Alternatives to Opioids in Treating Acute and Chronic Pain

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February 28, 2019 | 5:30 – 7:30 pm CST

Objectives

1) Discuss why opioids should be used only as a last resort in treating acute and chronic pain
2) Describe non-opioid medications and techniques for treating acute pain
3) Describe non-opioid medications and techniques for treating chronic pain

Disclosure

- None

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CME Accreditation and Designation

Aspirus Wausau Hospital is accredited by the Wisconsin Medical Society to provide continuing medical education for physicians.

Aspirus Wausau Hospital 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.

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Please complete the evaluation!

- To receive CME credit, please sign-in and complete the green evaluation/attestation form located on your seat. Thank you!

ASPIRUS CME/CPD PROGRAM EVALUATION

Alternatives to Opioids in Treating Acute & Chronic Pain

Speaker: Michael McNett, MD | Date: February 28, 2019

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I certify that I have participated in ____ of the 2.0 maximum credits designated for this activity

Please Print and Sign your Name:

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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.

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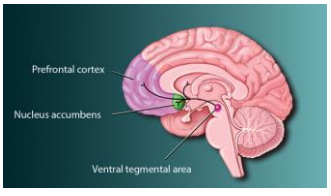
The Problem with Opioids #1
They reward their own use

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



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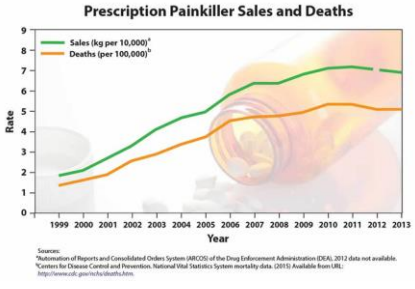
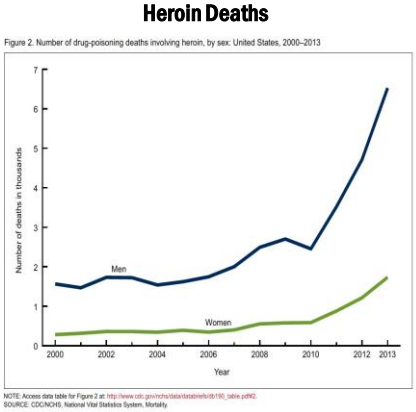
What are the consequences?





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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



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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

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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 persist 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

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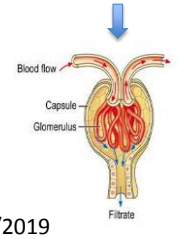
Alternatives to Opioids in Acute Pain: NSAIDs - General Considerations

- 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%



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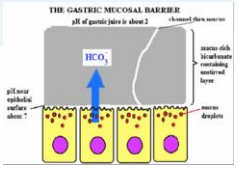
Alternatives to Opioids in Acute Pain NSAIDs – other ADRs



- 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
  ASA allergy
- Also associated with increased risk ASHD, bleeding problems

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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.

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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

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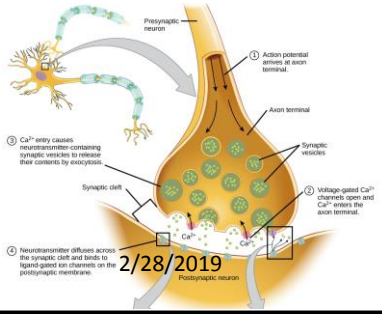
Alternatives to Opioids in Acute Pain Anticonvulsants: Physiology

- α-2-δ ligands (gabapentin, pregabalin)
  - Presynaptic inhibition by ↓ 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



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Anticonvulsants:α-2-δ 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

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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 (↑ 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 ↓ 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.)

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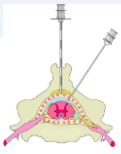
Alternatives to Opioids in Acute Pain
Interventional



- 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)

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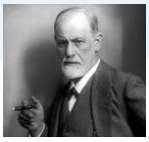
Alternatives to Opioids in Acute Pain Behavioral



- 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

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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

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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

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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

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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

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Non-opioid Treatment of Chronic Pain

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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

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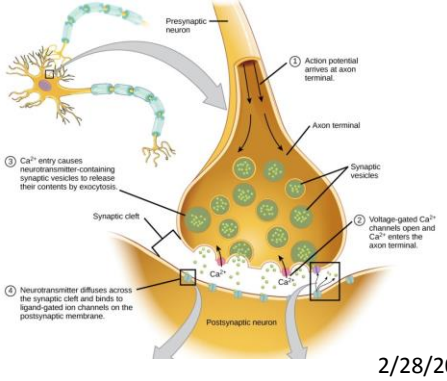
  - Presynaptic inhibition by ↓ neurotransmitter release



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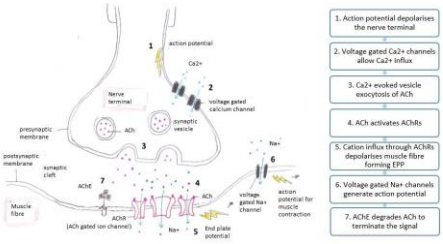
Alternatives to Opioids in Chronic Pain
Anticonvulsants: Physiology

Na channel agents

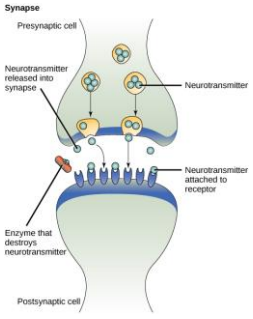
Postsynaptic inhibition

↓ action potential propagation



AMPA receptor agent

Postsynaptic inhibition



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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

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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 CO_2 at one month

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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_2 at 1 mo

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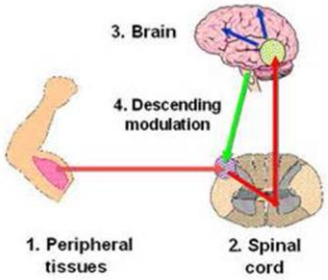
Alternatives to Opioids in Chronic Pain
TCA/SNRIs – mechanism of action

- Reduce pain by ↑ norepinephrine (and serotonin) at dorsal horn; hyperpolarize nerve



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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

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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

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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 despiramine

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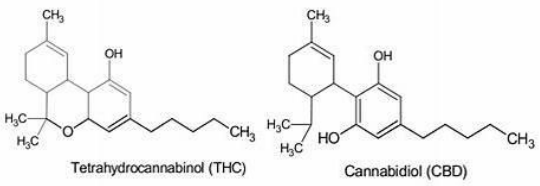
Medical Marijuana

- 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 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

THC vs. CBD



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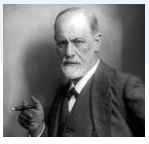
Alternatives to Opioids in Chronic Pain Behavioral



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Alternatives to Opioids in Chronic Pain
Physical Therapy

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

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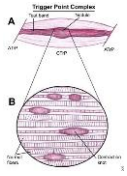
Alternatives to Opioids in Chronic Pain
Treating Myofascial Pain

- 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



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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

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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

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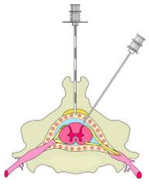
Alternatives to opioids in Chronic Pain Interventional approaches

- 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, …)



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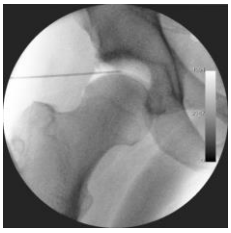
Corticosteroid Joint Injections

- 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



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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)

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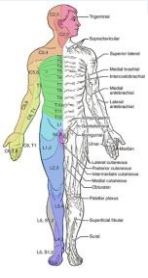
Epidural Steroid Injections

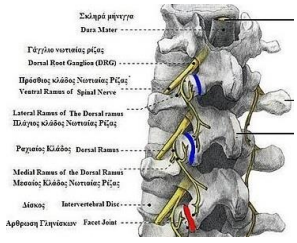
- Primarily benefit radicular pain associated with nerve impingement
  - May help annular tear pain
- Prefer < 3/yr, never > 6
- May benefit even if no nerve contact (inflammatory compound release)



2/28/2019

Nerve Ablations

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

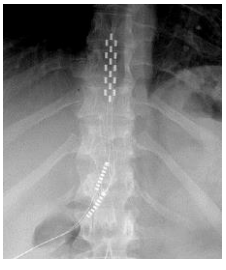


- Genicular Neurotomy
  - For chronic knee pain, if surgery undesirable
  - Trial block first
  - Usually lasts at least a year

2/28/2019

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



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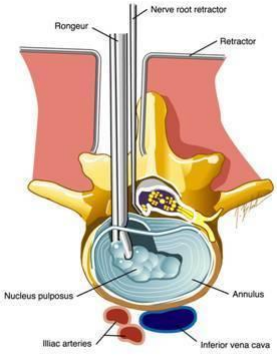
Intrathecal Pumps

- 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.)

2/28/2019

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.



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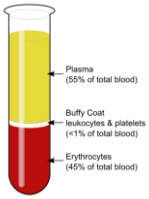
Coming Soon to a Procedure Room Near You

- 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



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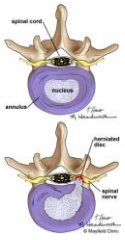
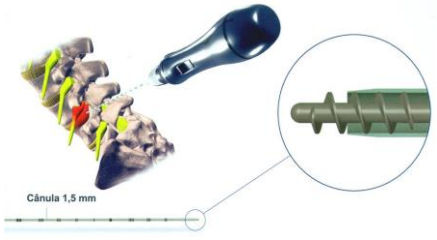
Coming Soon to a Procedure Room Near You

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





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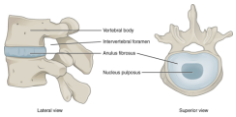
Coming Soon to a Procedure Room Near You

- 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



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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

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Questions?

Thank you for your time & attention!