Chronic Pain Management

CME Conference Swedish Hospital
February 23, 2010
Jonathan Clapp, MD

Colorado Comprehensive Spine Institute
3277 S. Lincoln St.
Englewood, CO 80113
Disclosures

(NOTHING)
Objectives

- Describe what chronic pain is and how it is thought to occur.
- Illustrate the many issues involved in a typical patient.
- Discuss the bio-psycho-social model of diagnosis and treatment.
- Outline medications and alternatives used to manage chronic pain.
What is Pain?

- Pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”. -IASP

- “Pain is a **subjective and entirely individual personal experience** influenced by learning, context, and multiple psychosocial variables”.

Chronic Pain

 Definitions

- “Pain lasting longer than anticipated within the context of the usual course of an acute disease or injury”.
- “Pain lasting 3-6 months following the inciting event, and in many cases may not be associated with any obvious ongoing noxious event or pathologic process”.
- “Pain that no longer serves as a physiologic protective mechanism”.

 DSM IV “Pain Disorder” Criteria:

- Pain in 1 or more anatomic sites.
- Pain causes significant distress or impairment.
- Psychological factors are judged to play an important role.
- Symptom(s) are not intentionally produced.
- Pain is not better accounted for by another condition.
Chronic Pain

- Often occurs with poor sleep and decreased function.
- Frequently results in dysfunctional behaviors, suffering and disability.
- Is different from acute pain in that it can involve biologic, psychologic and socioeconomic issues.
  - a multidisciplinary team approach the best means of comprehensive treatment.
Chronic Pain

- More than 75% of chronic pain patients display harmful behavioral characteristics.
  - Problems with job or housework, leisure activities, sexual function and vocational endeavors.
Chronic Pain

- **Epidemiology**
  - Approximately from 30-40% in gen. pop.
  - >70% in patients with a primary disability
    - SCI, MS, amputations & cerebral palsy
  - >36 million with arthritis, 70 million with chronic back pain, 20 million with migraines and additional millions with gout, myofascial pain syndromes, cancer and complex regional pain syndromes
  - By 2030 arthritis and related disability is expected to almost double, affecting 71 million Americans.
Chronic Pain

- Costs
  - $70-120 billion annually for healthcare and lost productivity.
  - Annually responsible for 90 million physician visits, 14% of all prescriptions, and 50 million lost workdays.
Types of Chronic Pain

- Somatic: Osteoarthritis, back pain, headaches, rheumatoid arthritis, osteomyelitis, post-surgical
- Visceral: pelvic pain, interstitial cystitis, pancreatitis, endometriosis
- Neuropathic: Complex regional pain syndrome (CRPS), post-herpetic neuralgia, diabetic neuropathy, phantom limb pain, post stroke, chronic radiculopathy, fibromyalgia, trigeminal neuralgia.

Pain Receptors & Pathways

- **Transduction: Receptor Activation**
  - Energy that is damaging or potentially damaging (thermal, mechanical or chemical energy) is converted into action potentials in primary nerve afferents.
  - Primary receptors for pain lie at the terminal branches of C and A-delta fibers that both respond to a painful stimulus at a cellular level.
Pain Receptors & Pathways

**Transmission**

- Impulses are transferred from primary afferents to the dorsal horn, brainstem, thalamus, and cortical structures.
  - C-fibers: 70% of skin nociceptors, slow, thin, unmyelinated
    - Transmit the slow, burning quality of pain
  - A-delta fibers: 10% of skin nociceptors, rapid, medium, thinly myelinated.
    - Transmit the fast, prickly quality of pain
    - Contribute to hyperpathia with sensitization.
  - A-beta fibers: 20% of skin nociceptors, fast, large, myelinated.
    - Carry non-painful impulses (touch, vibration, pressure), except with peripheral and central sensitization, which can result in allodynia.
Pain Receptors & Pathways

**Modulation**

- Primary afferents converge at the dorsal horn, with A-delta and C fibers synapsing on superficial laminae (I & II) and deep laminae (V & VI).
- Superficial laminae are involved primarily in nociceptive inputs.
- Deep laminae “respond to wide dynamic range neurons (WDR) of ‘wide’ stimulus intensities”.
  
  - Non painful afferent impulses in A-beta fibers, for example, release glutamate which acts on NMDA receptors to block it via magnesium release and on AMPA receptors to activate it via normal sodium channel opening.
  
  - However, prolonged post-synaptic depolarization causes voltage-dependent Mg removal, allowing additional Na and Ca to enter the cell, resulting in amplified/painful responses with further impulses.
Pain Receptors & Pathways

Figure 43-3 Organization of cutaneous, primary afferent input to the dorsal horn of the spinal cord. (From Millan 1999,104 with permission.)
Ascending & Descending Modulation

- **Endogenous Inhibition**
  - The periaqueductal gray in the pons is “important in modulating nociceptive inhibition and behavioral responses to potentially threatening stimuli” via endogenous opioids.
  - Serotonin, norepinephrine, acetycholine and GABA also, in general, act to inhibit pain signals.
  - Glutamate and substance P are excitatory neurotransmitters and ramp up the pain response.
Ascending & Descending Modulation

Key:
H = hypothalamus
IL = intralaminar thalamic nuclei
L = limbic system
PT = post. thalamic nuclei
VPL = ventral posterior thalamic nuclei
Figure 1. Pain signals are transmitted to the brain by two main pathways. The lateral system (A) is made up of long thick fibers that transmit information about the onset of injury, and its precise location and intensity. They are designed to carry a rapid flow of pain signals to the thalamus to stimulate an immediate antinociceptive response. The medial system (B) is composed of phylogenetically older fibers that carry slower signals and probably transmit information related to the persistence of injury and level of response induced.
The Role of Endogenous Opioids

- To reduce the level of perceived pain, endogenous opioids (enkephalins, dynorphin) are released by interneurons in the dorsal horn in response to severe/persistent pain. The opioids bind to G proteins associated with \( \mu \)-type opioid receptors, with the following results:
  - Inhibition of pre-synaptic release of glutamate
  - Increased potassium conductance across the post-synaptic membrane
- These events prevent the transmission of pain to the higher centers
- To combat pain, exogenous opioids (e.g. morphine) mimic the effects of endogenous opioids at the \( \mu \) opioid receptors.
fMRI studies in fibromyalgia patients suggest that similar levels of subjective pain result in similar central nervous system (CNS) activation in both fibromyalgia patients and controls. For a similar stimulus, however, fibromyalgia patients have a greater subjective sensation of pain. This increased sensitivity is accompanied with a decreased activity in brain regions implicated in the descending pain inhibitory pathways.

Psychologic Factors in Chronic Pain

- Affective & Cognitive factors have a large impact on the perception of pain.
  - Studies show depressed patients have higher levels of pain, decreased cognitive functioning, & greater disability.
  - Anxiety is a strong predictor of pain severity, disability and pain behavior.
    - Patients with pain-related fear had increased disability at 6 months.
Operant Behavior

- Operant, or “learned”, pain behavior can have a significant impact on the lives of chronic pain patients.
  - Patients learn to avoid potentially painful activities via punishment (pain) and achieve rewards (reduction of pain).
  - Reinforced by a physician lack of understanding of this chronic disease process.
    - “untreatable”
  - These principles can extend into other, more complicated, aspects of their lives based on:
    - Rewards: attention/affection, financial (disability), etc.
    - Punishment: returning to work, anxiety/fear with activity (kinesophobia), increased pain with independence, lack of understanding, etc.
Sleep & Chronic Pain

- 8-8½ hrs is considered “restorative”.
  - About 20% is spent in Stages 3 & 4 (delta-wave, slow-wave, or deep sleep) which is considered the most important/restorative part of the sleep cycle.
  - Is affected by many medications (opioids, benzo’s, etc.)
- 50-90% prevalence of disturbed sleep in chronic pain patients.
  - Possible role of decreased serotonin, besides the obvious pain that can wake patients.
Assessment

- **HPI**
  - Dx?
  - Onset
  - In temporal order, what was tried (surgery, injections, meds, PT, bracing, acupuncture, meditation, etc)?
    - Did each intervention help or not?
      - A 30% reduction in pain is considered clinically significant.
    - If they were in therapy, what did they specifically do? How often and how long?

- **Pain Hx**
  - For each complaint:
    - Where, ?, 10, constant or intermittent, quality (burning, sharp, ache, pins & needles, etc.), exacerbating/relieving factors, radiating?, am/pm differences?
Assessment

- **Functional Hx**
  - Is there anything they cannot, or have trouble doing? Assistance required? On disability or working?

- **Sleep Hx**
  - When do they go to bed? How long to fall asleep? Wake up how many times per night? How long to fall back asleep? What time do they wake for the day? Do they feel rested?

- **Psych Hx**
  - “A semistructured interview by an experienced psychologist/psychiatrist is the most comprehensive means of evaluating the psychologic state of the patient”.
  - Expectations of treatment?
    - DSM IV Criteria (+4/8 = major depression)
    - Sleep disturbances, decreased interests, guilt, energy, cognitive slowing, appetite changes, psychomotor slowing, decreased sex drive, suicidality.
Assessment

- **ROS**
  - check SE’s of current meds or sx’s that may be increased by additional interventions.

- **PMH**
- **PSxHx**
- **FH**
- **SH**

- **Meds**
  - Make sure that nobody else is prescribing pain medications.

- **Allergies**
- **Diagnostic tests**
  - Keep in close dialogue with other professionals involved in px’s care.

- **Vitals**
- **Detailed physical exam**
  - Affect, alertness, speech, pupils, provocative mov’ts, specialized tests, tenderness, asymmetry, swelling, redness, heat, cold, soft tissue abnormalities, hyperpathia or allodynia, radicular or nerve distribution.
Treatment

- Studies show multidisciplinary approaches are unequivocally the best model in px’s with short- & long-term disability.
  - Team should optimally include:
    - Physician, PT, OT, Pain Psychologist/Psychiatrist, Social Worker, Recreational Therapist, Biofeedback Specialist (may be covered by psych.), Nursing Educator, Vocational Counselor

- The team should work together to provide a unified diagnosis and comprehensive treatment program, in which the patient is an active participant.
Team Goals of Treatment

- Maximize & maintain physical activity and function
- Reduce the misuse or abuse of dependency-producing meds, invasive procedures, and passive modalities, fostered by a change toward active patient self management.
- Return to previous levels of activity at home, in the workplace and in leisure pursuits.
- Reduce subjective reported pain intensity and maladaptive pain behaviors.
- Assist patients in obtaining resolution and/or closure of contentious work-related or litigation aspects of the pain condition.
Treatment/Modalities

- **Heat & Cold**
  - Via unknown mechanisms, cutaneous heat & cold both serve to reduce muscle spasms by decreasing sensitivity of the muscle spindle’s firing rate and returning it to its normal length.
  - Cold is better for acute/inflammatory injuries, but can be used long-term based on px’s preference for muscle tightness.
  - Heat/Ultrasound is best tolerated in subacute/chronic conditions, but is better for loosening collagen and stiff joints than cryotherapy.
Treatment/Modalities

- Transcutaneous Electrical Nerve Stimulation Therapy (TENS)
  - Theoretically acts via the gate control theory, electrical stimulation preferentially activates large diameter fibers, inhibiting smaller pain fibers.
  - May involve release of endogenous opioids, as well.
  - No better than placebo for chronic LBP, but does help with CRPS, phantom limb pain, peripheral nerve injury and post-op incisional pain.
  - Contraindicated in px’s with pacemakers.
Treatment/Modalities: Exercise

- Muscles may shorten as a protective reaction to injury/pain.
  - Prolonged shortening can be a cause of pain and result in altered biomechanics.
  - Graded stretching and strengthening, massage and manual therapy can help restore normal body mechanics.

- Exercise itself is an important pain reducer, as well.
  - 20 minutes of aerobic exercise per day has been shown to decrease depression, increase self efficacy and increase the release of endogenous opioids.
Movement-Based Therapies

- **Aquatic Rehabilitation** is ideal for px’s with fear and anxiety related to movement.
  - Weight bearing is decreased 40% in chest deep water & allows for progressive loading.
  - Resistive force of water = force produced by px
  - Reports of reduced pain, anxiety, depression, fatigue and increased quality of life for up to 24 months.

- **Pilates** “focuses on core strengthening, power, concentration, breathing and kinesthetic awareness”.
  - Little literature, but reports of improved strength, flexibility & posture.

- **Yoga** has been reported to reduce pain possibly due to control of stress & depression as well as working on relaxation, stretching & strengthening of targeted muscles.
Behavioral Treatment Modalities

- Cognitive behavior modification teaches “self-coping statements and problem-solving cognitions” in attempts to alter their perception of their chronic disease.
  - Strategies of imaginative inattention, imaginative transformation of pain, focused attention & somatization in a dissociation manner are used.
  - The operant approach reinforces good behavior and ignores adverse pain behavior.
    - Exercises should be done at a level to avoid “punishment” for activity and reinforce the positive and reward them for achieving goals.

- Relaxation Methods involve voluntarily sequentially contracting and relaxing muscle groups.
  - Allows insight into sensing muscle tension, facilitating relaxation.
  - Strong support for use in treating anxiety, depression, HA, insomnia & chronic pain.

- Biofeedback teaches muscle relaxation and help teach the px self-regulation of pain.
  - Include imagery, hypnosis, meditation, diaphragmatic breathing.
  - Positive effects in chronic LBP, FM, HA, and temporomandibular disorders.
Alternative Therapies/Integrative Approach

- “When evaluating treatments for our patients, we shouldn’t only look at the number to treat, but we should also look at the costs and risks.” - Dr. Andrew Weil

- If there is something out there that may help our patients, when conventional medicine has failed; if it has little risk and is not overly expensive, should we be so quick to dismiss it?
  - TENS unit is a good example
Treatment/Modalities

- **Acupuncture**
  - 2,500 year old Chinese modality aimed at restoring the balance between the yin (blood) and the yang (spirit) which flow in 14 channels or meridians containing 361 acupuncture sites.
  - Two theories of action:
    - May stimulate large afferent fibers via the gate control theory
    - May induce endogenous “opiate-like substances” to effect pain control.
    - Insertion of a needle, regardless of substance injected, can reduce pain. Called the “needle effect”.
  - A NIH panel in 1997 concluded there is clear evidence that acupuncture is effective for pregnancy, postoperative and chemotherapy associated N/V, and post-op dental pain.
    - Also concluded that there are other pain-related conditions for which acupuncture may be effective, despite less convincing scientific data.
      - Addiction, stroke rehabilitation, headache, menstrual cramps, tennis elbow, fibromyalgia (general muscle pain), low back pain, carpal tunnel syndrome, and asthma.
Movement-Based Therapies

- **Feldenkrais** involves slow, fluid reaching, gentle stretching & postural changes for improved kinesthetic awareness & psychologic well-being.
  - Uses verbal cues and touch to facilitate movement.
  - Reported to improve QOL and self-efficacy in pain px’s. Also decreases anxiety & improves mood.
  - Can be done in gravity-eliminated positions, like laying down.

- **T’ai chi** “supreme ultimate boxing” integrates “sharp mental focus with slow, rhythmic, dancelike mov’t sequences & postures that unite mind & body by facilitating the flow of *qi* throughout the body.
  - Reports of helping with pain, strength & flexibility.
- Acupuncture
- Life Energy Flow Tai Yi®
- Reflexology
- Craniosacral Therapy
- Meditation
- Stress Management
- Healing Rhythms
- Movement Therapy
- Therapeutic Massage
- Laughter Yoga
- Nutrition Counseling
- Yoga and Yoga Therapy
Nutrition

- Vit D, B12, B6, and essential fatty acid deficiencies can cause pain.
- Excess Omega-6 fatty acids without appropriate balance with Omega-3 fatty acids results in inflammatory mediators that are more reactive.
Herbal Supplements

- **Inflammation:**
  - Via unknown mechanisms, S-adenosylmethionine (SAMe) 600mg BID shown to be as effective as celebrex in knee OA after 2 months of treatment and as effective as TCA’s in treatment of depression.
  - Omega-3 supplementation
    - 2.7g/day of EPA & DHA improves pain in RA, OA & IBS after 3 months. Rec BID dosing.
  - Ginger up to 4grams/day in divided doses.

- **Sleep dysfunction:**
  - Melatonin, passionflower, casein, 5-HTP, Valerian root

- **Nerve pain:**
  - Alpha-lipoic acid up to 600mg/day in divided doses.

(Najm WI, et al. BMC Musculoskelet Disord. 2004 Feb 26; 5:6)
WHO Pain Pyramid

- High Potency Opioids
- Low Potency Opioids
- NSAID’s
- Acetaminophen
Chronic Pain Pyramid

- High Potency Opioids
- Low Potency Opioids
- Tramadol & Adjuvant Drugs
- Acetaminophen

Gruft, 2005
NSAID’s

- Are ideal for acute conditions (2-3 weeks) to reduce inflammation (except Tylenol) and pain by selectively or non-selectively blocking COX-1&2 pain producing cascades and prostaglandin synthesis.
  - COX-2 is suggested to be more associated with pain via its involvement in peripheral and central sensitization and in mechanisms underlying neuroplastic changes in chronic pain.
  - Also inhibit tissue reaction to bradykinin, suppress release of histamine and decrease vascular permeability.

- All NSAID’s have a ceiling effect.
NSAID’s

- Should be avoided in chronic pain due to GI bleeding (most common 5-10%), renal toxicity, platelet dysfunction & cardiac complications.
  - In 2004, based on review of literature re: NSAID’s, the FDA concluded that adverse CV effects may be a class effect for all NSAID’s (except aspirin).
  - Other NSAID’s can actually block the cardioprotective effects of ASA.

- Ongoing monitoring of BP, hematologic status, and cardiac & kidney function is recommended for px’s on chronic selective & non-selective NSAID’s.
aspirin

- The original & standard NSAID.
- Only one with cardioprotective qualities.
  - Irreversibly blocks thromboxane A2 in platelets, blocking platelet aggregation.
    - Single dose can last 8-10 days.
- Higher rate of gastric irritation (up to 40%).
  - Misoprostol can help preserve gastric lining
- Do not give to children with flu like sx’s or chicken pox to prevent Reye’s Syndrome.
- Toxicity presents as HA, confusion, tinnitus, N/V & hyperventilation if severe.
- Analgesic Dose: 325-650mg/day (max 4g)
- Onset: 15-30 min
- ½ life: 3-6h
- May take 2 weeks for therapeutic response to arthritis.
acetaminophen

- Well tolerated NSAID in children and pregnancy. Usually 1st line.
- Dose: 325-1000mg Q4-6h (4g daily max).
- Onset: 15-30min
- ½ life: 3-6h
- Analgesic & antipyretic
  - Unclear mechanism
- 4g/day may produce fatal hepatic necrosis.
  - Less with EtOH
  - Look for N/V and abdominal pain
  - Give activated charcoal
- Can also produce renal tubular necrosis.
ibuprofen

- Good, inexpensive choice for acute pain conditions due to its ability to decrease inflammation & pain.
- Dose: TID or QID dosing
  - >1600mg/day needed for anti-inflammatory action. Don’t exceed 2400mg/day.
- Onset: 30 min
- ½ life: 2-4h
- Also inhibits platelet aggregation & antipyretic
- However, was shown to block the cardioprotective effects of ASA in a study of over 7,000 patients.
  - Should, therefore be avoided, along with other NSAID’s (except celecoxib) if px requires ASA.
celecoxib

- Only COX-2 inhibitor on the market.
- Less common GI effects through sparing COX-1.
- Dose: 100-200mg daily (200mg max dose)
- Onset: <60min
- ½ life: 9-10h
- Higher risk of CV events with COX-2’s than other NSAID’s.
  - “Black-Box Warning” from FDA.
  - Pfizer sponsored study showed no increased risk compared to other NSAID’s at doses of 200mg/day or less.
    - 400mg/day showed a 2.3-fold increase in risk
    - 800mg/day showed a 3.4-fold increase in risk
Opioids

- Work by binding 3 opioid receptors (mu, delta & kappa).
  - Presynaptically: inhibit calcium influx, decreasing release of excitatory neurotransmitters (serotonin, norepi-, substance P & glutamate).
  - Postsynaptically: hyperpolarize by increasing K influx.
  - In Brainstem: inhibit GABA’ergic transmission, causing enhanced descending inhibition.
Opioids

SE’s include:
- sedation, decreased cognition, poor concentration, lethargy, decreased mental & physical performance
- constipation, N/V
- hypothalamic-pituitary-adrenal/gonadal alterations.
  - Decreased testosterone, progesterone & estradiol causing decreased energy & libido, requiring supplementation.
  - Decreased cortisol response to stress
- tolerance, physical & psychological dependence
- possibly fatal impaired respiration or bradycardia.
- Some evidence that COAT may have a pronociceptive effect over time.
The CBME “strongly urges physicians to view effective pain management as a high priority in all patients”.

- “Tx may involve several drug and non-drug tx modalities, often in combination”.

- “Pain should be assessed and treated promptly, effectively, and for as long as pain persists”.

- “Drugs, particularly the opioid analgesics, are considered the cornerstone of treatment for pain associated with trauma, surgery, medical procedures, and cancer.”
CBME Guidelines for Prescribing Opioids

**Addiction vs. Physical Dependence**

- “Physical dependence and tolerance are normal physiologic consequences of extended opioid therapy and are not the same as addiction.”
- “Patients with chronic pain should not be considered addicts merely because they are being treated with opiates”.
- Tolerance resulting in decreased pain control is much rarer than decreased side effects, especially altered cognition.

“Addiction is a behavioral syndrome characterized by psychological dependence and aberrant drug-related behaviors”.

- “…compulsively uses drugs for non-medical purposes despite harmful effects”
Mixed opinions regarding chronic opioid analgesic therapy (COAT).

- Pain reduction is well documented, but debate occurs over whether there is an increase in function and whether risks of dependency, sedation, and other SE’s are worth the benefits.
  - Many different criteria used in these studies.
    - Chabal et al. “Conflicts arise when incomplete models are used to address a complex problem”
  - One study showed decreased function, increased pain & healthcare utilization with associated benzodiazepine use, but not opioids alone.
  - Haythornthwaite et al. showed reduced pain, anxiety & hostility without decreased cognition in 19 px’s.
    - Actually showed increase in psychomotor speed & sustained attention compared to untreated pain patients.
  - A review of 48 studies (Fishbain et al.) showed moderate evidence for no impairment of psychomotor abilities in opioid dependent px’s & strong evidence for no increase in MVA’s or violations vs. controls (also demonstrated in driving simulators).
    - Further supported by study reporting cognitive deficits in opioid naïve/healthy px’s and not in COAT px’s.
COAT & Chronic Pain

- For px’s with constant pain, it is agreed that scheduled long-acting opioids with short acting prn opioids are better to decrease pain, dependency and periods of breakthrough pain.
- Critical for the physician to cautiously increase or decrease dosing.
  - If px has SE’s 1 week after increasing dose, then it is too much.
  - When dose exceeds pain control, px’s start exhibiting SE’s, unless opioid sensitive.
    - Is an excellent marker for dose titration and should be monitored routinely, including px education to notify MD if they do develop SE’s.
  - “It is better to start too high than too low” to decrease anxiety and pain behaviors due to inadequate analgesia.
    - Also decreases central sensitization when decreasing pain before it starts
- Px should sign a contract re: informed consent & their responsibilities for tx.
  - Should understand that care may be terminated if non-compliant.
COAT & Chronic Pain

Graph showing pain levels throughout the day.
COAT & Chronic Pain

Graph showing pain control and pain course without medications.
COAT & Chronic Pain

![Graph showing pain control and pain course over a day with breakthrough/PRN medication and long-acting medication lines.](graph.png)
Opioids: Compliance

- Monitoring
  - “Monitoring also includes ongoing assessment of patient compliance with the controlled prescribing practice of the physician”. - CBME
    - Urine drug screens are recommended.
  - “Utilization of a single prescribing physician and a single pharmacy is advised”.
    - The Colorado Electronic Prescription Drug Monitoring Program
      - www.coloradopdmp.org
COAT & Chronic Pain

Watch for signs of noncompliance with opioid therapy.

- Unexpected results on tox screens
- Frequent requests for dose increases
- Concurrent use of nonprescribed psychoactive substances
- Failure to follow dosing schedule
- Failure to adhere to concurrently recommended tx’s
- Frequently reported lost prescriptions or meds
- Frequent ER visits for opioid therapy
- Missed f/u visits
- Frequent extra appointments
- Prescriptions from a 2\textsuperscript{nd} provider
- Tampering with prescriptions
COAT & Chronic Pain

Dosing

- Titration is generally accomplished by increasing or decreasing the next total daily dose by \( \frac{1}{4}-\frac{1}{2} \) the previous dose.

- Each dose of rapid acting q 4-6h prn opioids should be given at 10% of the px’s daily baseline opioid dose.
  - Or 40-60% of total daily dose.
COAT & Chronic Pain

Dosing

- If px is inpatient can convert 75% of previous opioid dose to long-acting with 25% short acting due to incomplete cross-tolerance.

- If outpatient, convert 50% of previous opioid dose to long-acting with 50% short acting.

  - For example: px is on 20mg of hydrocodone q6h (80mg/day), conversion dose of hydro- to oxycodone is 1:1, prescribe 20mg of oxycodone q12h and 10mg hydrocodone q6h prn.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Approximate equianalgesic oral dose</th>
<th>Approximate equianalgesic parenteral dose</th>
<th>Recommended starting dose (adults more than 50 kg body weight) oral</th>
<th>Recommended starting dose (children and adults less than 50 kg body weight) oral</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioid Agonist</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>30 mg q 3-4 hr (around-the-clock dosing)</td>
<td>10 mg q 3-4 hr</td>
<td>30 mg q 3-4 hr</td>
<td>0.3 mg/kg q 3-4 hr</td>
</tr>
<tr>
<td></td>
<td>60 mg q 3-4 hr (single dose or intermittent dosing)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Codeine</td>
<td>130 mg q 3-4 hr</td>
<td>75 mg q 3-4 hr</td>
<td>60 mg q 3-4 hr</td>
<td>1 mg/kg q 3-4 hr</td>
</tr>
<tr>
<td>Hydrocodone (in Lorcet, Lortab, Vicodin, others)</td>
<td>30 mg q 3-4 hr</td>
<td>Not available</td>
<td>Not available</td>
<td>Not available</td>
</tr>
<tr>
<td>Hydromorphone (Dilaudid)</td>
<td>7.5 mg q 3-4 hr</td>
<td>1.5 mg q 3-4 hr</td>
<td>6 mg q 3-4 hr</td>
<td>0.06 mg/kg q 3-4 hr</td>
</tr>
<tr>
<td>Hydrocodone (in Lorcet, Lortab, Vicodin, others)</td>
<td>30 mg q 3-4 hr</td>
<td>Not available</td>
<td>Not available</td>
<td>0.015 mg/kg q 3-4 hr</td>
</tr>
<tr>
<td>Levoephonol (Levo-Dromoran)</td>
<td>4 mg q 6-8 hr</td>
<td>2 mg q 6-8 hr</td>
<td>4 mg q 6-8 hr</td>
<td>0.04 mg/kg q 6-8 hr</td>
</tr>
<tr>
<td>Meperidine (Demerol)</td>
<td>300 mg q 2-3 hr</td>
<td>100 mg q 3 hr</td>
<td>Not recommended</td>
<td>0.75 mg/kg q 2-3 hr</td>
</tr>
<tr>
<td>Methadone (Dolophine, others)</td>
<td>20 mg q 6-8 hr</td>
<td>10 mg q 6-8 hr</td>
<td>10 mg q 6-8 hr</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Oxycodeone (Roxicodone, also in Percocet, Percodan, Tylox, others)</td>
<td>30 mg q 3-4 hr</td>
<td>Not available</td>
<td>Not available</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Oxymorphone (Numorphan)</td>
<td>Not available</td>
<td>1 mg q 3-4 hr</td>
<td>Not available</td>
<td>0.2 mg/kg q 3-4 hr</td>
</tr>
</tbody>
</table>

| **Opioid Agonist-Antagonist and Partial Agonist** | | | | |
| Buprenorphine (Buprenex)    | Not available                        | 0.3-0.4 mg q 6-8 hr | Not available | 0.004 mg/kg q 6-8 hr |
| Butorphanol (Stadol)        | Not available                        | 2 mg q 3-4 hr | Not available | Not recommended |
| Nalbuphine (Nubain)         | Not available                        | 10 mg q 3-4 hr | Not available | Not recommended |
| Pentazocine (Tailwin, others) | 150 mg q 3-4 hr                 | 60 mg q 3-4 hr | Not recommended | Not recommended |

**Note:** Published tables vary in the suggested doses that are equianalgesic to morphine. Clinical response is the criterion that must be applied for each patient; titration to clinical response is necessary. Because there is not complete cross tolerance among these drugs, it is usually necessary to use a lower than equianalgesic dose when changing drugs and to titrate to response.

**Caution:** Recommended doses do not apply to patients with renal or hepatic insufficiency or other conditions affecting drug metabolism and kinetics.

**Caution:** Doses listed for patients with body weight less than 50 kg cannot be used as initial starting doses in babies less than 6 months of age. Consult the Clinical Practice Guideline for Acute Pain Management: Operative or Medical Procedures and Trauma section on management of pain in neonates for recommendations.

**Caution:** Codeine doses above 65 mg often are not appropriate due to diminishing incremental analgesia with increasing doses but continually increasing constipation and other side effects.

**Caution:** Doses of aspirin and acetaminophen in combination opioid/NSAID preparations must also be adjusted to the patient's body weight.
tramadol

- Not a true opioid, but a weak opioid agonist.
  - Also norepi- & serotonin reuptake inhibitor.
  - Analgesic effect not well understood.
- Great 1st line medication for mild/mod pain, especially in the elderly due to lower SE profile.
- Dose: 25-50mg Q4-6h (max dose 400mg/day)
  - Start with 25mg/day and titrate up q3 days to 25mg qid
  - Then start 50mg/day & repeat
  - Then start 100mg/day & repeat up to 100mg qid
- Onset: 60 min
- ½ life: 7 hours
- Doses greater than 400mg/day associated with seizures.
acetaminophen/hydrocodone

- **1st line opioid.**
  - Is schedule III with proposed less abuse potential
  - Can write 2 refills and see 3 months later.

- **Dose:** 5-10mg q 4-6h (max dose 4g/day of acetaminophen)
  - Preferably prescribe 10/325 tablets, instead of 5/325, as 10’s can be split in half and have less acetaminophen.

- **Onset:** 10-30 min
- **½ life:** 3.8 hours
oxycodone

- 1st line long-acting opioid.
  - IR form is a good breakthrough medication, if Norco insufficient.
- Dose: 10-160mg BID (long-acting/”-contin”) or 10-30mg q4h (short acting/”-codone”).
  - 5mg q6h for OxyIR
  - max dose 4g/day of acetaminophen
- Onset: 40 min (CR) & 10-15 min (IR)
- ½ life: 4.5 hours (CR) & 3.2 hours (IR)
methadone

- Synthetic opioid.
- Has NMDA receptor blocking action which may reduce central sensitization and opioid tolerance.
  - Seems to have better neuropathic pain reducing properties than other opioids
  - Better choice in high abuse potential patients, but still can be abused!
- Dose: Initially, 2.5-10mg q6h prn, then after 6 days split average daily dose to BID scheduled.
  - 20-120mg/day for dependency tx
- Onset: 30-60 min
- ½ life: 7 hours-5 days!
  - Only increase dose at least every 5 days
- Less sedation & N/V than classic opioids.
  - Still has equivalent respiratory depressive effects & constipation.
fentanyl patch

- If px tolerating and stable on oxy-CR, can switch to a 72-hour patch for convenience, or increasing compliance.
- Dose: 25-100mcg/h q 72 hours
- Onset: steady state at 24h
  - If switching to fentanyl, prescriber should give normal dose of previous long-acting opioid for 1st 24hrs.
- ½ life: 17 hours
- SE’s: watch for skin reaction/ulceration (3-10%).
  - Avoid in liver or kidney disease.
  - Avoid heating sources, as can increase release of fentanyl.

<table>
<thead>
<tr>
<th>Patch Dose</th>
<th>codeine</th>
<th>oxy-/hydrocodone</th>
<th>morphine</th>
<th>hydromorphone</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 mcg/hr</td>
<td>150-447 mg/day</td>
<td>22.5-67 mg/day</td>
<td>45-134 mg/day</td>
<td>5.6-17 mg/day</td>
</tr>
<tr>
<td>50 mcg/hr</td>
<td>448-747 mg/day</td>
<td>67.5-112 mg/day</td>
<td>135-224 mg/day</td>
<td>17.1-28 mg/day</td>
</tr>
<tr>
<td>75 mcg/hr</td>
<td>748-1047 mg/day</td>
<td>112.5-157 mg/day</td>
<td>225-314 mg/day</td>
<td>28.1-39 mg/day</td>
</tr>
<tr>
<td>100 mcg/hr</td>
<td>1048-1347 mg/day</td>
<td>157.5-202 mg/day</td>
<td>315.49 mg/day</td>
<td>39.1-51 mg/day</td>
</tr>
</tbody>
</table>
Hydoxyzine

- Antihistamine that potentiates analgesic effects of opioids, as well as having intrinsic analgesic, anxiolytic and anti-nausea effects.
  - Unknown mechanism
- Dose: 25-50mg TID-QID
  - Can dose to give with opioids, like Norco.
  - If sedated, switch to 10mg TID-QID.
- Onset: 15-30 min
- ½ life: 3 hours
- SE’s: chest tightness (may be pleurisy from dry mucus membranes), tremor/convulsions, dry mouth.
lidocaine patch

- Can be great for focal superficial, especially neuropathic, pain.
  - Approved for post-herpetic neuralgia.
- Dose: 1-3 patches for 12 hours on and 12 hours off, daily.
  - One 12 hour patch contains 700mg of lidocaine (50mg/gram)
- Onset: peaks at 12 hours
- $\frac{1}{2}$ life: 81-149 min
- SE’s: watch for skin reaction/ulceration.
- Avoid in liver disease and non-intact skin
Benzodiazepines

- Benzo’s are the only class of drug that the withdrawal symptoms are the same symptoms the drug is designed to treat.
  - If someone is tolerant and trying to get off of it, they will have anxiety, palpitations & a jittery feeling purely from withdrawal. Not a psychologic disorder.
Anti-convulsants

- Older antiepileptic drugs have severe SE’s (hepatotoxicity, hematologic effects, etc) and require frequent monitoring.
- Newer agents have been shown to have good results treating neuropathic pain, sometimes “off-label”.
- Used more with HA’s (tegretol, topamax, depakote)
  - Tegretol FDA approved for migraines.
pregabalin

- Arguably 1\textsuperscript{st} line for neuropathic pain.
  - FDA approved for post-herpetic neuralgia, diabetic peripheral neuropathy & the first drug approved for fibromyalgia.
  - Off label for neuropathic pain, but approved in Europe.
- Less reports of lethargy & dizziness than with gabapentin, but can cause liver damage and “true” weight gain.
  - No intrinsic activity
  - If failed gabapentin trial, can still try Lyrica.
  - Modulates calcium voltage gated channels, decreasing release of excitatory neurotransmitters.
    - Via alpha-2-delta ligand agonist activity (like gabapentin)
- Dose: 75mg BID (unless sensitive, use 50mg BID)
  - If no improvement after 3 days, stop it.
  - If some improvement, double it (300mg BID is max dose).
- Onset: <60 min
- ½ life: 6.3 hours, steady state in 24-48 hours
gabapentin

- Older, cheaper and effective for neuropathic pain.
  - Off label for a number of neuropathic pain conditions.
  - Modulates calcium voltage gated channels, decreasing release of excitatory neurotransmitters.
    - Via alpha-2-delta ligand agonist activity (like gabapentin)
- Dose: 300mg daily to 1600mg TID
  - Increase dose by 300mg Q 3 days as outpx.
    - Daily in inpx setting.
  - If no effect at 300mg TID, stop it.
- $\frac{1}{2}$ life: 5-7 hours
- SE’s: dizziness, lethargy, tremors & dysmetria in elderly.
  - Initial mild SE’s may resolve in 2-3 d. Wait before stopping or increasing.
Antispasmodics

- Mechanism of action of muscle relaxers is unknown
  - Sedation?
- Treat muscle or nerve spasms.
- Works for neuropathic pain and myofascial pain with spasms.
baclofen

- GABA derivative.
- Appears to primarily inhibit spinal efferent & afferent pathways by functioning as an inhibitory neurotransmitter.
- The primary site of action is the spinal cord, where baclofen also reduces the release of excitatory neurotransmitters.
- Dose: 5mg TID
  - Can increase by 5mg/dose Q3 days
  - Max dose 80 mg/day
- Onset:
- ½ life: 2.5-4 hours
- SE’s: hypotonia, drowsiness, hypotension
tizanidine

- Centrally acting alpha blocker
  - Exact mechanism is unknown.
- Dose: 4-36 mg/day
  - Can increase in 2-4mg increments Q 6-8 hours for optimum effect.
- T max: 1.5 hours
- ½ life: 2.5 hours
- SE’s: hypotension, impotence, drowsiness, orthostatic hypotension.
clonidine

- Can be used for spasticity, but great for new-onset CRPS, especially in children.
- 1st line for opioid withdrawal sx’s.
  - Stuffy nose, N/V/D, bone aches (like a bad flu).
- Dose: 0.1-0.3mg BID for withdrawal
  - 0.1-0.3mg QHS for hot flashes perimenopausal women.
- Onset: 30-60 min
- ½ life: 12-16 hours
- SE’s: hypotension, impotence, drowsiness, orthostatic hypotension.
Tricyclic Antidepressants

- Older antidepressants
- Have serotonergic > noradrenergic effects and all have antihistaminergic effects.
  - Except for desipramine
- Also antagonize Na channels, alpha-2 & H1 receptors
- All are a little distinct from each other.
- TCA’s don’t work for pain until 7-14 days, but work for sleep immediately & depression in up to 1 month.
- All should be given at 25-100 mg QHS
  - Except desipramine which is BID
- Dangerous at high doses
  - Can cause irreversible liver necrosis and may be a poor choice for severely depressed.
amitriptyline

- Large muscarinic effects (dry mouth, sedation, orthostatics).
- Has the highest incidence of SE’s than other TCA’s discussed.
- Dose: 25-100mg QHS
- ½ life: 10-28 hours
- SE’s: weight gain due to increased appetite
doxepin

- Accomplishes what amitriptyline does with fewer SE’s.
- Dose: 25-100mg QHS
- ½ life: 8-24 hours
desipramine

- Has the least anticholinergic and sedative effects of the 1st generation TCA’s.
- Has similar analgesic effects.
- Only TCA that selectively block norepinephrine reuptake > serotonin.
- Dose: 10-50 mg BID
- Onset: 28-31 hours
trazodone

- A heterocyclic antidepressant (4 rings)
- Great for sleep, as well as having some analgesic effects (less than TCA’s, however).
  - Serotonin reuptake inhibitor
  - Shorter ½ life than other TCA’s resulting in less daytime sleepiness.
- Dose: 25-100mg QHS
- ½ life: biphasic 3-6 hours & 5-9 hours
- SE’s: lower anticholinergic profile than TCA’s.
  - Can cause priapism (less likely to prescribe to men), and up to 30% have vivid dreams that may be tolerated.
Sleep Medications

- Stage III & IV sleep are restorative.
  - Benzo’s and opioids can both decrease these stages of sleep.
    - Non-benzo’s don’t.
- Sleep is crucial to chronic pain management.
- Need to find if trouble falling and/or staying asleep to prescribe right meds.
  - Pain or anxiety a factor?
    - If pain, use a TCA and can use ambien/flexeril combinations.
    - Anxiety might benefit from clonazepam, which affects the sleep cycle the least of the benzodiazepines and has a convenient 8hr half-life.
Sleep Medications

- If mild insomnia use over-the-counter supplements:
  - 5-HTP at 50-100mg QHS.
    - Crosses the BBB and converted to serotonin.
  - Valerian Root at 400-800mg QHS
    - Has a mild serotonin, norepi- and dopamine reuptake blocker.
  - Melatonin: a hormone that is good for jet-lag.
    - Take for 3 days before a trip at the time you will be going to sleep.
zolpidem

- Non-benzodiazepine hypnotic
  - Interacts with GABA-benzodiazepine complex to facilitate GABA transmission.

- Classic medication for trouble falling, not staying asleep
  - Quickly metabolized with least amount of am sedation.

- Dose: 5-10mg QHS

- ½ life: 2.6 hours (CR has a delayed release)

- SE’s: sleep walking and driving.
  - Do not give to px’s with hx of sleep walking and advise px to monitor.
clonazepam

- Benzodiazepine with least effect on decreasing Stage III & IV sleep.
  - temazepam, diazepam, lorazepam & triazolam are worse.
- Better for px’s with frequent sleep interruptions or with anxiety component.
- Dose: 0.5-2.5mg QHS
- T max: 1-4 hours
- ½ life: 30-40 hours
- SE’s: Hepatotoxicity.
  - Monitor LFT’s.
eszopiclone

- New longer acting non-benzodiazepine hypnotic
  - Interacts with GABA-benzodiazepine complex to facilitate GABA transmission.
- FDA approved for long-term management of insomnia.
- Dose: 1-3mg QHS
- ½ life: 6 hours
cyclobenzaprine

- Is a actually a TCA, but has different effects
  - Is also a serotonin reuptake blocker that helps deepen sleep.
- Dose: 10 mg QHS initially for sleep.
- Onset: 1 hour
- ½ life: 1-3 days
Summary

- Chronic Pain is persistent pain that no longer serves a purpose.
- It is a complicated entity that is intimately linked to psychological well-being, sleep patterns, function & relationships.
- The bio-psycho-social model of diagnosis and treatment is the most effective means of treatment and involves a multidisciplinary team approach.
- Medications are only a small part of treating chronic pain and should be used with caution with appropriate monitoring and follow-up.
- The goal is not to eliminate pain, but to empower the patient to be in charge of their pain so that they may lead a full and active life.
Bibliography

Video Clip References


Bibliography

- http://www.georgiapainphysicians.com/l2_edu_pharma_mod2_slides.htm
- Williams GW. Identifying appropriate patients for NSAIDS. CMEZone.com Sept. 2007.

Special Thanks to Dr. James Gruft!