



Alternatives to Opioids in Treating Acute and Chronic Pain

Michael McNett, MD
Medical Director, Aurora Pain Program GMS-PSM

© Aurora Health Care, Inc.

CME Accreditation and Designation

Aurora Health Care is accredited by the Wisconsin Medical Society to provide continuing medical education for physicians.

Aurora Health Care designates this Live Activity for a maximum of 2 AMA PRA Category 1 Credit(s)[™]. Physicians should only claim credit commensurate with the extent of their participation in the activity.

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

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.

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

Disclosures

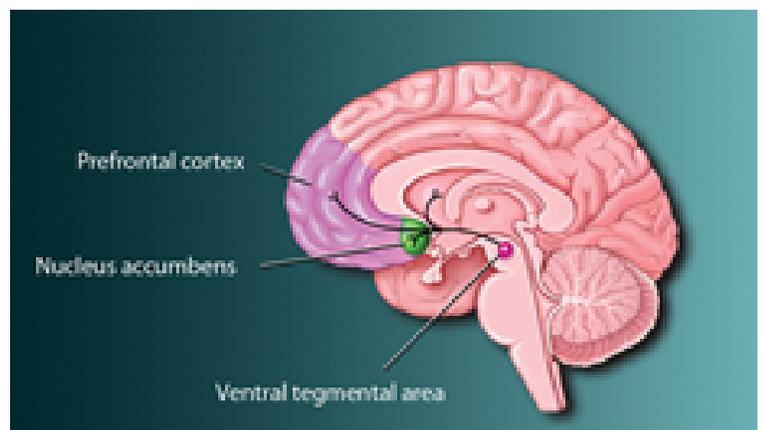
The following faculty speakers/planning committee members have disclosed the following:

Faculty Name	Name of Commercial Interest	Nature of relationship

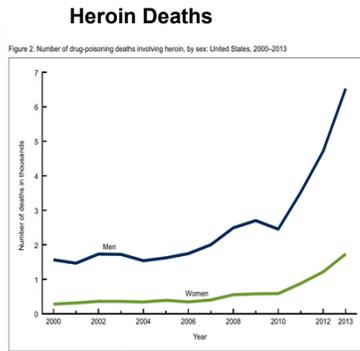
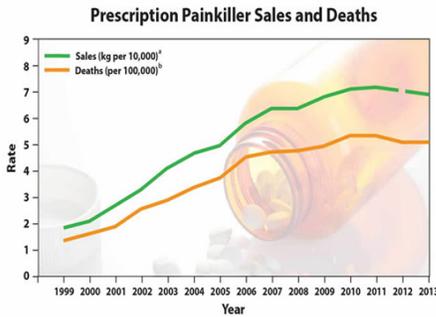
All other presenters, planners, and anyone controlling content completed conflict of interest forms and no one else has any relevant financial relationships to disclose.

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?



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



© Aurora Health Care, Inc.

Alternatives to Opioids in Acute Pain Acetaminophen

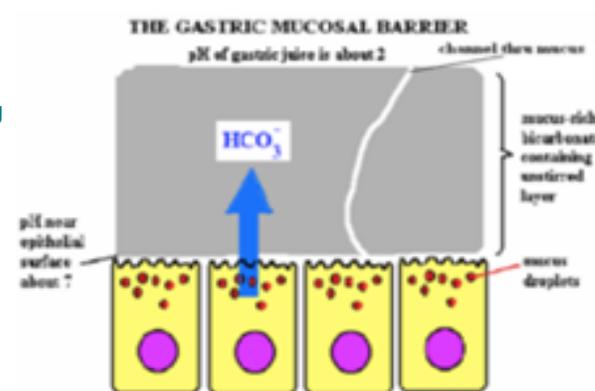
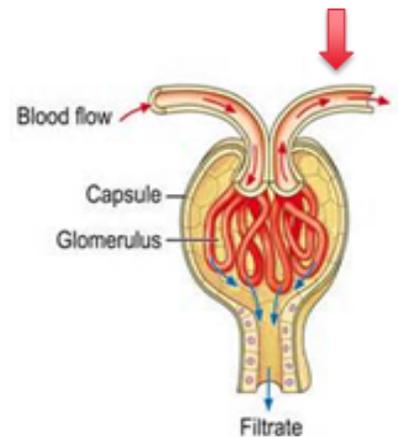
- Highly effective, despite OTC status
- IV now available but pricey
- Rectal suppositories also available
- Dosing:
 - Acute: up to 6 g/d
 - Chronic: try to keep < 3 g/d, never > 4 g/d
 - Beware of combination opioids w/ APAP
- Avoid if poor liver function, heavy drinker
 - ↑ LFTs a relative contraindication, ↑↑ 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 ≥ 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 > 50 yo
 - Hx neuropathy DM
- Contraindicated if:
 - Bleeding disorder
 - Hx bleeding ulcer
 - ASA allergy
 - Anticoagulation
 - ≥ 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 Anticonvulsants: Physiology

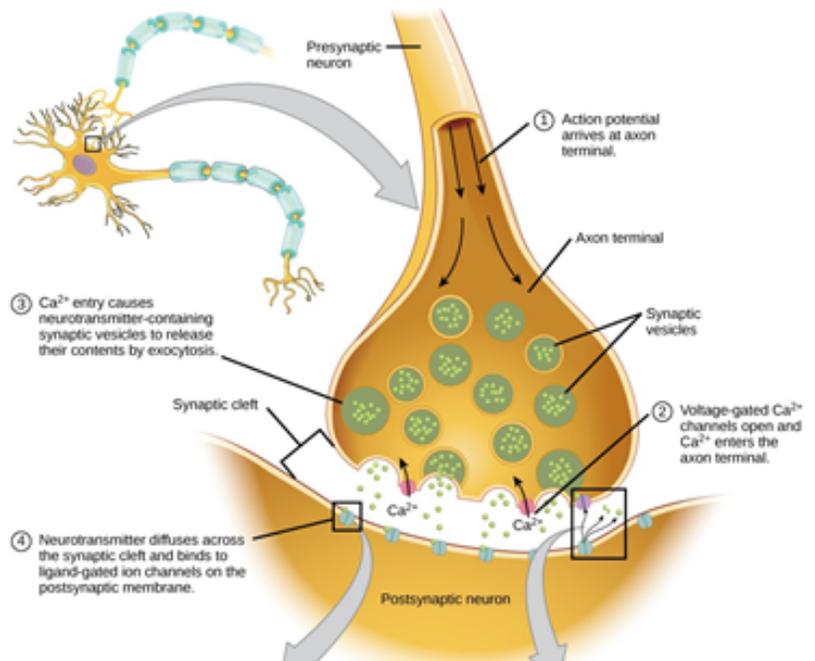
- α -2- δ ligands (gabapentin, pregabalin)
 - Presynaptic inhibition by \downarrow neurotransmitter release
 - Key component of pre-emptive analgesia (despite common conception that they only slowly take effect)
- Common ADRs:
 - Sedation
 - Cognitive dysfunction
 - Weight gain
 - Edema
 - Dizziness

Anticonvulsants: α -2- δ ligands Gabapentin (Neurontin)

- Typically dosed 300-600 tid
- Optimal titration:
 - 600 mg $\frac{1}{2}$ tab qhs, increase by $\frac{1}{2}$ 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 \downarrow renal function

Alternatives to Opioids in Acute Pain Muscle Relaxants

- Optimal:
 - Baclofen 10-20 tid
 - Tizanidine (Zanaflex) 2-4 mg tid
 - Metaxalone (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



Anticonvulsants: α -2- δ 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 (\uparrow to tid if needed)
 - Some may need to go slower (25 mg at 1st)
 - 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 \downarrow 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 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 Integrative Medicine

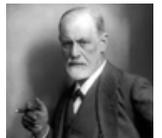
- Manipulation: chiro, osteo, PT, nurse
- Energy Medicine: therapeutic touch, Reiki, homeopathy, etc.
- Physical modalities: massage, yoga, tai chi, qi gong, etc.
- Acupuncture, acupressure, suction
- Music, light, aromatherapy
- Prolotherapy



Alternatives to Opioids in Acute Pain Physical Therapy

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

Alternatives to Opioids in Acute Pain Behavioral



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

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, α blockers, APAP, regional/spinal/epidural block

Check out: 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

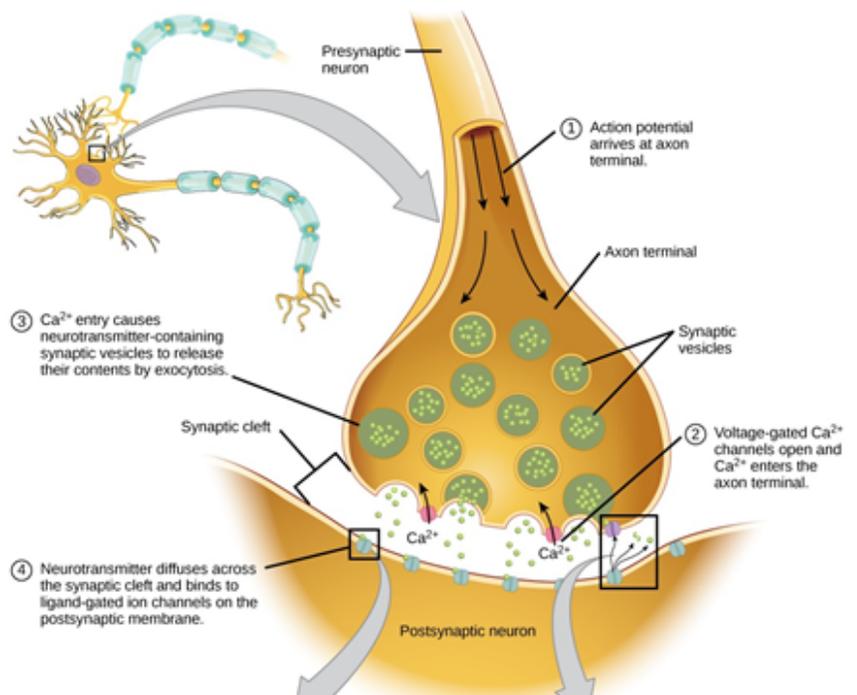


All of the above, plus...

- 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

Alternatives to Opioids in Chronic Pain Anticonvulsants: Physiology

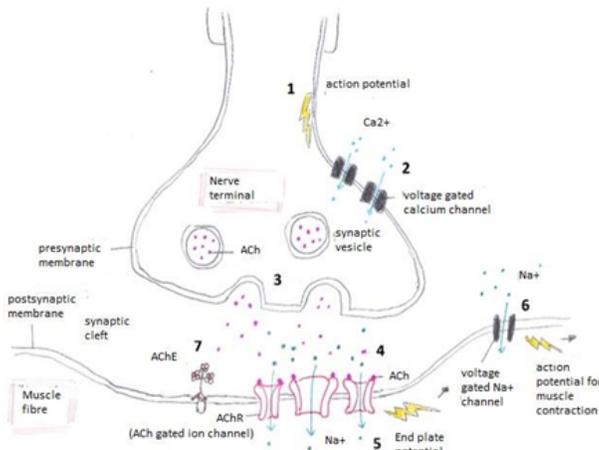
- α -2- δ ligands (gabapentin, pregabalin)
 - Presynaptic inhibition by \downarrow neurotransmitter release



Alternatives to Opioids in Chronic Pain

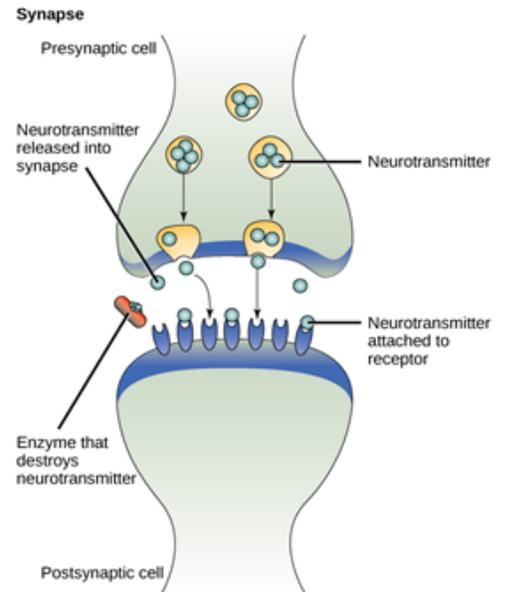
Anticonvulsants: Physiology

- Na channel agents
- Postsynaptic inhibition
- ↓ action potential propagation



1. Action potential depolarises the nerve terminal
2. Voltage gated Ca²⁺ channels allow Ca²⁺ influx
3. Ca²⁺ evoked vesicle exocytosis of ACh
4. ACh activates AChRs
5. Cation influx through AChRs depolarises muscle fibre forming EPP
6. Voltage gated Na⁺ 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

- **α-2-δ 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 10th 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 CO₂ at one month

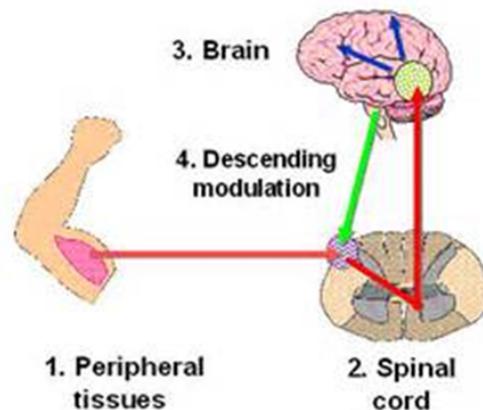
Anticonvulsants; other considerations

- 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 CO₂ at 1 mo

Alternatives to Opioids in Chronic Pain

TCA/SNRIs – mechanism of action

- Reduce pain by ↑ 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

Recommended initial titration for patients with significant pain

- Gabapentin 600 mg ½ qhs, increasing by ½ 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 desipramine

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 signif benefit; 135 human studies underway (OA, neuropathic pain, central pain, low back pain, seizures, anxiety, depression, addiction, schiz, etc.)
- “Hemp oil” vs “CBD oil”
- Encourage standardized products for consistent dosing
- NOTE: CBD does *not* test + as THC

Alternatives to Opioids in Chronic Pain TCAs 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

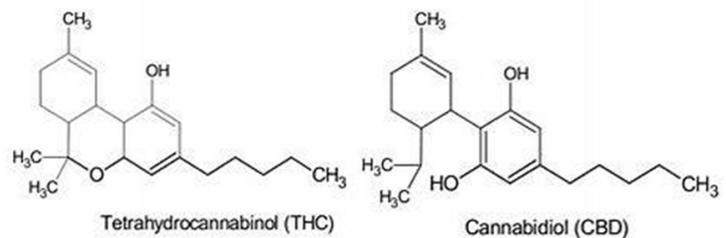
Avoid in elderly: all except desipramine are on the Beers Criteria

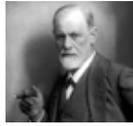


Medical Marijuana

- 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

THC vs. CBD





Alternatives to Opioids in Chronic Pain Behavioral

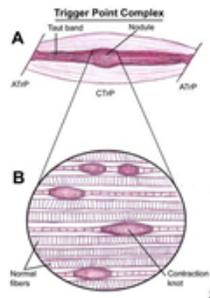
- Distraction: ↑ desc. inhibition at dorsal horn
- CBT: proven beneficial (esp. for poor copers)
- Stress-reducing mindfulness meditation: may provide similar benefit
- Biofeedback: shown to ↓ pain (esp. chronic)
- Hypnosis: highly effective if patient susceptible
- Other psych Tx may help: grief, family,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

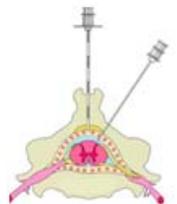
- Teach how to use skills to full capacity
- Prevent disability
- Maintain functionality/capabilities
- Establish new abilities to replace lost ones
- Modify environment to maximize function with lost abilities

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



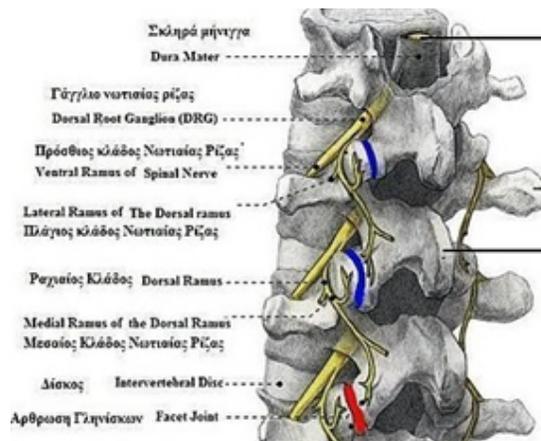
Epidural Steroid Injections

- 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

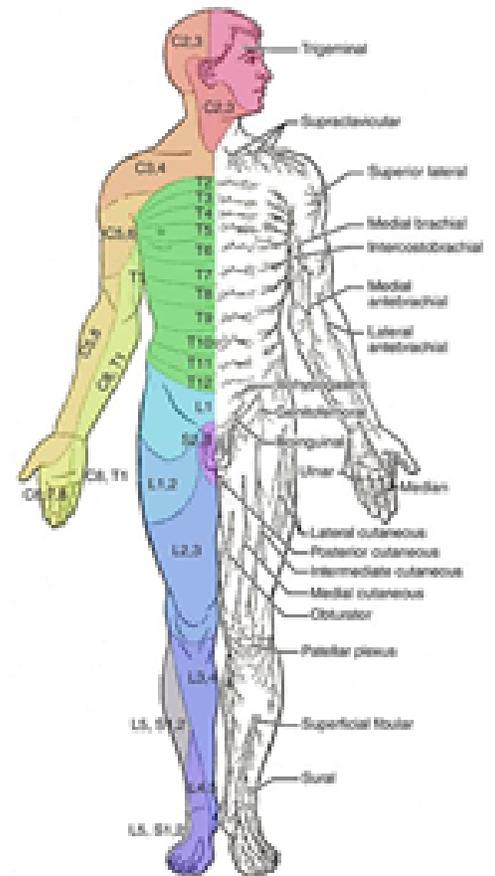
- Medial Branch Block – Radiofrequency Ablation
 - For nonradiating facet pain
 - Trial of block first
 - If pain <50%, do ablation
 - Lasts ~9-24 months



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)



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



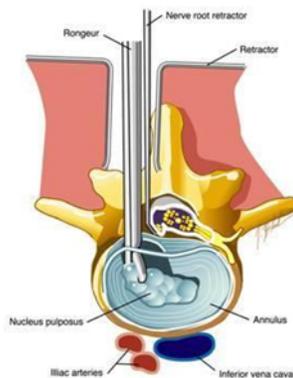
Intrathecal Pumps

- 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

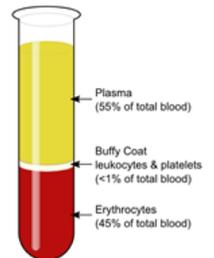
- For when a small disc piece has extruded and is pushing on a nerve
- Low risk, outpatient procedure
- Increasingly popular
- A much less invasive alternative to laminectomy, fusion, etc.



Coming Soon to a Procedure Room Near You!

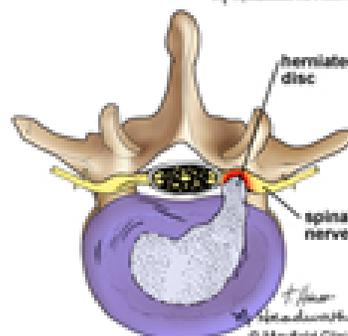
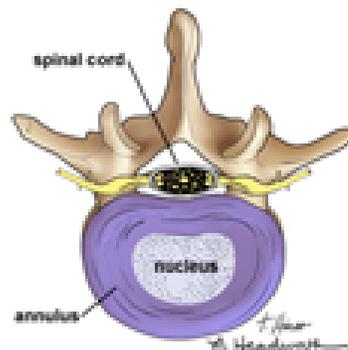
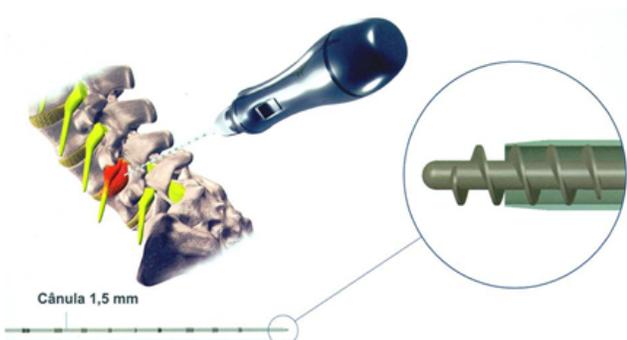
Platelet Rich Plasma Injections

- 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



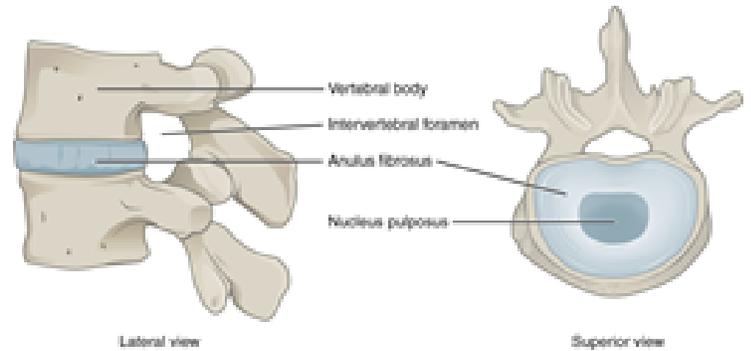
Coming Soon to a Procedure Room Near You!

- 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!

- 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!

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

- Select Opioid-Related Morbidity and Mortality Data for WI, November 2016, WI DHS, Division of Public Health, 1/2017
- CDC Opioid Overdose Data, <https://www.cdc.gov/drugoverdose/data/overdose.html>
- Cochrane analyses on acute pain:
 - Naproxen for postop pain, 2011 (C Derry & Derry, 2009)
 - Oxycodone for postop pain, 2010 (Gaskell, Derry, Moore, & McQuay, 2009)
 - Ibuprofen plus acetaminophen for post-op pain. (CJ Derry, Derry, & Moore, 2013)
- Opioid Therapy for Chronic Pain, Ballantyne J, Mao J. NEJM 2003; 349:1943-1953
- Efficacy and Safety of Opioid Agonists in the Treatment of Neuropathic Pain of Nonmalignant Origin Eisenberg E, McNicol ED, Carr DB. JAMA 2005; 293(24):3043-52
- Opioids for Chronic Non-Cancer Pain: a Meta-Analysis of Effectiveness and Side Effects, Furlan AD, Sandoval JA, Mailis-Gagnon A, Tunks E. CAMJ 2006; 174(11):1589-94

References

- Clinical Importance of Changes in Chronic Pain Intensity Measured On An 11-point Numerical Scale, Farrar JT, Young JP Jr, LaMoreaux L, Werth JL, Poole RM. Pain, 2001; 94:149-58
- Opioids in chronic non-cancer pain: systematic review of efficacy and safety, Kalso E1, Edwards JE, Moore RA, McQuay HJ. Pain. 2004 Dec;112(3):372-80.
- Pharmaceutical treatment patterns for patients with a diagnosis related to chronic pain initiating a slow-release strong opioid treatment in Sweden, Gustavsson A1, Bjorkman J, Ljungcrantz C, Rhodin A, Rivano-Fischer M, Sjolund KF, Mannheimer C. Pain. 2012 Dec;153(12):2325-31
- A population-based survey of chronic pain and its Tx with prescription drugs, Toblin RL1, Mack KA, Perveen G, Paulozzi LJ. Pain. 2011 Jun;152(6):1249-55.
- A population-based cohort study on chronic pain: the role of opioids, Sjogren P1, Grønbaek M, Peuckmann V, Ekholm O. Clin J Pain. 2010 Nov-Dec;26(9):763-9.

Questions?



Thank you for your time & attention!