, when would it be appropriate to use an opiate as an analgesic agent, alone or in combination?
4. What are adjuvants?

#### REFERENCES

American Pain Society. Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain, 6th, American Pain Society, Glenview, IL 2008

WHO guideline 2017: <http://www.who.int/csr/don/archive/year/2017/en/>

WHO analgesic pain ladder available online. [www.who.int/cancer/palliative/painladder/en/](http://www.who.int/cancer/palliative/painladder/en/) (Accessed on September 06, 2011).

Caraceni A, Martini C, Zecca E, Portenoy RK, et al. Breakthrough Pain Characteristics and Syndromes in Patients with Cancer Pain: An International Survey. *Palliat Med* 2004;18:177-83.

Delaney A, Fleetwood-Walker SM, Colvin LA, Fallon M. Translational Medicine: Cancer Pain Mechanisms and Management. *Br J Anaesth* 2008;101:87-94.

Mantyh PW, Clohisy DR, Koltzenburg M, Hunt SP. Molecular Mechanisms of Cancer Pain. *Nat Rev Cancer* 2002; 2:201-9.

Pamela J. Goodwin, Eduardo Bruera, and Martin Stockler. Pain in Patients With Cancer. *Journal of Clinical Oncology* 2014 32:16, 1637-1639

Portenoy RK, and et al. Cancer pain management: General principles and risk management for patients receiving opioids. 2017 April. Uptodate.

Quigley C. Role of Opiates in Cancer Pain. *BMJ* 2005;331:825-9.

Wiffen PJ, Wee B, Derry S, Bell RF, Moore RA. Opioids for cancer pain - an overview of Cochrane reviews. 2017 Jul 6;7. *Cochrane Database Syst Rev*.

Zech D, Grond S, Lynch J, Hertel D, Lehmann K. Validation of World Health Organization Guidelines for cancer pain relief: a 10-year prospective study. *Pain* 1995;63:65-76.

# **ACUPUNCTURE AND PAIN MANAGEMENT**

*Jiang-Ti Kong, MD*

## **DEFINITION:**

Acupuncture refers to an Ancient Asian medical therapy where long, thin needles are inserted to discrete points on the body surface for the treatment of disease.<sup>1</sup>

Acupuncture has been used extensively to treat both organ dysfunction and pain disorders. The focus of this monograph is on the treatment of acute and chronic pain.

## **HISTORY AND MECHANISMS OF ACTION:**

Acupuncture was first documented in the Yellow Emperor's Internal Canon which was written in China around 200 BC. Acupuncture is traditionally believed to work via the reinforcement of the flow of Qi (or vital energy) along 12 principle meridians on the body surface, each of which is directly connected to an internal organ.

Acupuncture has gained widespread medical attention since the 1970's after President Nixon visited China, where one of his aides had acupuncture anesthesia for an appendectomy.<sup>2</sup> Since that time, numerous research studies have been conducted to explain its mechanisms of action in a manner compatible with Western medicine. Below is a brief summary of neurologic and physiologic pathways affected by acupuncture.

1. **Peripheral nervous system**: histo-anatomical studies have shown acupuncture points to be shallow areas of lowest electrical resistance along fascial planes where the peripheral nerve fibers concentrate.<sup>3-5</sup> Needle stimulation of these points results in activation of A $\beta$ , A $\delta$ , C fibers at the subcutaneous level as well as group II and III fibers at the muscle receptor level.<sup>4</sup> Injection of local anesthetics in the muscle layers surrounding acupuncture points blocks acupuncture-induced analgesia, supporting the role of group III fibers.<sup>6</sup>
2. **Central nervous system**: two distinct analgesic pathways are activated by electro-acupuncture<sup>7</sup>: low frequency (4Hz) stimulation results in slow onset endorphin-mediated analgesia reversed by naloxone; while high frequency stimulation (>70Hz) results fast onset mono-amine-mediated (5HT and NE) analgesia unaffected by naloxone or hypophysectomy.<sup>4</sup> The analgesic pathway appears to involve both spinal (interneurons) and supraspinal levels (the raphe magnus, the nucleus ceruleus, PAG, and the dorsolateral funiculus).<sup>8</sup>
3. **Neuro-humeral system**: Acupuncture also exerts profound effects on the midbrain and hypothalamic-pituitary axis (HPA), resulting in the release of endorphins in both the CSF and peripheral circulation. As such, by systemic and CNS administration of naloxone has been shown to abolish acupuncture induced analgesia.<sup>9</sup>

## **INDICATIONS:**

1. **NIH Consensus**: in **November 1997**, the NIH held a national, multidisciplinary convention assessing the utility of acupuncture.<sup>10</sup> The consensus asserted the “**efficacy of acupuncture in adult postoperative and chemotherapy nausea and vomiting, and in postoperative dental pain.**” With less definitive evidence, the consensus stated that “acupuncture **may** be useful as an adjunct treatment or an acceptable alternative or may be included in a comprehensive management program for the following conditions: “**addiction, stroke rehabilitation, headache, menstrual cramps, tennis elbow, fibromyalgia, myofascial pain, osteoarthritis, low back pain, carpal tunnel syndrome, and asthma.**”

2. **More recent evidence:** Since 1997, more clinical trials have been conducted, further supporting the efficacy of acupuncture in the following conditions:
  - a. **Low back pain:** in a meta-analysis of 35 randomized clinical trials from 1996 to 2003, Furlan et al concluded that “For chronic low back pain, acupuncture is more effective for pain relief and functional improvement than no treatment or sham treatment immediately after treatment and in the short-term only. Acupuncture is not more effective than other conventional and ‘alternative’ treatments.”<sup>11</sup>
  - b. **Acute postoperative pain:** in a systematic review of 15 randomized clinical trials from 1996 to 2007, Sun et al concluded that compared with sham control, **acupuncture** treated group reported **less pain**, consumed 9.14mg less morphine equivalent at 72hr, and had less opiate-related complications in patients in the **acute postoperative** period.<sup>12</sup>
  - c. **Chronic headaches:** Sun and Gan concluded in their systematic review from 2008 that **acupuncture was more effective than sham or medication therapy** in reducing pain intensity, frequency and improving function in patients with chronic migraine, tension headaches, or both.<sup>13</sup>
  - d. **Knee pain:** the results on knee pain have been **equivocal**. Manheimer et al reports in their meta-analysis from 2007 that for knee pain due to osteoarthritis, there is no difference between acupuncture and sham controls, but some benefits when compared to no treatments at all.<sup>14</sup> Another group, led by White A et al, reported benefits of acupuncture compared to sham or no treatment in knee pain regardless of etiology.<sup>15</sup>

#### ACCESSING ACUPUNCTURE RESOURCES AT STANFORD:

1. **When to use it:** Acupuncture has a clearly defined role in acute post-operative pain, nausea and vomiting, and in chronic settings including low back pain, headaches, and potentially knee pain and chemical addiction.<sup>16</sup> It may be used as an adjunct to a comprehensive pain management plan, or by itself in patients intolerant of conventional therapies.
2. **Where to find it:** At Stanford Hospital, acupuncture is offered to chronic pain patients via referrals. However, it is not customarily offered on the acute service.
  - a. **Outpatient:** Drs. Brenda Golianu and Julie Good both offer acupuncture in the pediatric pain clinic. For adults, one may refer the patient to the Stanford Integrative Medicine where acupuncture service is available. One may also directly refer the patient to Dr. Emily Ratner in the department of Anesthesia.
  - b. **Inpatient:** acupuncture is not routinely offered on the inpatient, acute adult pain service. However, other in-hospital services may still request it. Such requests are handled on a case-by-case basis. Routine, conventional therapies are first recommended to the primary team if they have not already been tried. Next, if the acute pain team feels that the indication is appropriate, they may contact Dr. Emily Ratner for further suggestions. On the pediatric side, one may direct requests to Drs. Golianu and Good.

#### CONCLUSIONS

Acupuncture is an evolving medical therapy that originated from China over three thousand years ago. Compared to conventional therapies, it has the advantages of low cost and minimal complications.<sup>2</sup> The most common complication with acupuncture is “needle shock,” a vasovagal reaction which often resolves with removal of the needles, supine positioning, and patient reassurance.<sup>2,z</sup>

Emerging clinical evidence supports the role of acupuncture in treating acute postoperative pain, nausea and vomiting, chronic low back pain, headaches, and potentially knee pain. It may be used as part of a comprehensive plan, by itself as initial therapy, or in patients who failed conventional pain management approaches.

At the present, the use of acupuncture at the Stanford Pain Management Clinic and the Adult Acute Pain service is relatively limited. Hopefully this will change with increasing patient demand, provider availability, and research studies clarifying its mechanisms of action and efficacy.

#### BIBLIOGRAPHY

Stedman TL: Stedman's medical dictionary for the health professions and nursing, Illustrated 6th Edition. Philadelphia, Wolters Kluwer Health/Lippincott Williams & Wilkins, 2008

Ballantyne J, Massachusetts General Hospital.: The Massachusetts General Hospital handbook of pain management, 3rd Edition. Philadelphia, Lippincott Williams & Wilkins, 2006

Hyvarinen J, Karlsson M: Low-resistance skin points that may coincide with acupuncture loci. Med Biol 1977; 55: 88-94

Helms JM: Acupuncture energetics : a clinical approach for physicians, 1. Edition. Berkeley, Calif. [u.a.], Med. Acupuncture Publ. [u.a.], 2007

Liu Y, Varela M, Oswald R: The correspondence between some motor points and acupuncture loci. Am J Chin Med (Gard City N Y) 1975; 3: 347-58

Chiang CY: Peripheral afferent pathway for acupuncture analgesia. Scientia Sinia 1973; 16: 210-217

Cheng RS, Pomeranz B: Electroacupuncture analgesia could be mediated by at least two pain-relieving mechanisms; endorphin and non-endorphin systems. Life Sci 1979; 25: 1957-62

Li A, Wang Y, Xin J, Lao L, Ren K, Berman BM, Zhang RX: Electroacupuncture suppresses hyperalgesia and spinal Fos expression by activating the descending inhibitory system. Brain Res 2007; 1186: 171-9

Pomeranz B, Stux G, Han C-s: Scientific bases of acupuncture. Berlin ; New York, Springer-Verlag, 1989

NIH Consensus Development Panel on Acupuncture: NIH Consensus Conference: Acupuncture. JAMA 1998; 280: 1518-1524

Furlan AD, van Tulder M, Cherkin D, Tsukayama H, Lao L, Koes B, Berman B: Acupuncture and dry-needling for low back pain: an updated systematic review within the framework of the cochrane collaboration. Spine (Phila Pa 1976) 2005; 30: 944-63

Sun Y, Gan TJ, Dubose JW, Habib AS: Acupuncture and related techniques for postoperative pain: a systematic review of randomized controlled trials. Br J Anaesth 2008; 101: 151-60

Sun Y, Gan TJ: Acupuncture for the management of chronic headache: a systematic review. Anesth Analg 2008; 107: 2038-47

Manheimer E, Linde K, Lao L, Bouter LM, Berman BM: Meta-analysis: acupuncture for osteoarthritis of the knee. Ann Intern Med 2007; 146: 868-77

White A, Foster NE, Cummings M, Barlas P: Acupuncture treatment for chronic knee pain: a systematic review. *Rheumatology (Oxford)* 2007; 46: 384-90

Liu TT, Shi J, Epstein DH, Bao YP, Lu L: A meta-analysis of acupuncture combined with opioid receptor agonists for treatment of opiate-withdrawal symptoms. *Cell Mol Neurobiol* 2009; 29: 449-54