

# **Alternatives to Opioids in Treating Acute and Chronic Pain**

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# Learning Objectives



Upon completion of this educational activity, the participant will be able to demonstrate an understanding of:

1. Why opioids should be used only as a last resort in treating acute and chronic pain
2. Non-opioid medications and techniques for treating acute pain
3. Non-opioid medications and techniques for treating chronic pain

# CME Accreditation and Designation



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This activity also meets the requirements of the Wisconsin Medical Examining Board for opioid-related continuing education necessary for licensure recertification.

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# Why non-opioids?



- For too long, healthcare practitioners have relied on opioids as a first-line treatment for pain
- This has resulted in a devastating epidemic of opioid abuse
- It is now clear that we need to focus on non-opioid treatments, using opioids only briefly and as a last resort if needed
- Current guidelines (including those of the CDC and WI MEB) reinforce this approach.

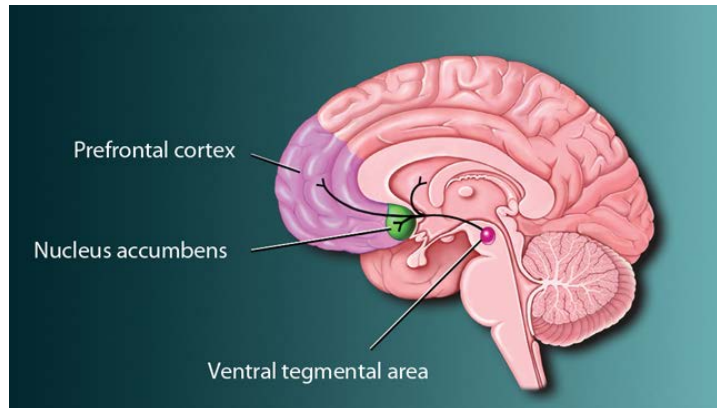
# The Problem with Opioids #1

## They reward their own use



### The Reward System

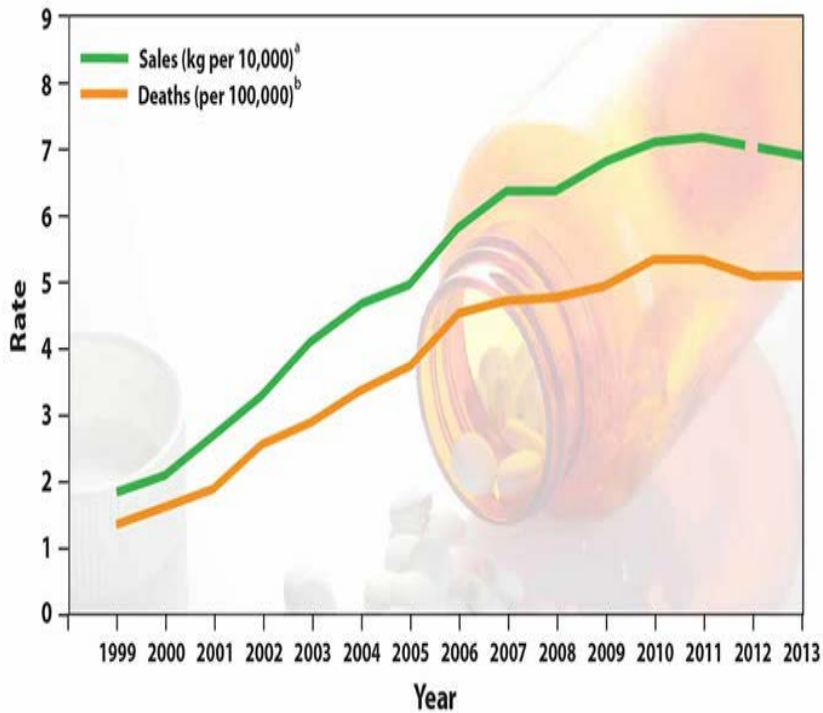
- Opioids bind in the VTA, causing it to release dopamine on the nucleus accumbens
- The nucleus accumbens then affects the motivation system, increasing the drive to repeat whatever action caused its stimulation
- Continued stimulus strengthens the drive
- This can ultimately result in drug-liking or addiction



# What are the consequences?



## Prescription Painkiller Sales and Deaths



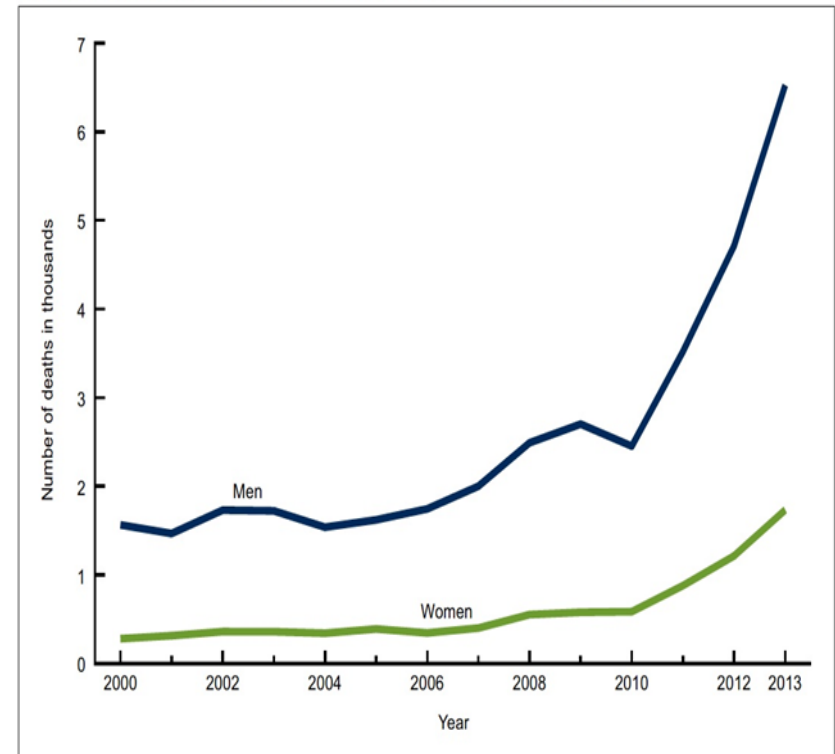
Sources:

<sup>a</sup>Automation of Reports and Consolidated Orders System (ARCOS) of the Drug Enforcement Administration (DEA), 2012 data not available.

<sup>b</sup>Centers for Disease Control and Prevention, National Vital Statistics System mortality data. (2015) Available from URL: <http://www.cdc.gov/nchs/deaths.htm>.

## Heroin Deaths

Figure 2. Number of drug-poisoning deaths involving heroin, by sex: United States, 2000–2013



NOTE: Access data table for Figure 2 at: [http://www.cdc.gov/nchs/data/databriefs/db190\\_table.pdf#2](http://www.cdc.gov/nchs/data/databriefs/db190_table.pdf#2).

SOURCE: CDC/NCHS, National Vital Statistics System, Mortality.

# A serious epidemic of drug abuse



## Rx opioid abuse is rampant in our society

- WI opioid OD deaths are more than twice those from MVAs
- Opioid-related deaths are reducing the life expectancy of US Caucasians
- 80% of patients dying from heroin OD started with Rx drugs
- **Every 3 weeks**, as many Americans die of opioid ODs as died in 9/11
- In 2017, as many Americans died from opioids as died in the Vietnam War
- Middle-aged whites are at highest risk of prescription opioid OD death

**Since the two worst adverse effects of opioids are overdose and addiction, prescribers must have high index of suspicion**





# The Problem with Opioids #2

## They aren't very effective



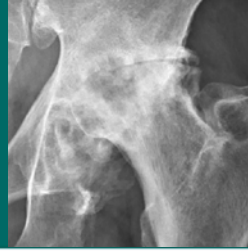
- In **acute** pain, they're mildly effective, with many adverse drug reactions
- In **chronic** pain, they provide less benefit than a patient can appreciate

# Acute Pain



- Multiple studies show that the patients who receive the highest # opioids during hospitalization have the lowest HCAHPS scores
- Cochrane:
  - 1 ibuprofen 200 mg + 1 acetaminophen 500 mg is ~3x as likely to cut pain in half as 15 mg of OxyIR (NNT 1.7 vs. 4.7)

# Chronic pain



- Multiple meta-analyses have shown trivial benefit from opioids if used longer than 2 months.
  - Average level of pain reduction ~15%
- Another meta-analysis has shown that pain patients need 20-30% improvement to consider a treatment “mildly effective”

# The Optimal Approach to Acute Pain



1. Use all reasonable non-opioid treatments
2. If inadequate, add opioids at the lowest dose possible and for the shortest duration possible, avoiding oxycodone
3. If pain persists longer than expected, check for a complication
  - If not present, wean off opioids and onto non-narcotic meds for chronic pain

# Common Alternatives to Opioids



- Acetaminophen
- NSAIDs (acute, inflammatory)
- SNRIs: venlafaxine, duloxetine, milnacipran
- TCAs: desipramine, amitriptyline, nortriptyline
- Anticonvulsants: gabapentin, pregabalin, topiramate, carbamazepam, etc.
- Topicals: lido, NSAID, capsaicin
- Procedures: blocks, epidurals, facet block
- PT, OT, braces, stimulators
- CBT, hypnosis, meditation, acupuncture



# Non-opioid Treatment of **Acute** Pain

# Alternatives to Opioids in Acute Pain

## Acetaminophen

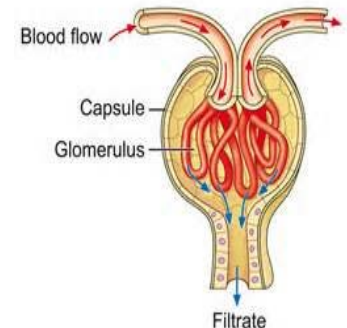


- Highly effective, despite OTC status
- IV now available but pricey
- Rectal suppositories also available
- Dosing:
  - Acute: up to 6 g/d
  - Chronic: try to keep < 3 g/d, never > 4 g/d
  - Beware of combination opioids w/ APAP
- Avoid if poor liver function, heavy drinker
  - ↑ LFTs a relative contraindication, ↑↑ absolute



# Alternatives to Opioids in Acute Pain: NSAIDs - General Considerations

- Anti-inflammatory, some analgesic effects
  - Most acute pain is caused by tissue damage, which is often associated with inflammation
- Paralyze renal compensatory mechanisms
  - Constriction of efferent arteriole is prostaglandin-dependent
  - Avoid if  $\geq$  Stage II CKD
  - Consider APAP, tramadol instead
    - If GFR  $<$  30, cut tramadol dose 50%





# Alternatives to Opioids in Acute Pain

## NSAIDs – other ADRs

- Can cause ulcers

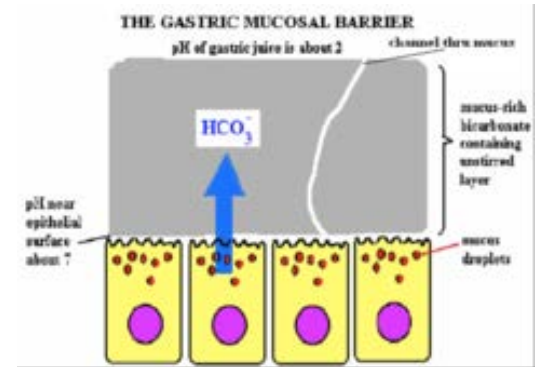
Indications for gastroprotection:

Hx ulcers, dyspepsia

Hx neuropathy

50 yo

DM



- Contraindicated if:

Bleeding disorder

Anticoagulation

Hx bleeding ulcer

≥ Stage III kidney disease

- Also associated with increased risk ASHD, bleeding problems

# Alternatives to Opioids in Acute Pain

## NSAIDS commonly used



- **Nonacetylated:** salsalate, diflunisol, choline Mg trisalicylate
- **Propionic acids:** ibuprofen, naproxen, ketoprofen
- **Indoles:** indomethacin, sulindac, tolmetin, etodolac
- **Others:** diclofenac, meloxicam, piroxicam, nabumetone, ketorolac  
(available IV)
- **Cox-II:** celecoxib

If tolerance develops, may try changing to a different class.

# Alternatives to Opioids in Acute Pain

## Muscle Relaxants



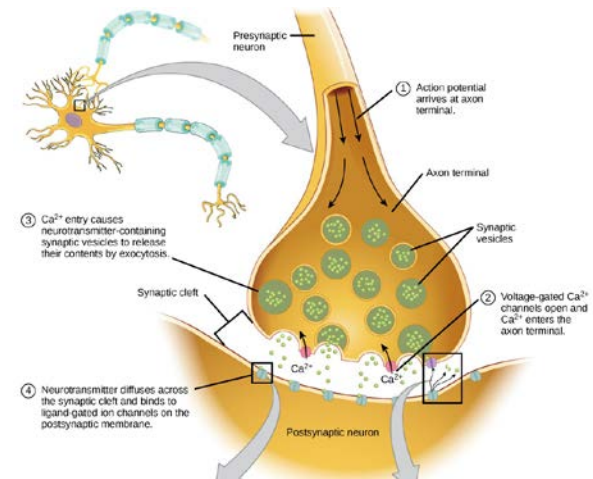
- Optimal:
  - Baclofen 10-20 tid
  - Tizanidine (Zanaflex) 2-4 mg tid
  - Metaxolone (Skelaxin) 800 tid-qid
- OK: (work mostly by sedation)
  - Orphenadrine (Norflex) 100 bid
  - Methocarbamol (Robaxin) 750 2 qid
  - Chlorzoxazone (Parafon Forte) 250-500 tid-qid
  - Cyclobenzaprine (Flexeril) 5-10 tid (a TCA)
- Avoid:
  - Dantrolene (Dantrium) - liver problems
  - Carisoprodol (Soma) - addictive



# Alternatives to Opioids in Acute Pain Anticonvulsants:

## Physiology

- $\alpha$ -2- $\delta$  ligands (gabapentin, pregabalin)
  - Presynaptic inhibition by  $\downarrow$  neurotransmitter release
  - Key component of pre-emptive analgesia (despite common conception that they only slowly take effect)
- Common ADRs:
  - Sedation
  - Cognitive dysfunction
  - Weight gain
  - Edema
  - Dizziness



# Anticonvulsants: $\alpha$ -2- $\delta$ ligands

## Gabapentin (Neurontin)



- Typically dosed 300-600 tid
- Optimal titration:
  - 600 mg ½ tab qhs, increase by ½ tab nightly to 3 tabs (or maximum tolerated), change to 600 mg tid in 1-2 mo (after drowsiness has worn off)
  - Some patients may require much slower
  - If unable to tolerate at least 900 mg/d, d/c
  - Preemptive analgesia: 600 qhs start 3-7 d preop
- Common ADRs
  - Drowsiness, vertigo, weight gain, blurred vision
  - Reduce dose if ↓ renal function

# Anticonvulsants: $\alpha$ -2- $\delta$ ligands

## Pregabalin (Lyrica)



- Typically dosed 150 bid-tid
- Optimal titration:
  - 50 mg qhs x 1 wk, bid x 1 wk, tid x 1 wk, qid x 1 wk, then 150 mg bid (↑ to tid if needed)
  - Some may need to go slower (25 mg at 1<sup>st</sup>)
  - If unable to tolerate 300 mg/d, d/c
  - Preemptive analgesia: 150-300 qhs 3-7 d preop
- Common ADRs
  - Weight gain, drowsy, edema, blurred vision
  - Reduce dose if ↓ renal function

# Alternatives to Opioids in Acute Pain

## Topicals

- Work best for superficial pathology
- NOTE: occlusive seal ↑ absorption 10-40 x!
- Lidocaine (Lidoderm)
- NSAIDs (Voltaren patch/gel/liquid, Flector patch)
- Capsaicin (mostly OTC, except Zostrix)
- Salicylates (OTC: “BenGay”)
- Compounded (Rx: mix of multiple meds)
- Advantages: lack of systemic ADRs
- Disadvantages: \$\$\$, often limited benefit, poss. messy



# Alternatives to Opioids in Acute Pain

## Physical Therapy

- Thermal
- Electrical
- Mechanical traction
- Phoresis
- Bracing
- Exercise
- Manual treatments (stretch, massage, trigger points, etc.)

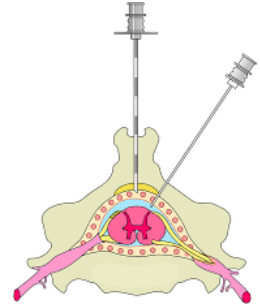




# Alternatives to Opioids in Acute Pain

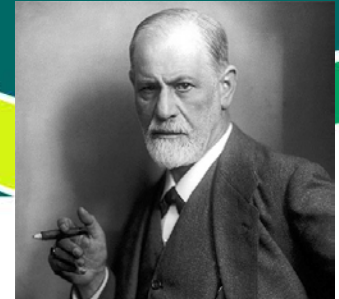
## Interventional

- Trigger point/muscle injections
- Joint/Bursa injections
- Regional (peripheral nerve) Blocks or Infusions
- Hematoma Block (for Colles Fx)
- Bier Block (for extremity surgery)
- Epidural Blocks or Infusions (surgery)
- Spinal Blocks or Infusions (surgery)



# Alternatives to Opioids in Acute Pain

## Behavioral



- Distraction:  $\uparrow$  desc. inhibition at dorsal horn
- CBT: proven beneficial (esp. for poor copers)
- Stress-reducing mindfulness meditation: may provide similar benefit
- Biofeedback: shown to  $\downarrow$  pain (more for chronic)
- Hypnosis: highly effective if patient susceptible
- Other psych Tx may help: grief, family, anxiety/depression

# Alternatives to Opioids in Acute Pain

## Integrative Medicine



- Manipulation: chiro, osteo, PT, nurse
- Energy Medicine: therapeutic touch, Reiki, homeopathy, etc.
- Physical modalities: massage, yoga, tai chi, qi gong, etc.
- Acupuncture, acupressure, suction
- Music, light, aromatherapy
- Prolotherapy



# Integrative Medicine Tx of Pain

## Summary by Level of Evidence



### **Recommendation level: High**

- **Moderate quality evidence**

- Exercise
- Multidisciplinary rehabilitation
- Acupuncture
- Mindfulness-based stress reduction (Vipassana)

- **Low quality evidence**

- Tai chi
- Motor control exercises
- Progressive relaxation
- Electromyography biofeedback
- Low level laser therapy
- Operative therapy
- Cognitive behavioral therapy
- Spinal manipulation

# Alternatives to Opioids in Acute Pain

## Pre-emptive analgesia



May include any/all, depending on surgery:

- Preoperative
  - Celecoxib, gabapentinoid, APAP, steroids
- Intraoperative
  - Incisional block, regional block, ketamine
- Postoperative
  - Celecoxib, gabapentinoid,  $\alpha$  blockers, APAP, regional/spinal/epidural block

Check out: [www.postoppain.org](http://www.postoppain.org)

# Alternatives to Opioids in Acute Pain

## Effects of pre-emptive analgesia



- Dramatic reduction in opioid need
  - Many patients get by without using any
- Better compliance with PT/rehab
- Better overall outcomes
- Data on shorter LOS mixed
- Markedly improved HCAHPS Scores





# Non-opioid Treatment of **Chronic** Pain

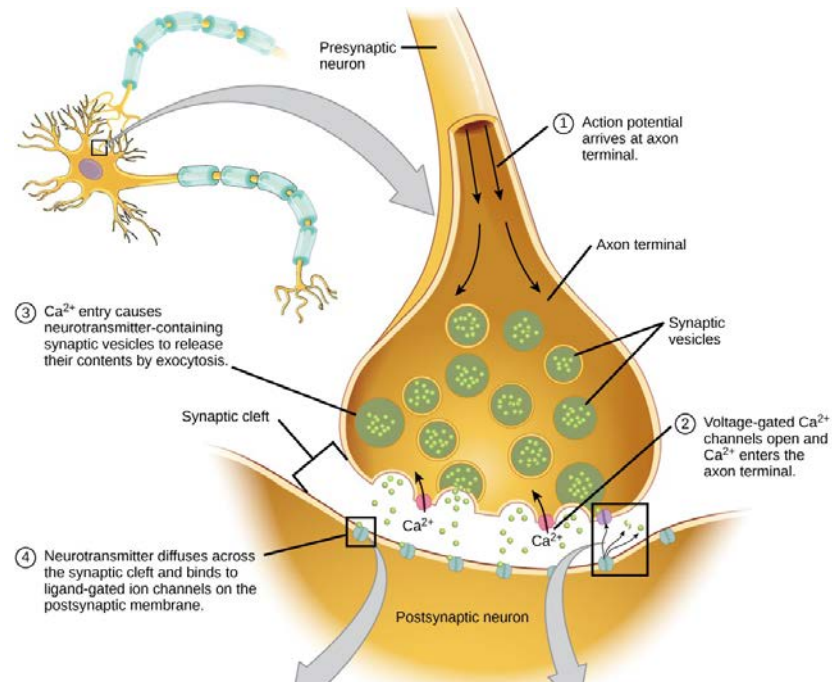
# All of the above, plus...



- Virtually all non-narcotic acute pain treatments can be used chronically.
- Opioids, however, have imperceptible benefit in chronic pain
- Chronic pain often has a neuropathic component (neuroplasticity)
- APAP requires a lower dose (3 g/day)
- Regional blocks less applicable
- NSAIDs: only for inflammatory conditions (RA, etc.) and OA
- Psych Tx's probably more important



- $\alpha$ -2- $\delta$  ligands (gabapentin, pregabalin)
  - Presynaptic inhibition by  $\downarrow$  neurotransmitter release



# Alternatives to Opioids in Chronic Pain Anticonvulsants:

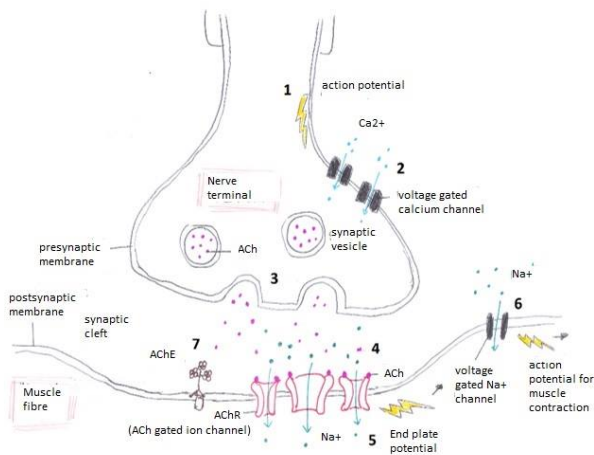
## Physiology Part 2



Na channel agents

Postsynaptic inhibition

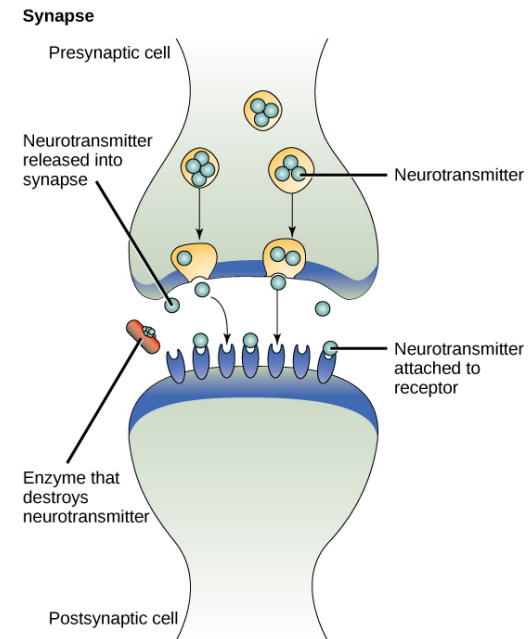
↓ action potential propagation



1. Action potential depolarises the nerve terminal
2. Voltage gated Ca<sup>2+</sup> channels allow Ca<sup>2+</sup> influx
3. Ca<sup>2+</sup> evoked vesicle exocytosis of ACh
4. ACh activates AChRs
5. Cation influx through AChRs depolarises muscle fibre forming EPP
6. Voltage gated Na<sup>+</sup> channels generate action potential
7. AChE degrades ACh to terminate the signal

AMPA receptor agent

Postsynaptic inhibition



# Alternatives to Opioids in Chronic Pain Anticonvulsants commonly used for pain



- **$\alpha$ -2- $\delta$  ligands**

gabapentin (Neurontin)

pregabalin (Lyrica)

- **Na channel agents**

carbamazepine (Tegretol)

valproic acid (Depakote)

lamotrigine (Lamictal)

levetiracetam (Keppra) tiagabine (Gabitril)

zonisamide (Zonegran)

- **AMPA Receptor Blocker**

topiramate (Topamax) – also some Na activity

**NOTE:** Agents of each type can't be used together but can be used with one of the other types

# Alternatives to Opioids in Chronic Pain Anticonvulsant considerations



- All can cause birth defects; avoid if trying to get pregnant and before 10<sup>th</sup> week of pregnancy
- All can cause rash, though SJS rare
- Topiramate:
  - Dosing: titrate slowly to 200 bid max (often effective at lower doses, like 50 tid)
  - ADRs: weight loss (☺), cognitive dysfunction, paresthesias, fatigue, taste change (esp. soda), metab acidosis (→ osteoporosis, kidney stones)
  - Check CO<sub>2</sub> at one month

# Anticonvulsants; other considerations

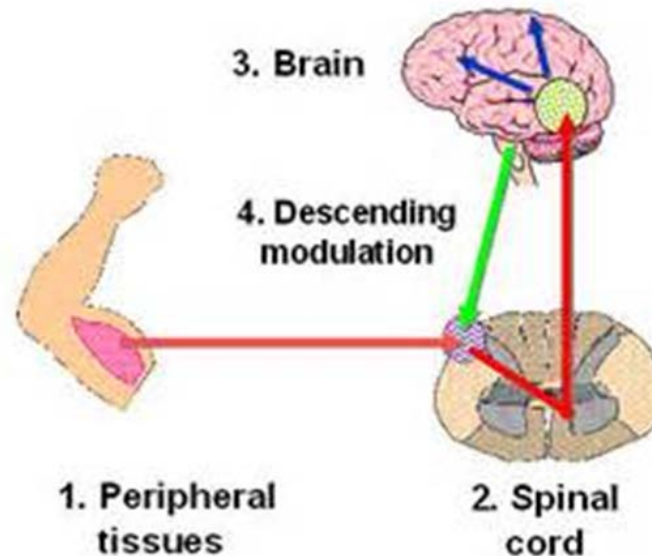


- Carbamazepine (Tegretol)
  - Dosing: 200 mg bid
  - ADRs: bone marrow suppression, rash (poss SJS), drowsy: need to check CBC, drug levels
  - Need to check blood level at 2 wk
  - Check CBC at baseline and 3 mo
- Lamotrigine (Lamictal)
  - Dosing: starter pack → 200 mg/d max
  - ADRs: rash (poss SJS), drowsy, dizzy, vision, incoordination
- Zonisamide (Zonegran)
  - Dosing: start 100/d, ↑ by 100 q 2 wk to 600/d max
  - ADRs: Vertigo, drowsy, ataxic, N/V, vision, rash
  - Can cause metab acidosis: check CO<sub>2</sub> at 1 mo

# Alternatives to Opioids in Chronic Pain

## TCA/SNRIs – mechanism of action

- Reduce pain by  $\uparrow$  norepinephrine (and serotonin) at dorsal horn; hyperpolarize nerve



# Alternatives to opioids in Chronic Pain SNRIs commonly used



**NOTE: pain patients commonly also have depression/anxiety,  
and these can help them all!**

- Duloxetine (Cymbalta)
  - 30 mg/d x 1 wk, then 60 mg/d
  - Generally well-tolerated (80%). Avoid if ↑ LFTs
- Venlafaxine (Effexor)
  - 75 mg/d x 1 wk, then 150 mg/d
  - Lots of ADRs: venlafaxine ER less so
  - Wicked withdrawal syndrome: taper, can use fluoxetine
  - Oddly, desvenlafaxine (Pristiq) doesn't seem to work
- Milnacipran (Savella)
  - Don't use titration pack: do 12.5/d x 2 wk, 12.5 bid x 2 wk, 25 bid x 2 wk, then 50 bid – many must titrate even slower
  - High CV ADRs (effective dose ↑ pulse 8 BPMs!)
  - Honestly, few patients tolerate effective doses

# Alternatives to Opioids in Chronic Pain

## TCA's commonly used



- **Desipramine** – pure NE (safe w/ SSRIs, tramadol)
  - 25 mg ½ tab qam, ↑ by ½ weekly to 2 qam (50 mg/d)
    - Max 300/d, but rarely see added benefits over 100/d
  - ↓ muscarinic effects, so fewer cognitive ADRs
  - ↓ metabolism by some SSRIs (esp. Paxil, Prozac)
    - Titrate slowly, checking desip levels as you go
- Amitriptyline – sedating, lots of cognitive dysfunction
- Nortriptyline – sedating, possibly fewer ADRs

Watch for ↑ QTc

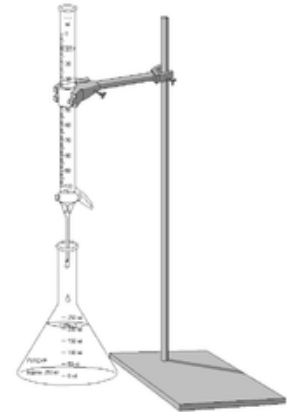
Avoid in elderly: all except desipramine are on the Beers Criteria



# Recommended initial titration for patients with significant pain



- Gabapentin 600 mg  $\frac{1}{2}$  qhs, increasing by  $\frac{1}{2}$  nightly to 3 tabs or max tolerated (*after several months, redistribute to tid*)
- Wait 1 week, then
- Duloxetine 30 mg qam x 7 days, then
- Duloxetine 60 mg qam
- If probs w/ gaba, consider pregabalin, carbamazepine, or topiramate
- If probs w/ dulox, consider venlafaxine or despiramine



# Medical Marijuana



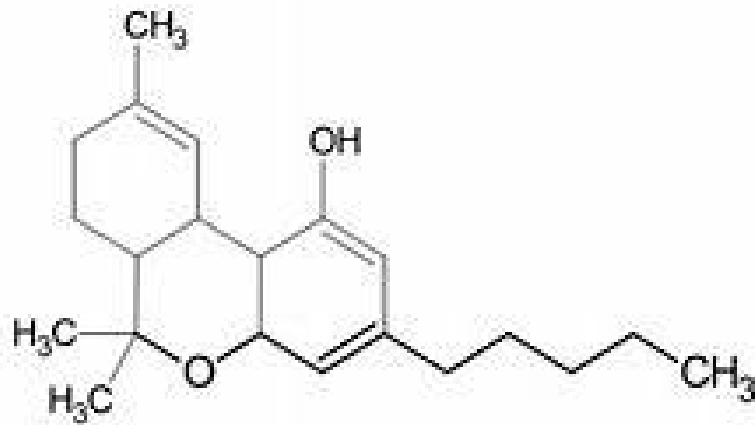
- Marijuana is significantly effective for many forms of pain, but:
  - It's illegal in WI (and federally)
  - It causes serious cognitive dysfunction
  - It can be psychologically addicting
  - It can cause long-lasting effects in children
- If a patient is on it, they should not be prescribed opioids
  - Unless they live in a state where it's legal
- Consider CBD instead

# Cannabidiol (CBD)

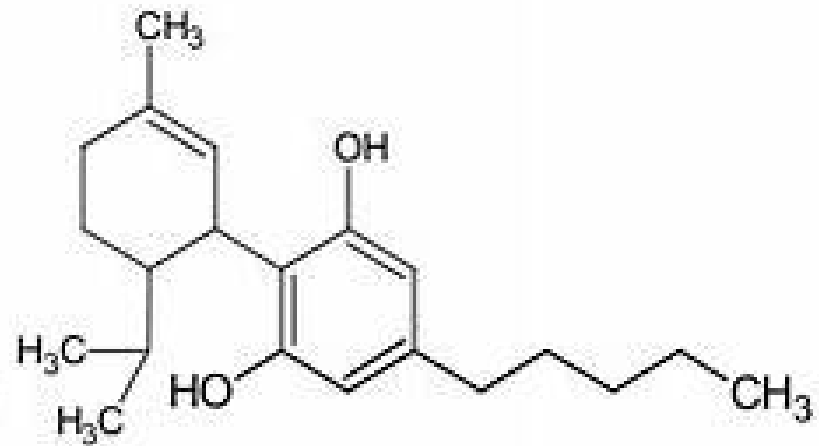


- CBD is legal in WI, but a patient must have a letter from a physician saying they have a condition for which it could be beneficial
- Animal models show significant benefit; 135 human studies underway (OA, neuropathic pain, central pain, low back pain, seizures, anxiety, depression, addiction, schizophrenia, etc.)
- “Hemp oil” vs “CBD oil”
- Encourage standardized products for consistent dosing
- NOTE: CBD does *not* test positive as THC

# THC vs. CBD



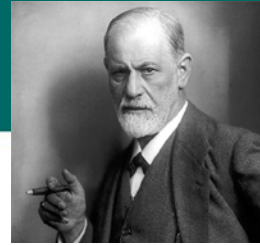
Tetrahydrocannabinol (THC)



Cannabidiol (CBD)

# Alternatives to Opioids in Chronic Pain

## Behavioral



- Distraction:  $\uparrow$  desc. inhibition at dorsal horn
- CBT: proven beneficial (esp. for poor copers)
- Stress-reducing mindfulness meditation: may provide similar benefit
- Biofeedback: shown to  $\downarrow$  pain (esp. chronic)
- Hypnosis: highly effective if patient susceptible
- Other psych Tx may help: grief, family, anxiety/depression

# Alternatives to Opioids in Chronic Pain

## Physical Therapy



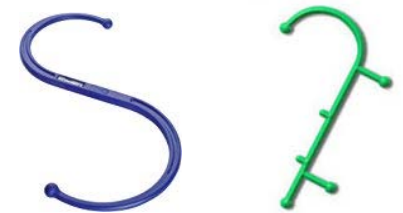
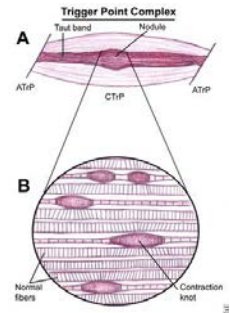
- Thermal
- Electrical
- Mechanical traction
- Phoresis
- Bracing
- Exercise
- Manual treatments (stretch, massage, trigger points, etc.)



# Alternatives to Opioids in Chronic Pain

## Treating Myofascial Pain

- Probably the most underdiagnosed chronic pain problem
- Often develops around sites of chronic pain
- Muscle tension → microtears → TrPs
- TP injection of limited benefit by itself
  - Don't use steroids; no addl. benefit, ↑ ADRs
  - Botox is very expensive
- PT helpful, but not frequent enough
- Best to have patient do self-care tid
- Heat 10 min, firm but gentle massage 5 min/area just below pain threshold
- Can use a cane, ball in nylon stocking, Backnobber, Theracane



# Alternatives to Opioids in Chronic Pain

## OT approaches may be helpful



- Teach how to use skills to full capacity
- Prevent disability
- Maintain functionality/capabilities
- Establish new abilities to replace lost ones
- Modify environment to maximize function with lost abilities



# Alternatives to Opioids in Chronic Pain

## Integrative Medicine



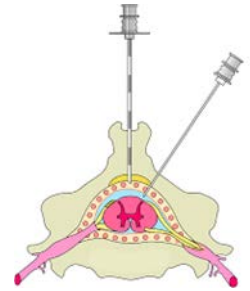
- Manipulation: chiro, osteo, PT, nurse
- Energy Medicine: therapeutic touch, Reiki, homeopathy, etc.
- Physical modalities: massage, yoga, tai chi, qi gong, etc.
- Acupuncture, acupressure, suction
- Music, light, aromatherapy
- Prolotherapy



# Alternatives to opioids in Chronic Pain

## Interventional approaches

- Corticosteroid injections (epidural, SI, facet, other joints)
- Nerve Blocks
- Nerve ablations (knees, facets, SI joints, etc.)
- Adhesiolysis
- Spinal stim
- Intrathecal pumps (baclofen, ziconitide)
- Etc. (discectomy, MILD, ...)



# Corticosteroid Joint Injections



- Primarily for anti-inflammatory effect
- Can also be in bursa, around enthesis
- Prefer < 3/year total (regardless of site)
- Often tend to wear off relatively quickly
- May delay need for surgery



# Nerve Blocks

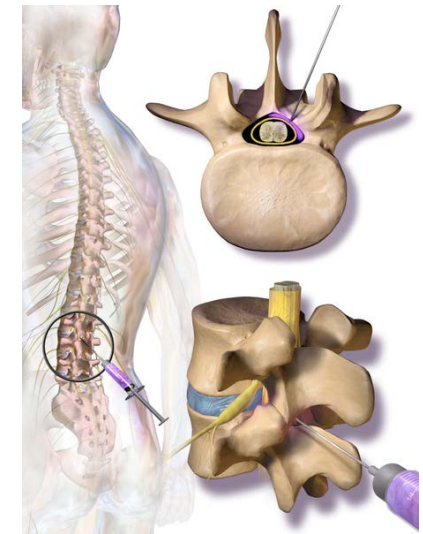
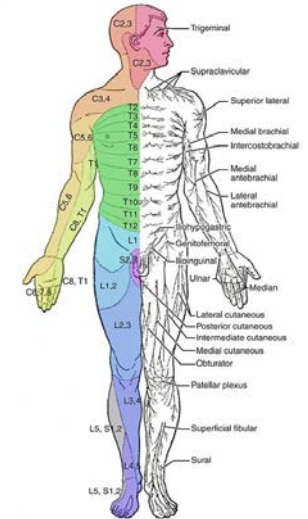


## Commonly used:

- Trigeminal: Trigeminal neuralgia/face pain
- Axillary/stellate ganglion: arm pain/CRPS
- Celiac: internal upper abdomen
- Superior hypogastric: internal low abd/pelvic
- Ilioinguinal/iliohypogastric: hernia/genital
- Impar: pelvic/genital/rectal pain
- Lumbar sympathetic: leg pain/CRPS
- Genicular block: knee pain (to see if should have neurotomy)

# Epidural Steroid Injections

- Primarily benefit radicular pain associated with nerve impingement
  - May help annular tear pain
- Prefer < 3/yr, never > 6
- May benefit even if no nerve contact (inflammatory compound release)

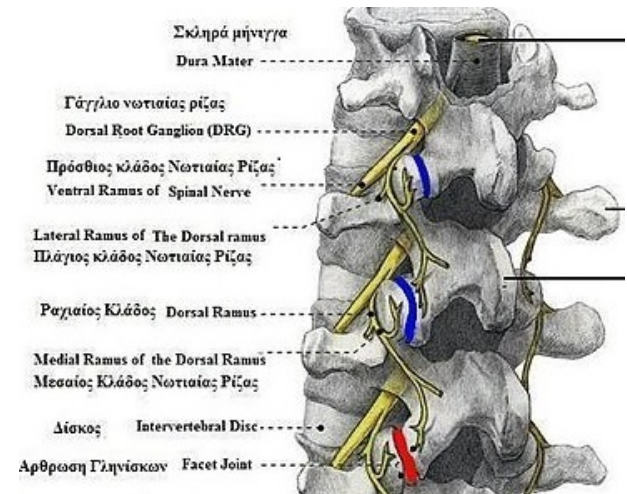


# Nerve Ablations



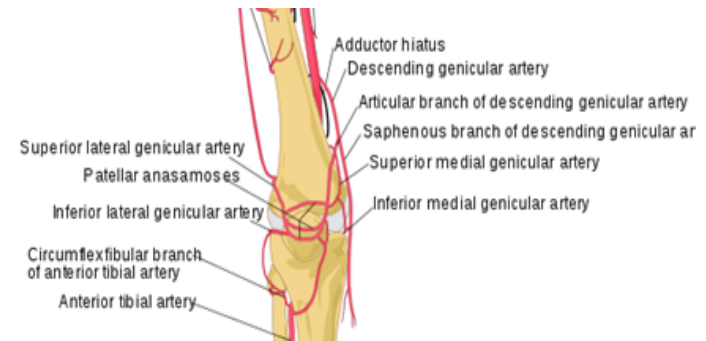
## Medial Branch Block – Radiofrequency Ablation

- For nonradiating facet pain
- Trial of block first
- If pain <50%, do ablation
- Lasts ~9-24 months



## Genicular Neurotomy

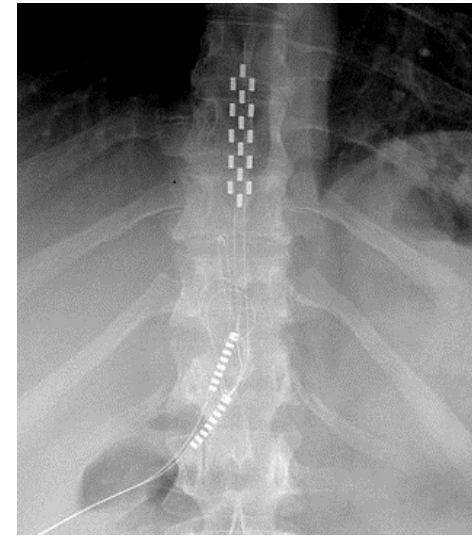
- For chronic knee pain, if surgery undesirable
- Trial block first
- Usually lasts at least a year



# Nerve Stimulation



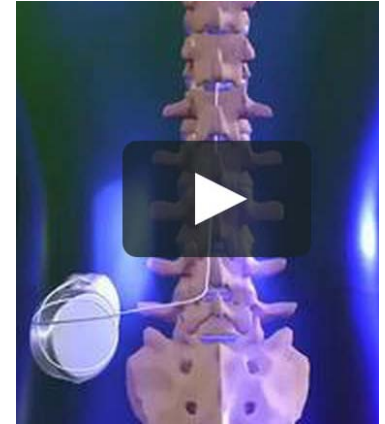
- One of the most promising new forms of Tx; usage increasing rapidly
- FDA approved as early Tx for back pain
- Often used for failed back syndrome
- Spinal and dorsal root ganglion stimulators block pain as it enters/is processed by the spine
- Peripheral stimulators block efferent nerve
- Many different modalities, based on frequency, wave form
- Requires psych eval
- Electrodes and battery pack implanted



# Intrathecal Pumps



- Basically used as a last resort
- Surgically implanted, prone to blockage
- May be used for 1-level opioid infusion (micro-dosing) in intolerant patients
- Ziconitide (Prialt)
  - From sea snail venom
  - Presynaptic inhibitor of pain neuroTx
  - Very potent
  - Many ADRs, requires very slow titration
- Baclofen – for severe spasm (CP, post-stroke, etc.)

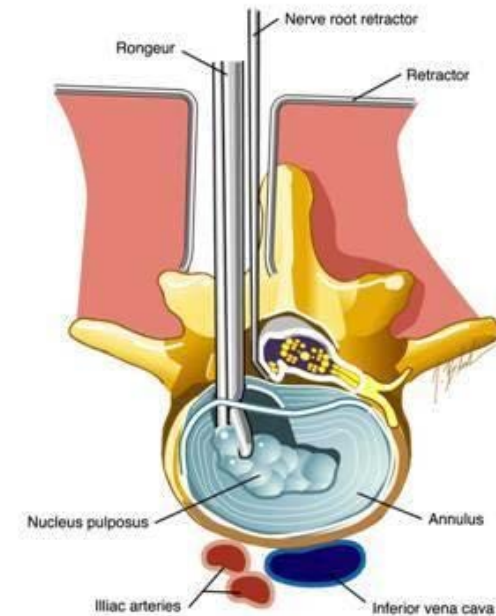




# Endoscopic Microdiscectomy



- For when a small disc piece has extruded and is pushing on a nerve
- Low risk, outpatient procedure
- Increasingly popular
- A much less invasive alternative to laminectomy, fusion, etc.



# Coming Soon to a Procedure Room

## Near You! Part 1



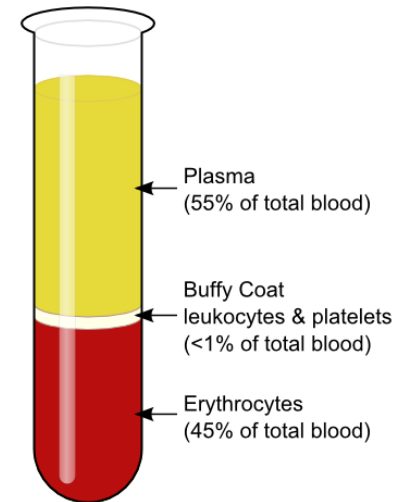
- Platelet Rich Plasma Injections

- Indications:

- OA
- Muscle tears
- Tendon/ligament sprains

- Early studies:

- Seem to improve function more than pain
- Speed recovery from acute injuries
- Better than viscosupplementation in OA

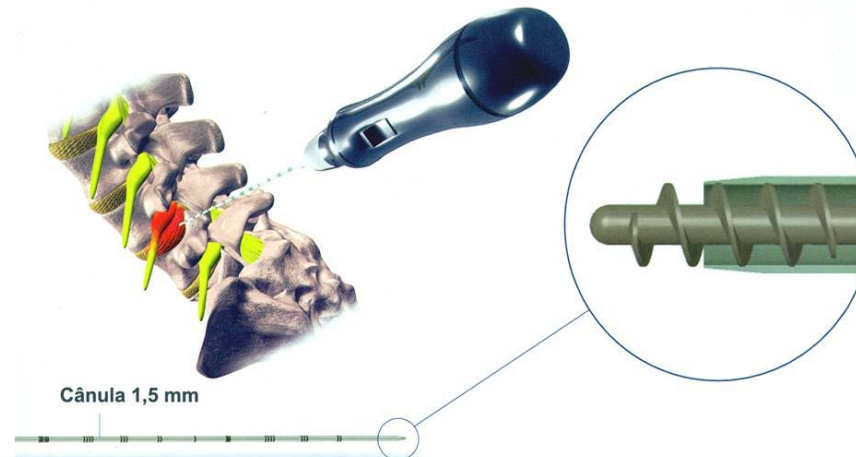
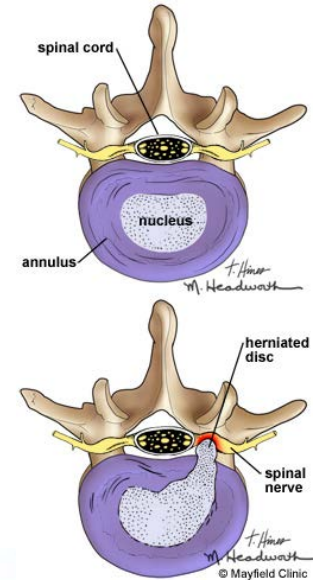


# Coming Soon to a Procedure Room Near You! Part 2



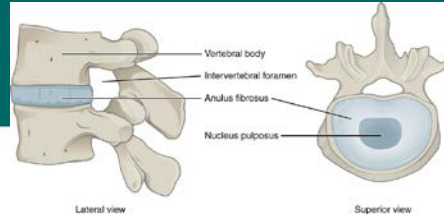
## Nucleoplasty

- Few well-done studies
- 66-75% report > 50% improvement
- As more studies done, expect use to increase



# Coming Soon to a Procedure Room

## Near You! Part 3



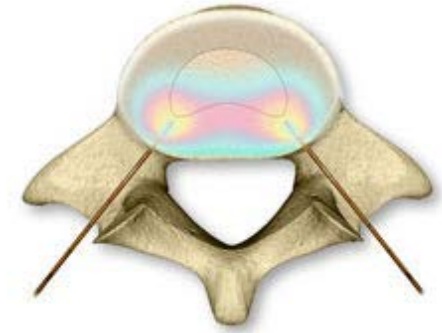
- Intradiscal Electrothermal Annuloplasty (IDET)
- Was common, waned, now coming back; still somewhat controversial
- For pain from a torn annulus
- Annulus cauterized, causing fibrosis and stabilization, may kill pain receptors
- Much less invasive alternative to fusion
- Few well-done studies; those available show mild-moderate improvement

# Coming Soon to a Procedure Room Near You! Part 4



## Biacuplasty

- May replace IDET
- Goal is to denervate and numb disc
- Cooled electrodes apply RF energy to posterior disc, where nerves grow in
- Early studies promising



# References



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# Questions?



Thank you for your time & attention!