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Back Talk: The Medicine Cabinet

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Back Talk: The Medicine Cabinet

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Disclosure

- None

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"I'M THE ONE WITH THE MEDICAL DEGREE, I'LL DETERMINE
IF YOUR BACK IS BOTHERING YOU, OR NOT..."

Objectives

- Differentiate between traditional therapies for back pain of nociceptive origin
- Discuss the debate regarding long-term opioid use & its impact on psychosocial functioning
- Differentiate between neuropathic back pain agents

General Back Pain Details

- Lifetime incidence ~50-80%
- Peak onset ages 30-40
- Direct US medical costs \$12.2-90.6 **BILLION**/yr
- Lost productivity & disability compensation
- Frequently associated with depression or anxiety

Duffy. Prim Care Clin Office Pract. 2010;37:729-741.

Chou. Drugs. 2010;70:387-402.

Schnitzer, et al. J Pain Symptom Manage. 2004;28:72-95.

Definition & Classification

- Low back pain (LBP): pain localized to lumbar area between inferior ribcage & waistline
 - May include sciatica, with pain radiating down to posterior-lateral thigh distal to the knee

Classification	Duration
Acute	<6 weeks
Subacute	6-12 weeks
Chronic	>12 weeks

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4 Main Classes of Low Back Pain

	Non-specific	Mechanical	Visceral / referred	Non-mechanical
Prevalence	70%	27%	2%	1%
Attributed Conditions	<ul style="list-style-type: none">• Lumbar sprain• Lumbar strain• No identifiable origin	<ul style="list-style-type: none">• Degenerative disc disease• Herniated disc• Osteoporotic compression fracture*• Spinal stenosis	<ul style="list-style-type: none">• Aortic aneurysm• Pelvic organ disease• GI disease• Renal disease*	<ul style="list-style-type: none">• Cancer• Infection*• Inflammatory arthritis• Paget disease of bone

Chronic LBP: A Mixed Pain Syndrome

- Nociceptive pain component (nonspecific pain)
 - Inflammatory response from tissue injury
 - Dull, aching, or throbbing pain
 - Usually adaptive & temporary once injury heals
- Neuropathic pain component (mechanical pain)
 - Lesion or disease affecting somatosensory system
 - Originates from lumbar spine and/or nerve roots
 - Paroxysmal, dysaesthetic and/or thermal

Acute nociceptive pain → Chronic nociceptive & neuropathic pain

LBP Treatment Goals

- Effectively reduce, if not resolve, **pain**
 - Fewest interventions (meds) necessary
 - Shortest duration at lowest dose
 - Most cost-effective
- Prevent and/or minimize treatment-related side effects
 - Avoid drug-drug & drug-disease interactions
- Restore **physical functioning**
- Decrease disease burden on patient & society

Factors Influencing Nonspecific LBP Pharmacologic Treatment Choice

- Symptom duration – acute vs. chronic
- Symptom intensity & quality
- Evidence
- Prior response to medications
- Adverse effect profile
- Drug-drug & drug-disease interactions
- Cost
- Convenience - # doses/day

Methodological Limitations

Most studies of only moderate quality

- Limited description of randomization & blinding
- Few active comparisons; most placebo only
- Small sample size
- Safety reporting limited & vague
- Short study duration & insufficient follow-up period
- Variation in pain assessment & efficacy criteria
- Multiple pain assessment scales used

Treatment Pearls

- 2/3 cases resolve within 6 weeks of onset
- LBP >12 weeks = ↓ likelihood for improvement
- Medication does not alter natural course
 - Meds target symptoms & functional status
- Best evidence for acute, short-term use
- Use shortest duration necessary, stop when no longer pain relief
- Chronic LBP does not mandate long-acting meds

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Traditional Back Pain Options

- Acetaminophen (APAP)
 - Nonsteroidal anti-inflammatory drugs (NSAIDs)
 - Corticosteroids
 - Muscle relaxants
 - Tramadol
 - Opioids
- Indications
 - Efficacy
 - Place in therapy
 - Side effects, contraindications
 - Monitoring

Acetaminophen (APAP)

- 1st line agent for acute & chronic LBP
- May be equivalent NSAIDs for **acute** back pain
 - Possibly inferior for **chronic** back pain
 - Ineffective for neuropathic pain
- Max 4 grams in 24 hours
 - 1000mg 4x/day, up to 28 days studied
 - Educate patients on APAP-containing meds!
- Caution use in alcohol users

NSAIDs

- 1st line agent for acute & chronic LBP
- Superior vs. placebo
 - Strongest evidence for acute pain
 - Better data for chronic pain vs. APAP
 - Ineffective for neuropathic pain
- No agent superior NSAIDs \approx celecoxib
- Toxicities limit more prevalent use
 - Studies not designed to assess GI & CV outcomes
 - Avoid in age >75, GI/CV disease history

NSAID & Dose	Duration (days)	LBP Type
Ibuprofen 400mg TID	2, 7	Acute
Ibuprofen 600mg TID	10	Acute
Ibuprofen 800mg TID	7	Acute
Naproxen 250mg TID	42	Acute
Naproxen 250mg 3-4x/day	15	Acute
Naproxen 250mg 4x/day	14	Acute
Naproxen 550mg BID	14	Chronic
Diflunisal 500mg BID	7-15	Acute
Diflunisal 500mg BID	14, 28	Chronic

NSAID Toxicities

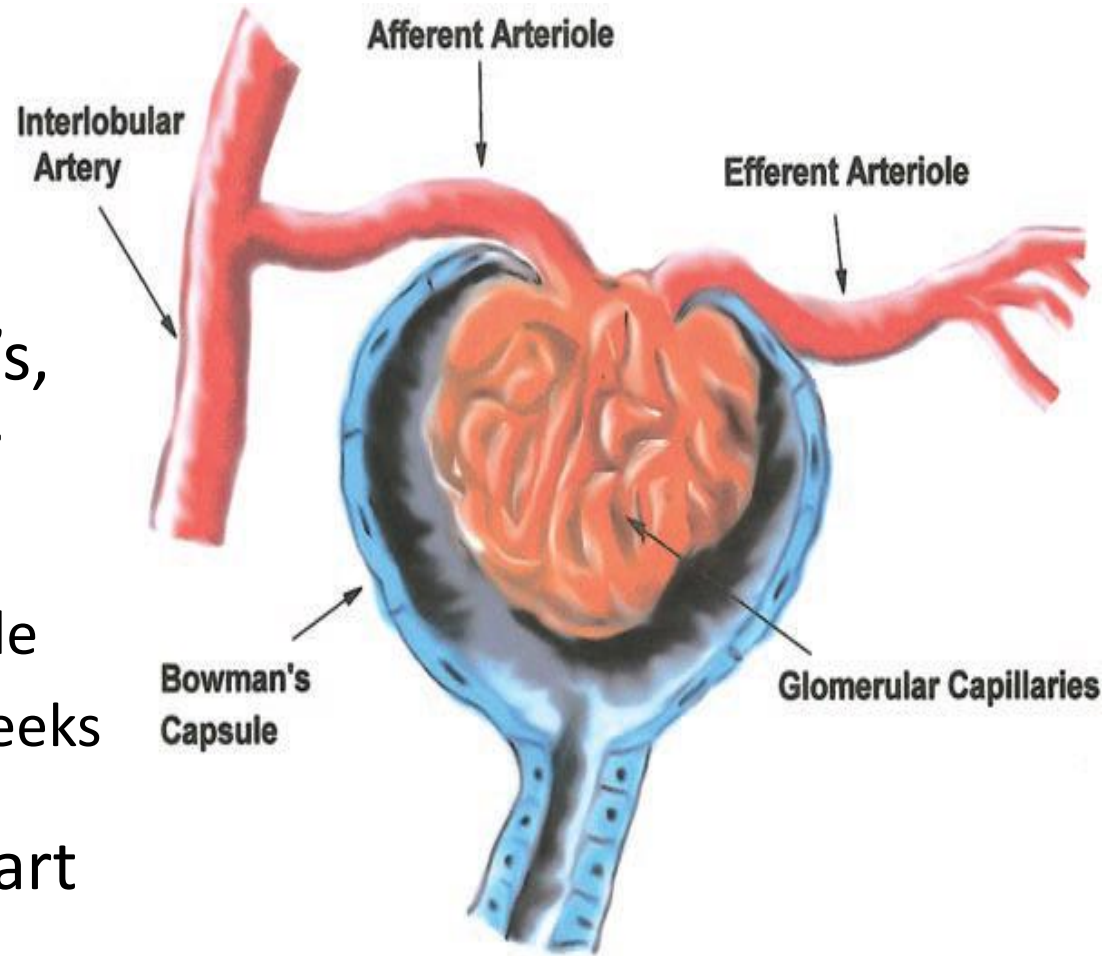
- Gastrointestinal
 - Dyspepsia (~30-40%)
 - Gastroduodenal ulceration 1-2 cases/1,000 patients/year
- Cardiovascular
 - Concurrent aspirin
 - ASA doses <150mg/day

Risk for ulcer on NSAIDs

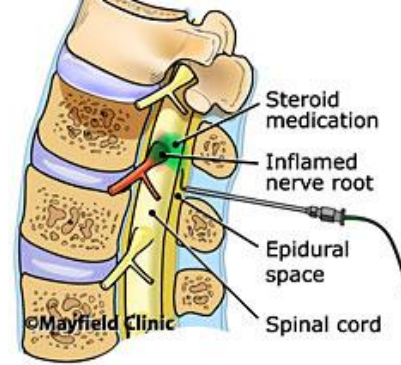
- Age >60
- H/o peptic ulcer disease
- Multiple NSAIDs
- High-dose NSAIDs
- Long-term use
- Concurrent corticosteroids

NSAIDs & Nephrotoxicity

- ↓ Renal blood flow
- ↑ Na⁺, H₂O retention
- Caution use with ARB's, ACE inhibitors, and/or diuretics!
 - Elderly, CKD susceptible
 - Monitor Cr, K in 1-2 weeks
- Caution CKD, HTN, heart failure, cirrhosis



Corticosteroids



- Epidural injections for radiculopathy (sciatica)
 - Benefit minimal, variable & only short-term
 - IM, IV methylprednisolone 160mg, 500mg x 1
- No benefit for any corticosteroid vs. placebo via any route for acute or chronic LBP
- Adverse events poorly described
 - Rare injection site infection risk
- **Not recommended for acute or chronic LBP**

Muscle Relaxants (MRs)

- Superior to placebo for **acute** LBP
- **2nd line or adjunct option due to side effects**
 - Short courses (2-7, max 14 days) recommended
 - Tizanidine + APAP/NSAID = better pain relief
- No single MR superior or best tolerated
- Not recommended for chronic LBP
 - Limited evidence, sedation, dizziness, dependence
 - No benefit for neuropathic pain (sciatica)

Duffy RL. Prim Care Clin Office Pract. 2010;37:729-741.

Chou, et al. Ann Intern Med. 2007;147:505-514.

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Variation in Selecting a MR

- Tizanidine (Zanaflex[®]) 2-4mg q6-8h
 - Dose-dependent hypotension, dry mouth, sedation
 - Monitor LFTs at baseline, 1 month, 3 months
- Cyclobenzaprine (Flexeril[®]) 5-10mg TID
 - Anticholinergic
 - 5mg=10mg, but less sedation
- Carisoprodol (Soma[®]) – avoid use!
 - Physical or psychological dependence possible

Tramadol (\pm APAP)

- Combination with APAP provides synergy
 - Lower doses, longer duration, better pain relief
- Caution SSRI, SNRI drugs
- No evidence in acute LBP
- **2nd line agent for moderate-severe chronic LBP**
 - Benefits similar to NSAIDs, weak opioids
 - Abuse & withdrawal potential
 - Potential benefit in nociceptive & neuropathic LBP

Tramadol + APAP Literature

- Tramadol 37.5mg TID – 75mg 4x/day + APAP x 12 weeks vs. placebo in moderate chronic LBP
 - Moderate improvement in chronic LBP
 - Minimal improvement in functional status
- Side effects: nausea (~13%), sedation (~12%), constipation (~11%) generally less vs. opioids
- Promising results, yet little data >12 weeks

Opioids for Acute LBP

- Potent, short-term pain relief vs. placebo
- May be no better vs. NSAIDs or SMRs
- No specific opioid superior
- Effective for nociceptive & neuropathic pain
- **2nd or 3rd line for severe, disabling acute pain not controlled/not likely to respond to APAP/NSAIDs**
 - Alternative for high risk of NSAID-induced toxicity
 - Screen for substance abuse prior to initiation
 - Time-limited course (1 month) to determine response

Dose-Dependent Side Effects

Complaint	Incidence	Comments
Constipation**	20-40%	Prophylactic bowel regimen
N/V	30%	Resolves days-weeks
Sedation	30%	Usually decreases with time
Dry mouth	25%	Caution dental carries
Dizziness	14%	Risk for falls, caution elderly
Pruritis	13%	Antihistamines?
Hypogonadism	??	Monitor fatigue, libido

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 Colameco S, et al. J Am Osteopath Assoc. 2009;109:20-25.

Morlion B. Curr Med Res Opin. 2011;27:11-33.
 Chou R, et al. J Pain. 2009;10:113-130.
 Jamison RN. Spine. 1998;23:2591-2600.

Chronic Opioid Debate in LBP

- Limited quality data for long-term effectiveness
 - Reduce pain VAS score ~30% vs. placebo
 - Opioid naïve & experienced with moderate-severe pain
- Initially improve pain, but long-term pain relief unproven combined with known side effects
 - Mood improvement ≠ pain improvement
- Do not improve activity or facilitate return to work!
- **Generally not appropriate for chronic LBP**
 - Requires monitoring of benefit, side effects & misuse

Grady D, et al. Arch Intern Med. 2011;E1-E2.

Kalso E, et al. Pain. 2004;112:372-380.

Deshpande A, et al. Cochrane Database Syst Rev. 2007;18:CD004959.

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Kuijpers T, et al. Eur Spine J. 2011;20:40-50.

Chou, et al. Ann Intern Med. 2007;147:505-514.

Long-Term Use: What Formulation?

- Chronic LBP \neq continuous 24/7, unrelenting pain
- More consistent opioid exposure may reduce euphoric effects & reduce abuse potential
- **No evidence long-acting formulations are more effective vs. short-acting or PRN doses**
 - Continuous exposure may facilitate tolerance
 - Tolerance \rightarrow dose escalations \rightarrow endocrine problems
- No reason to switch to long-acting opioids if doing well on a short-acting, PRN regimen

Serious Concerns for Opioids

- Analgesic tolerance
 - increasing doses to attain same pain relief
 - vs. disease progression vs. addiction vs. diversion
- Abuse, misuse, addiction, diversion - **INSPECT**
 - major depression, psychiatric conditions: more likely to initiate, abuse & not respond to opioids
- Physical dependence
- Overdose – incidence on the rise
 - dose-related, formulation-dependent
 - depression, substance abuse, benzodiazepines

Opioids & Psychosocial Functioning

- Opioids do not improve functional status or facilitate return to work
- Duration >7 days, ↑ dose, >1 prescription within 6 weeks of acute back injury associated with notable increase in work disability at 1 year
- Opioids may:
 - impair cognition
 - contribute to poor treatment outcomes
 - foster reliance on the healthcare system

Jamison RN. Spine. 1998;23:2591-2600.

Franklin GM. Spine. 2008;33:199-204.

Moore JE. Phys Med Rehabil Clin N Am. 2010;21:801-815.

Opioids & Addiction in Chronic LBP

- Most trials not designed to assess
- Few use a validated detection tool
- Poor quality trials used to define prevalence
- Current prevalence estimate of aberrant opioid-related behavior in chronic back pain: 5-24%
- Possible predictors for addiction
 - Additional comorbidities
 - Other substance abuse disorders
 - Younger age
 - Female

Methadone

- Less potential for abuse
- Long, variable half-life 15-60 hours
 - Not used for PRN or breakthrough pain
- No active metabolites
- Variable pharmacokinetics & pharmacodynamics
- High risk for side effects – start low, go slow!
- QTc interval prolongation & arrhythmias
 - Dose-related, concomitant drugs, drug interactions

My Patient is on Chronic Opioids....

- Evaluate pain, functional status & side effects regularly
- No max dose, but total doses >200mg/day morphine equivalent should permit evaluation of effectiveness
 - Switch to another opioid at reduced dose
 - Taper & discontinue opioid therapy altogether
 - Consider pain specialist referral
- Reemphasize opioid use as a therapeutic trial run
- Lack of alternatives not reason to continue unproven & unsafe chronic opioids when no clear end point exists

Neuropathic Back Pain Options

- Tricyclic antidepressants (TCAs)
- Duloxetine (Cymbalta[®])
- Gabapentin (Neurontin[®])
- Pregabalin (Lyrica[®])
- Opioids

TCA's – Nortriptyline, Desipramine

- Target neuropathic component of LBP
- Analgesia independent of antidepressant actions
- TCA's might be more effective vs. placebo for **chronic** pain; no data in acute LBP
 - Mild reduction in pain
 - No benefit on functional impairment, ADL
- Side effects: S.L.U.D.G.E. , sedation, weight gain
- **2nd/3rd line agent for chronic LBP after insufficient relief to other agents**

TCA Prescribing Considerations

- Undiagnosed depression
- Body mass
- Social drug use history & abuse potential
- Baseline cardiac arrhythmias
- Seizure history
- Elderly comorbidities
 - BPH, diabetes, constipation, dementia
 - Beer's Criteria
- Existing medications – tramadol, opioids

Duloxetine

- Quality & overall favorable data for reducing chronic LBP vs. placebo
- Maintained benefit up to 41 weeks duration
- Duloxetine 60mg daily
 - Usually start at 30mg, then increase after 1 week
 - Fewer side effects (nausea, dry mouth) vs. 120mg
- **Reliable option for chronic LBP**
 - Also useful if underlying depression

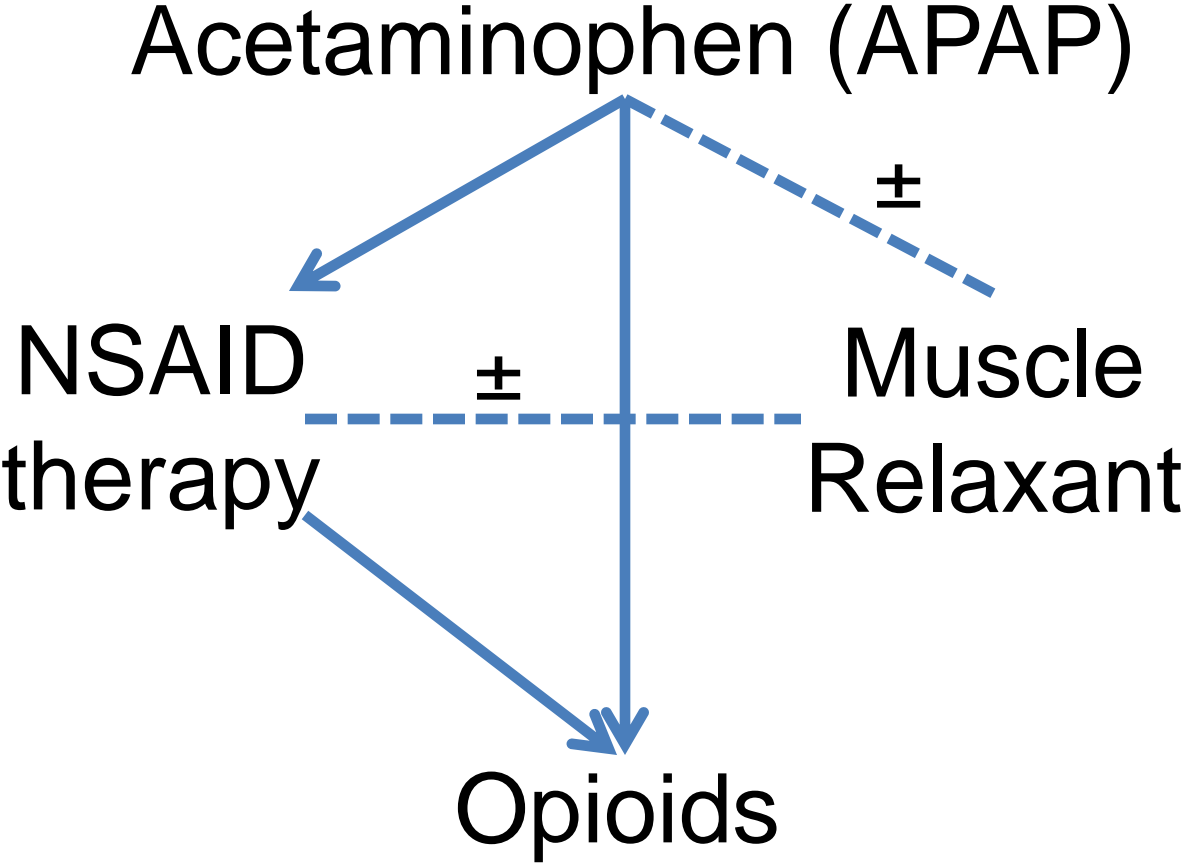
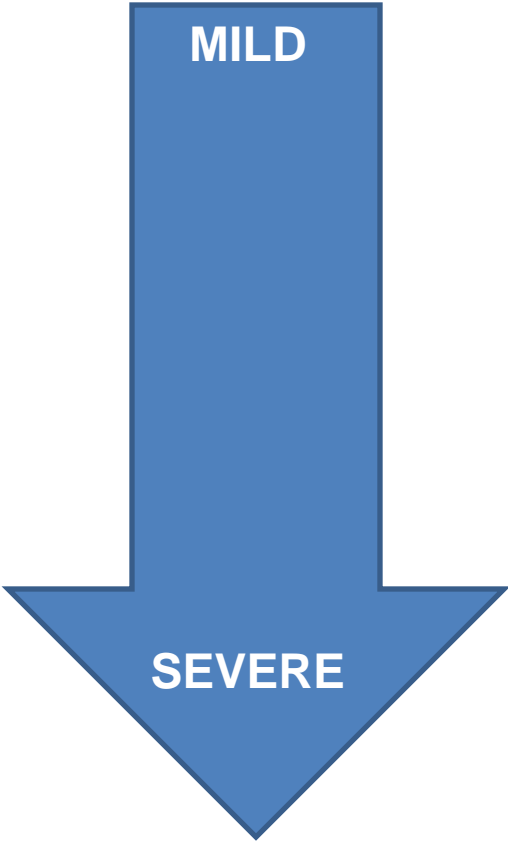
Gabapentin

- Limited data specifically in chronic back pain
- Reduced pain, increased walking distance in lumbar spinal stenosis, lumbar disc hernia vs. placebo
- TID dosing titrated to target 2400mg/day
- Well tolerated
 - Mild, transient sedation, dizziness
- **Well-tolerated option with possible benefit in neuropathic chronic back pain**

Pregabalin

- No more effective as monotherapy vs. placebo for chronic LBP
- No benefit for refractory neuropathic chronic back pain due to spinal stenosis or radiculopathy
- Not proven useful as monotherapy for chronic LBP

Acute LBP Treatment Algorithm



Chronic LBP Treatment Algorithm



Acetaminophen (APAP)

NSAID ← → Tramadol

Opioids

Evaluate use for duloxetine, gabapentin, or TCAs at any severity

Take Home Points

- Screen for depression
- Determine potential for neuropathic pain involvement
 - Assess not only pain intensity, but also pain quality
- Individualize treatment decisions
 - Caution polypharmacy in the elderly
- Meds may reduce pain; little effect on functional status
- Opioids – clear evidence for harm; ?? long-term benefit
- False perceptions & expectations about opioid use drive patient requests for chronic opioids when risk > benefit
- Never overlook non-pharmacologic approaches
- Active comparator, combination therapy , topical & long-term quality safety/efficacy studies desperately needed

Questions



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