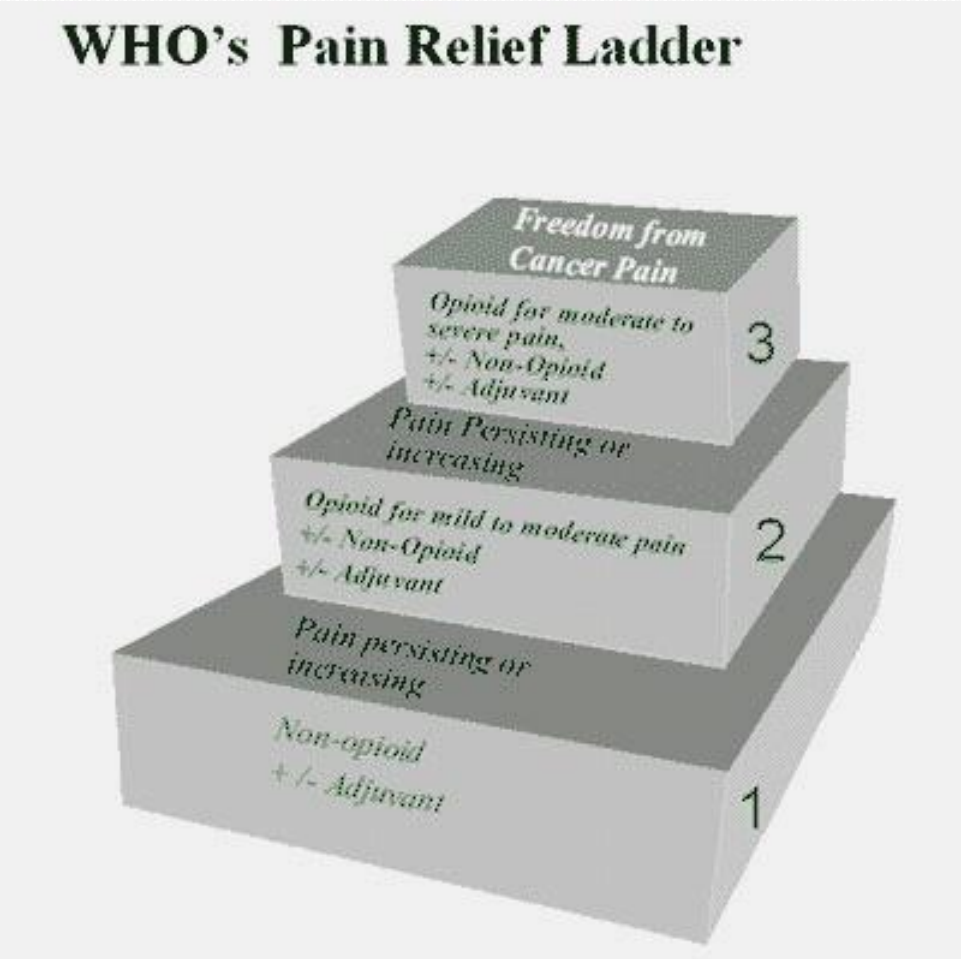
Medications and Pain

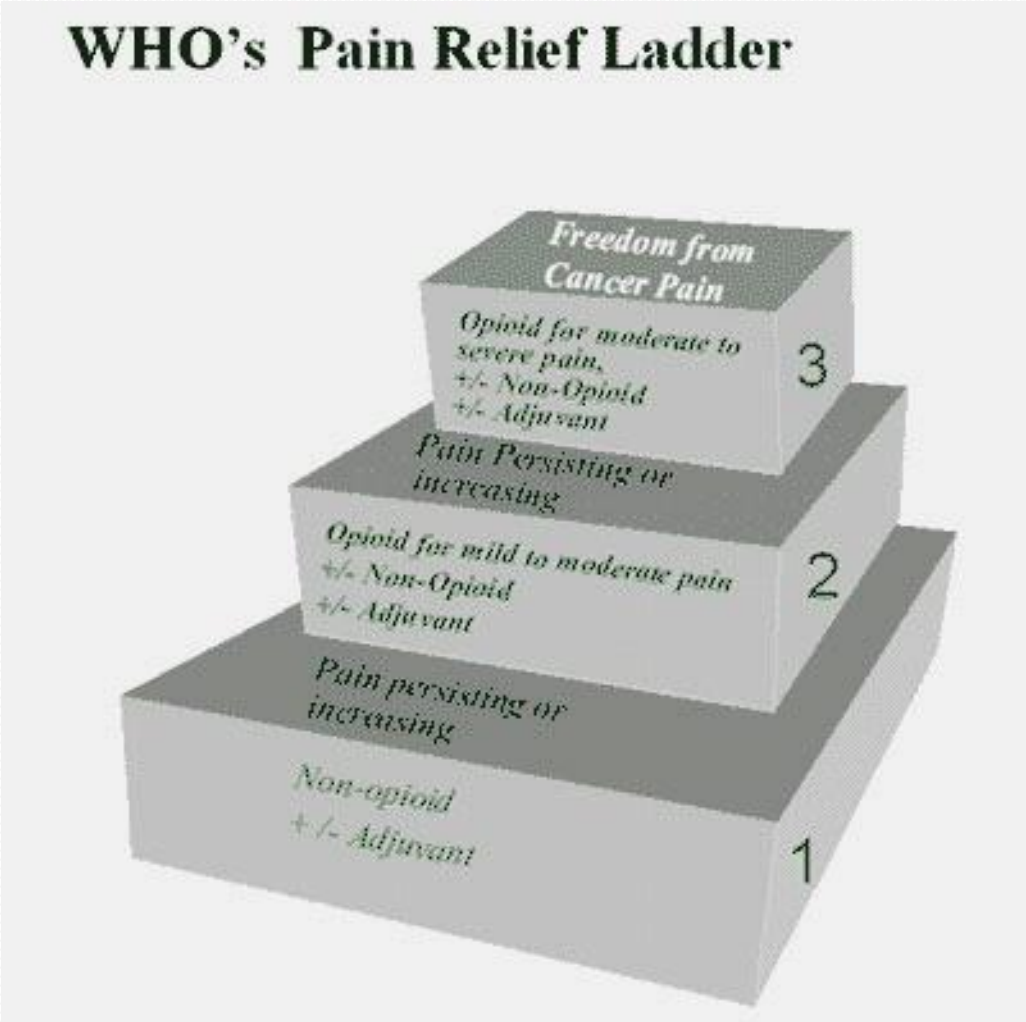
Symptom Management: Medical Treatment of Pain

WHO's pain ladder
- developed for cancer pain, now applied for nonmalignant chronic pain as well



Step 1: Non-Opioid Analgesics

- Aspirin
- Tylenol
- Other NSAIDs



Tylenol(acetaminophen) toxicity

- Chronic tylenol ingestion of 4000 mg per day (8 vicodin) can produce liver damage
- Lower doses can be toxic when fasting/not eating well or if taken with alcohol

- Extra strength tylenol has 500 mg
- Vicodin, norco, lortab have from 325 – 750 mg per tab
- Many cold and flu medicines have acetaminophen in them as well

Adverse effects of NSAIDs (Anti-inflammatory drugs):

- Stomach and GI tract
  - Ulcers and internal bleeding
  - Leaky Gut: Increased intestinal permeability
- Bones and Joints
  - Bone necrosis and cartilage destruction
  - Inhibition of cartilage synthesis
- Other organs
  - Liver damage
  - Kidney injury
- Death

NSAIDs and the Stomach

- 107,000 patients hospitalized per year for stomach complications
- **16,500 NSAID-related deaths occur each year among arthritis patients**

Am J Med. 1998 Jul 27; 105(1B): 31S-38S

The “safer” anti-inflammatories?

Merck to Withdraw Vioxx Because of Heart Risks

Sept. 30 (Bloomberg) -- Merck & Co. withdrew its Vioxx painkiller, which generated $2.5 billion in sales last year, because of a link to heart attacks and strokes. The company's shares slid as much as 28 percent, wiping out $28 billion in market value.

New three-year data from Merck suggested that patients taking Vioxx for more than 18 months faced twice the risk of a heart attack compared with those taking a placebo.

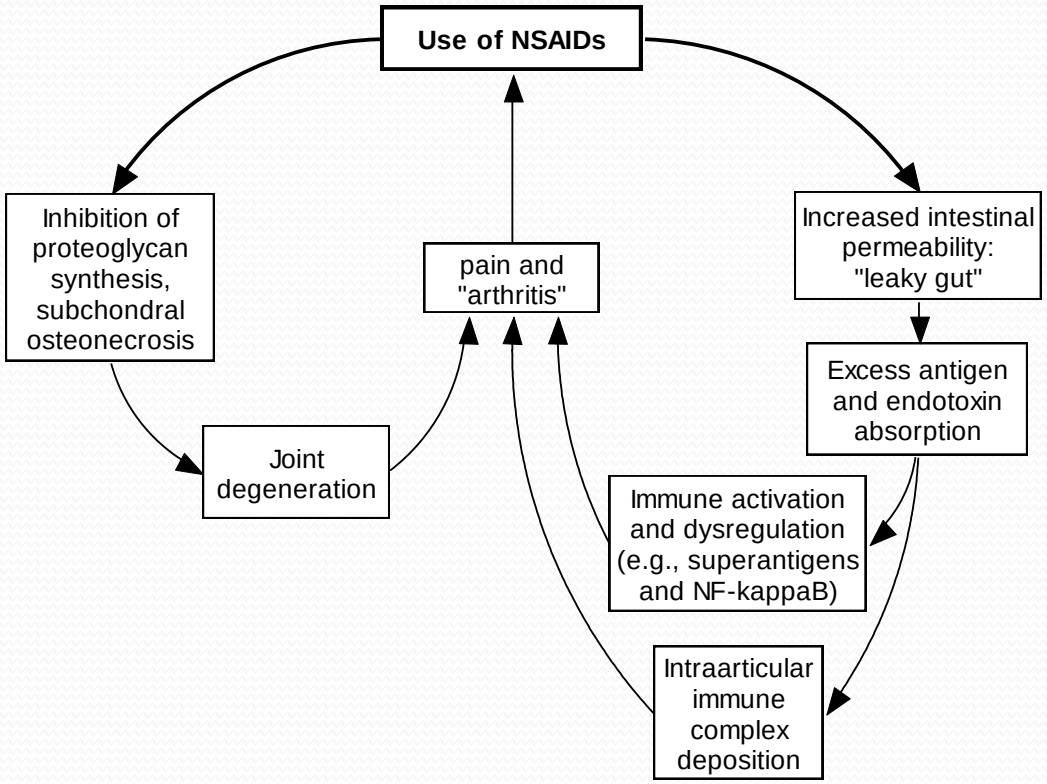
NSAIDs Block Joint Repair

In vivo studies with NSAIDs at physiologic concentrations have shown that several NSAIDs reduce glycosaminoglycan synthesis.

- Salicylate
- Acetylsalicylic acid
- Fenoprofen
- Isoxicam
- Tolmetin
- Ibuprofen

- "…femoral head collapse and **acceleration of osteoarthritis have been well documented in association with the NSAIDs…**" *Lancet*. 1985 Jul 6; 2(8445): 11-4

Vicious Cycle of NSAID Use: Chondrolysis and Intestinal Injury



Rheum Dis Clin North Am. 1991 May;17(2):309-21

If you have to take an NSAID. . .

- Safer in combination with
  - Misoprostol
  - Proton Pump Inhibitor like prilosec
    - But that has a whole host of other side effects. . . .

Another non-narcotic option: Devil's Claw

- Harpagophytum procumbens (Devil's claw) – 60 mg harpagoside per day
- Primarily analgesic, not much anti-inflammatory activity; in one study was as effective as vioxx for low back pain
- Try for 4-8 weeks

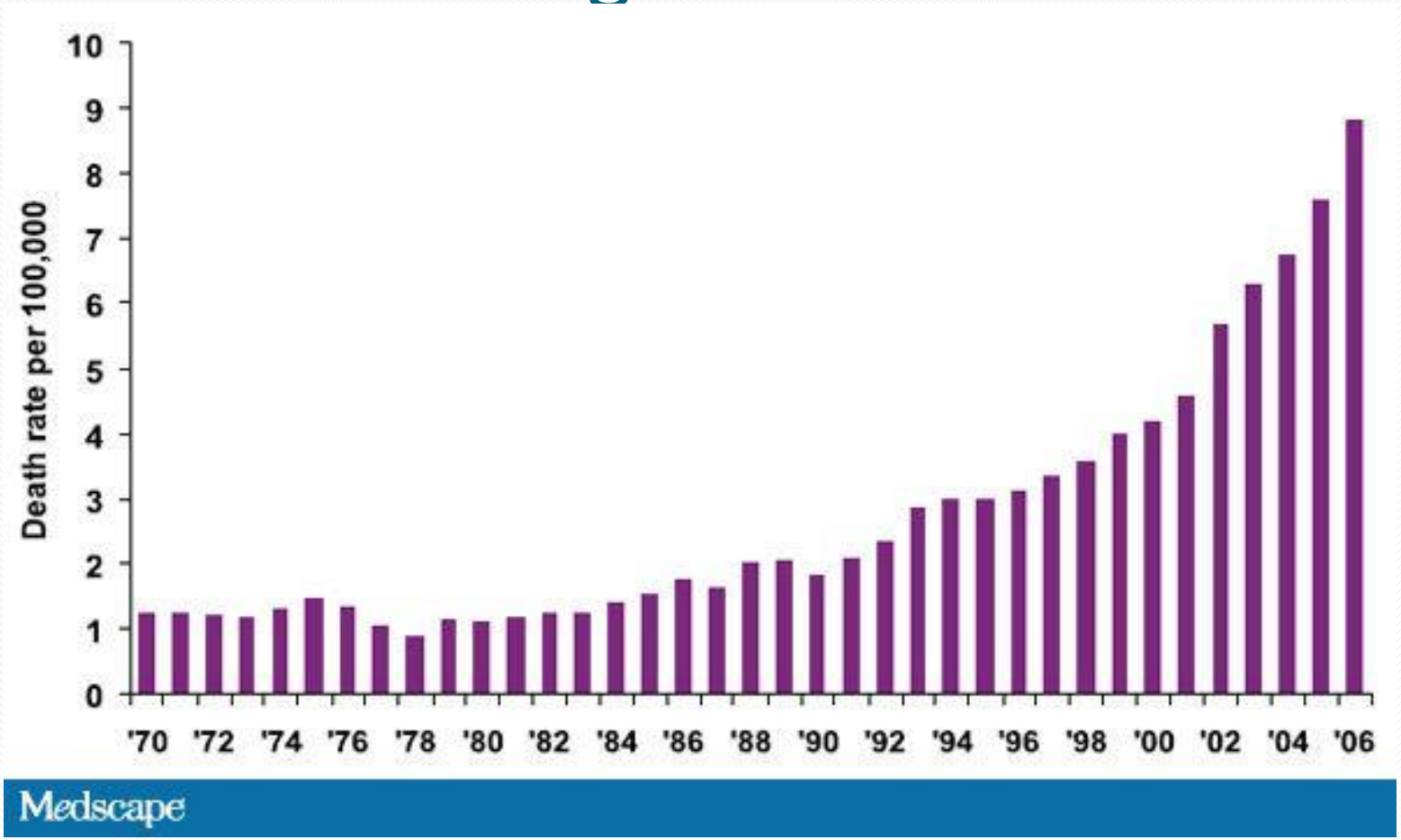
Tramadol = Ultram

- Milder version of an opioid
- Morphine and others bind to kappa and mu opioid receptors
- Tramadol binds to kappa but not mu
  - Less addictive potential
  - Works better in women than men
- Risk of seizures in excessive doses or in combination with some antidepressants

Opioids in Chronic Pain Management

- Benefits and Risks

Unintentional Drug Overdose Deaths



In 2007, there were over 28,000 unintentional drug overdose deaths in this country

Opioids in Chronic Nonmalignant Pain

- Side effects: constipation, sleep disruption, altered mental status, itching, nausea, respiratory depression
- Addiction vs. Dependence

- Bottom line:
  - Assessing whether medication improves quality of life and participation in life or diminishes them

Questions to Ask Before Starting:

- Have there been any other chemical (alcohol or drug) abuse problems in the person's life?
- Is there a family history of substance abuse?
- Is there a history of sexual abuse prior to adolescence?
- Is there psychological disease? (Depression, bipolar, OCD, ADHD, etc.)

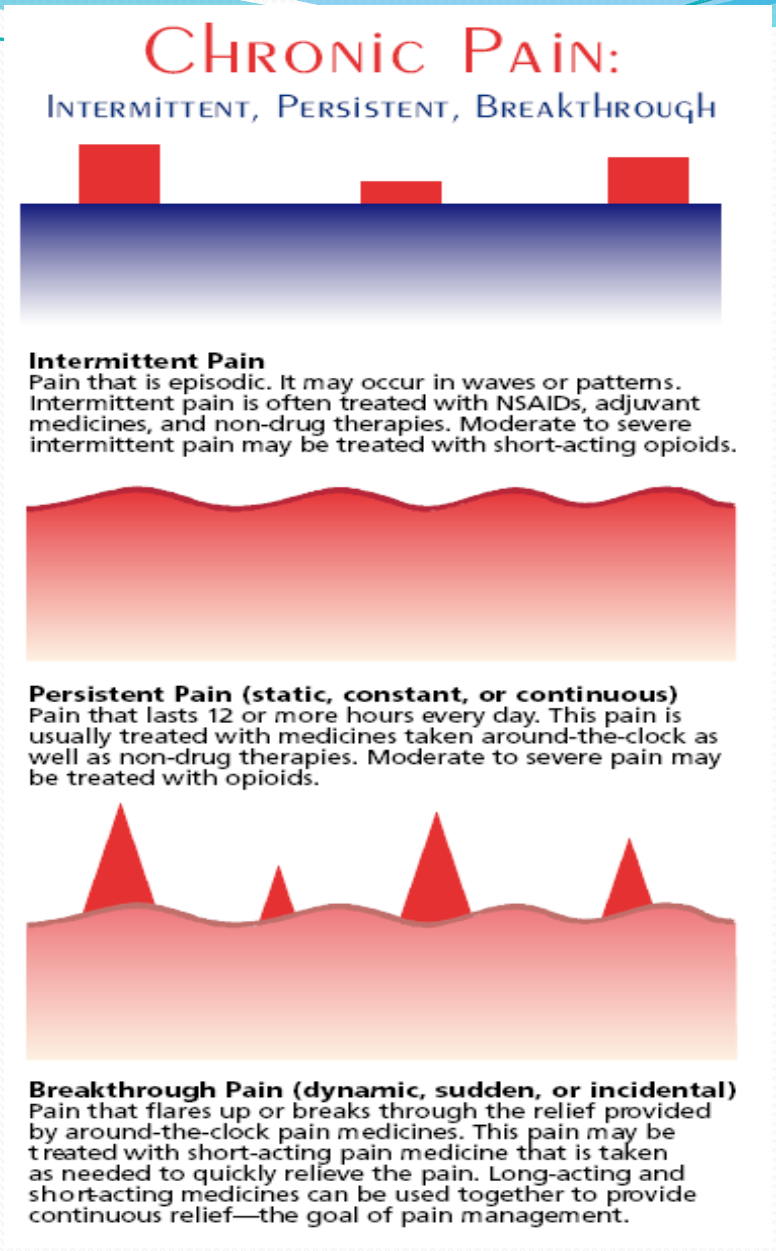
Questions to Ask When Taking:

- *Is your day centered around taking medication?*
- *Do you spend most of the day resting, avoiding activity, or feeling depressed?*
- *Are you able to function (work, household chores, and play) with pain medication in a way that is clearly better than without?*

Signs Someone is Being Harmed more than Helped by Pain Medication

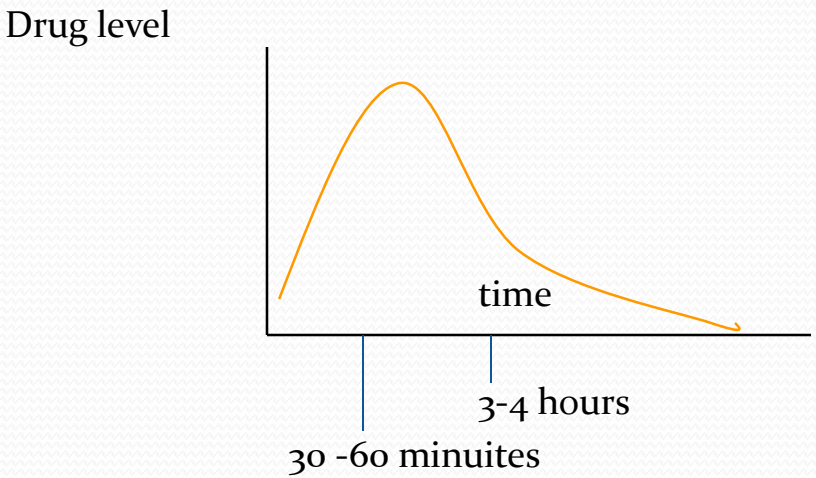
- Sleeping too much or having days and nights confused
- Decrease in appetite
- Inability to concentrate or short attention span
- Mood swings (especially irritability)
- Lack of involvement with others
- Difficulty functioning

Proper use of opioid pain medications

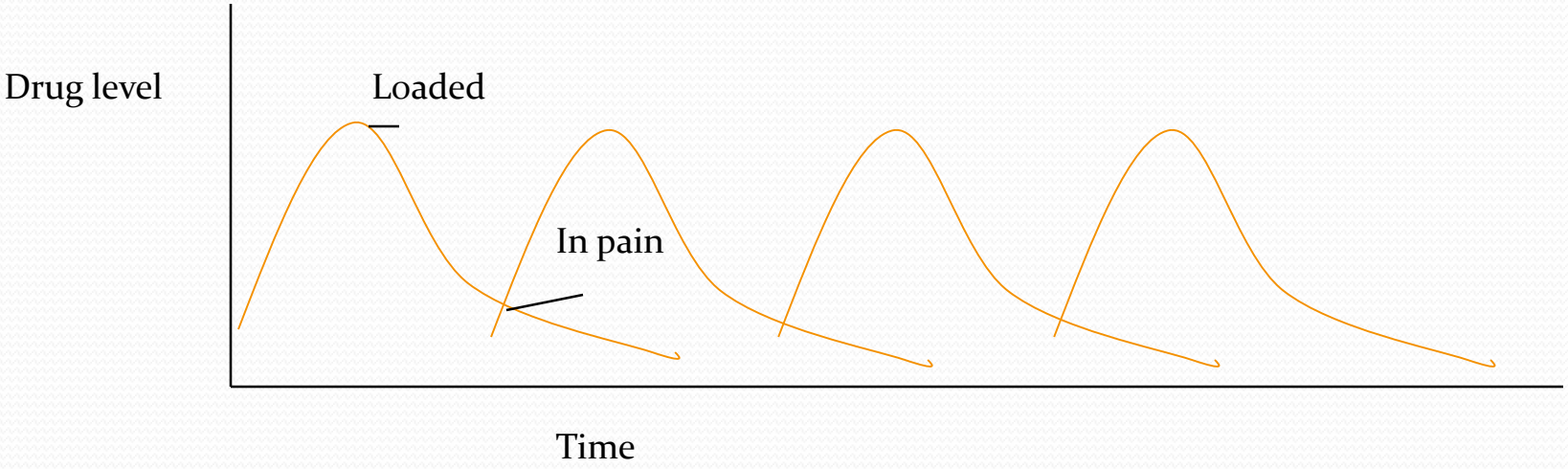


Timing

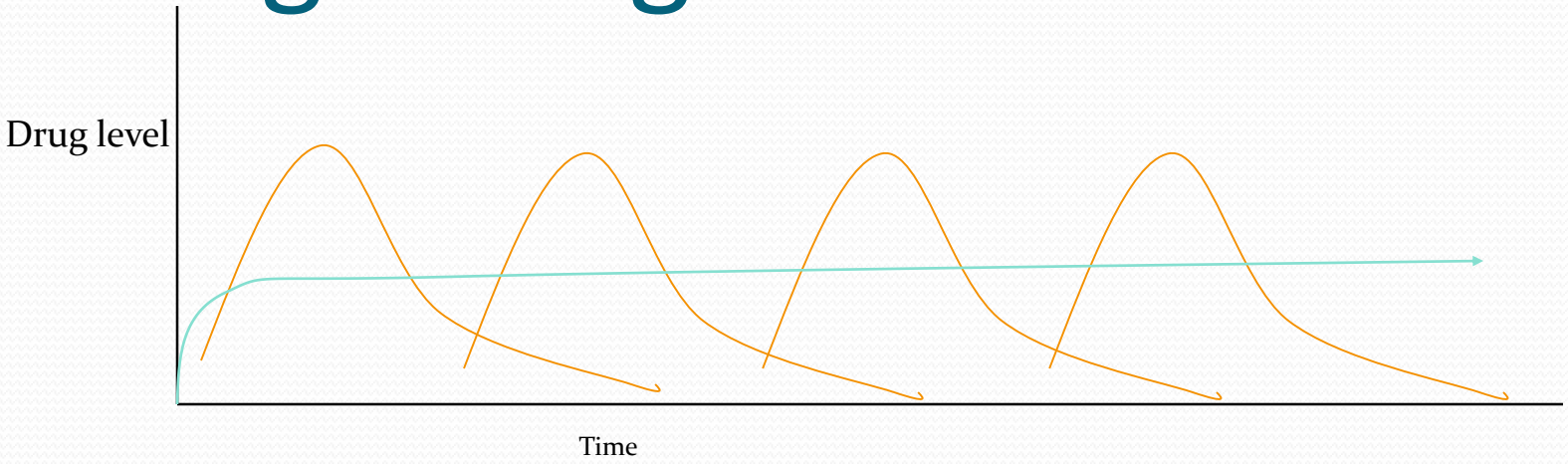
- Short-acting/Rescue medications: codeine, hydrocodone, oxycodone, morphine



Problems with Short-acting Medications



Long-acting narcotics:



- Fentanyl patches (Duragesic)
- Methadone
- MS Contin
- OxyContin
- Exalgo
- Opana ER
  - Need to be dosed on a schedule, <u>not</u> prn

Opioid-induced Hyperalgesia

- Animal studies show that repeated opioid administration. . . can lead to a progressive and lasting reduction of baseline nociceptive thresholds, resulting in an

  increase in pain sensitivity.

- The decreased baseline nociceptive thresholds lasted as long as 5 days after the cessation of four fentanyl bolus injections

Opioid-induced Hyperalgesia

- Six chronic low back pain patients
- Quantitative sensory testing (cold and heat) before and after starting oral morphine
- Preliminary results showed hyperalgesia and tolerance with cold but no hyperalgesia with heat or analgesic tolerance to heat pain.

- Chu L.F., Clark D.J., Angst M.S.: Opioid tolerance and hyperalgesia in chronic pain patients after one month of oral morphine therapy: a preliminary prospective study. *J Pain* 7. (1): 43-48.2006

Opioid-induced Hyperalgesia

- Patients treated intraoperatively with remifentanil reported more postoperative pain than the matched nonopioid controls

- Vinik H.R., Igor K.: Rapid development of tolerance to analgesia during remifentanil infusion in humans. *Anesth Analg* 86. 307-311.1998;
  Crawford M.W., Hickey C., Zaarour C., et al: Development of acute opioid tolerance during infusion of remifentanil for pediatric scoliosis surgery. *Anesth Analg* 102. (6): 1662-1667.2006;
- Guignard B., Bossard A.E., Coste C., et al: Acute opioid tolerance: intraoperative remifentanil increases postoperative pain and morphine requiremnt. *Anesthesiology* 93. (2): 409-417.2000;

Opioid-induced Hyperalgesia

- **A number of case reports document decreases in pain with stopping opioids**

- Wilson G.R., Reisfield G.M.: Morphine hyperalgesia: a case report. *Am J Hosp Palliat Care* 20. (6): 459-461.2003
  Mercadante S., Ferrera P., Villari P., et al: Hyperalgesia: an emerging iatrogenic syndrome. *J Pain Symptom Manage* 26. (2): 769-775.2003;
- Heger S., Maier C., Otter K., et al: Morphine induced allodynia in a child with brain tumour. *BMJ* 319. (7210): 627-629.1999;
- Sjogren P., Jensen N.H., Jensen T.S.: Disappearance of morphine-induced hyperalgesia after discontinuing or substituting morphine with opioid agonists. *Pain* 59. 313-316.1994;

- Mechanism may be NMDA receptor-mediated central sensitization

So why/when use them?

- Opioids are most helpful in Acute Pain

- In Chronic Pain, I recommend them as a bridge:
  - Premedicate to increase activity level
  - Medicate to get good, deep sleep

  - As sleep improves and activity improves, try to wean

Stopping or Tapering Opioids

- Withdrawal Symptoms
  - Anxiety/Restlessness
  - Sweating
  - Insomnia
  - Diarrhea
  - Nausea, vomiting
  - Yawning, rhinorrhea (runny nose)
  - Transient increase in pain

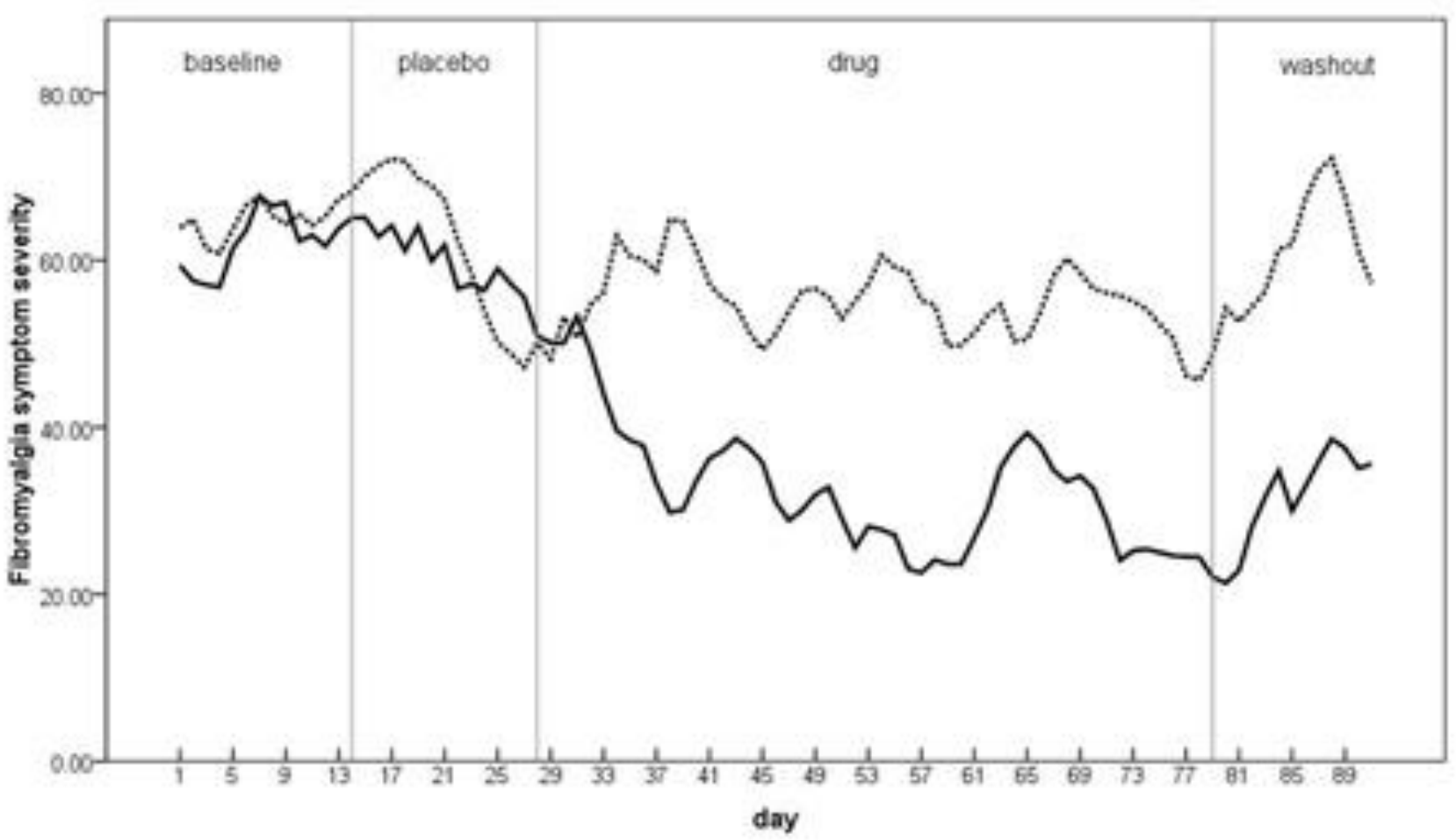
Treatment of Withdrawal

- Each of the symptoms of withdrawal can be treated, and herbal support is also available for opioid withdrawal
  - Suboxone
  - Passionflower
  - Clonidine
  - Lomotil
  - Hydroxyzine
  - Trazodone
  - Etc.

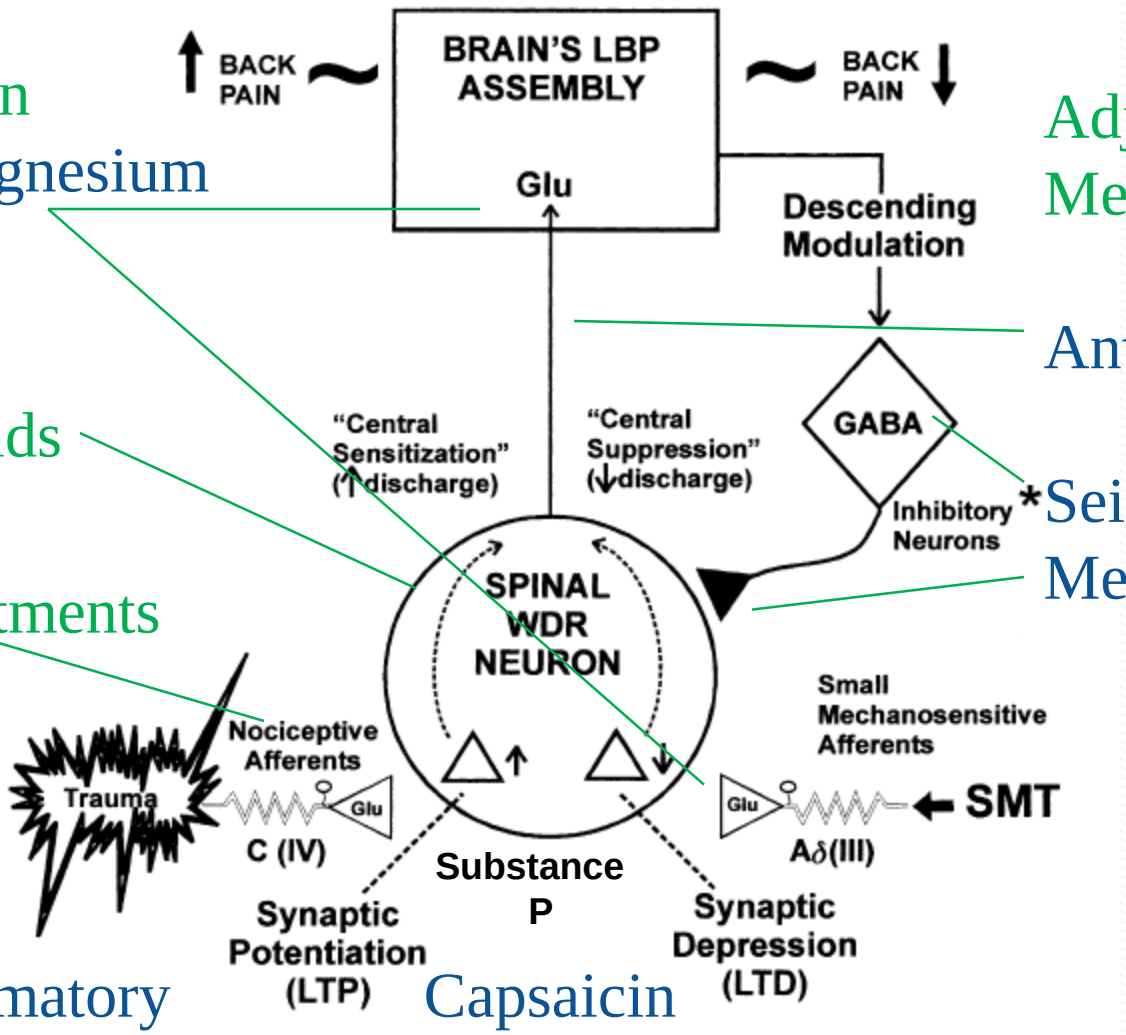
Adjunctive Medications

- Topical – lidocaine, capsaicin, anti-inflammatories, other
- Antidepressants
- Anticonvulsants
- Antiarrhythmic drugs

And for something completely different: Low Dose Naltrexone - LDN



Adjunctive Therapies



Nutrition

Magnesium

Opioids

Topical treatments

Anti-inflammatory

Turmeric

Capsaicin

Lidocaine

Adjunctive Medications

Antidepressants

*Seizure Medications

Antidepressants for Pain

- Work by affecting neurotransmitters
- Do not only work for treating pain by improving depression.
  - Work as well in non-depressed people as in people with depression
  - Effectiveness for pain does not correlate with effectiveness for depression
- Do not work for all types of pain.

Adjunctive Medications

- Topical – lidocaine, capsaicin, anti-inflammatories, other
- Antidepressants – especially amitriptyline, cymbalta
- Anticonvulsants – esp gabapentin, carbamazepine, lyrica
- Antiarrhythmic drugs

Oh, and for tacks:

- Botanicals and nutriceuticals may help directly with cartilage repair, decreasing inflammation, etc.

Highlights:

- Glucosamine sulfate
- Hydrolyzed Collagen
- Pycnogenol or Grape seed extract
- Vitamin D
- Fish oil
- Boswellia, Cat's Claw, Cherry, Curcumin, Ginger and others