CHRONIC MUSCULOSKELETAL PAIN
DIAGNOSIS, MANAGEMENT AND TREATMENT

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Pain Medicine
Chronic Musculoskeletal Pain

I. Introduction

II. Evaluation for Chronic Pain

III. Non-pharmacologic Therapies for Chronic Pain

IV. Pharmacotherapy for Chronic Pain

V. Conclusion
Definition of Chronic Musculoskeletal Pain

- Involves bones, muscles, tendons, ligaments and nerves
- > 3 months duration
- Localized or widespread

(Cleveland Clinic)
Classifications of Chronic Musculoskeletal Pain

- **Muscular Pain**
  - Chronic low back pain
  - Myofascial pain syndrome

- **Inflammatory Pain**
  - Rheumatoid arthritis
  - Ankylosing spondylitis
  - Osteoarthritis

- **Mixed/Central Pain**
  - Fibromyalgia
Fibromyalgia

• Controversial

• Several abnormal findings

• Centrally-mediated augmentation of pain and sensory process
Abnormal Findings in Fibromyalgia

- Allodynia
- Central sensitization
- Neurotransmitter system abnormalities
- ANS dysfunction
- Diminished grey matter volume of the brain
- Genetic factors
- Neuroendocrine abnormalities
- Exposure to a variety of stressors
- Small-fiber neuropathy (in a sub-group of fibromyalgia patients)
- Chronic inflammatory neuropathy (sub-group)
- Abnormal cutaneous arteriole venule shunts
CHRONIC PAIN: ALTERED NEURAL STRUCTURE

Chronic Pain is Accompanied by Cortical Reorganization: Flor, Neurosci Lett, 1997

Chronic Back Pain is accompanied by Brain Atrophy: Apkarian, Neurosci, 2004
Central Sensitization

- Increased levels of various pain neurotransmitters, glutamate and substance P

- fMRI data show cerebral responses to low-intensity stimuli that are comparable to responses of high-intensity stimuli in healthy controls
Clinical Presentation

- Pain
- Fatigue
- Insomnia
Diagnosis of Fibromyalgia

Classic:

Presence of tender points
Fibromyalgia Tender Points

Front of the neck above the collar bone
Breastbone below the collar bone
Outer forearm below the elbow
Inner side above the knees
Base of the skull
Back of neck towards shoulder
Upper back on shoulder blades
Hips
Upper outer side of buttock
The 2010 American College of Rheumatology Diagnostic Criteria for Fibromyalgia

- Widespread pain and symptoms for 3 or more months
- Widespread Pain Index (WPI) of 7 or greater and Symptom Severity (SS) scale score of 5 or greater

OR

- WPI of 3-6 and SS of 9 or greater

AND

- NO disorder that would otherwise explain the pain
<table>
<thead>
<tr>
<th>Criteria</th>
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<tbody>
<tr>
<td>A patient satisfies the diagnostic criteria for FMS if the following 3 conditions are met:</td>
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<tr>
<td>1. WPI ≥ 7 and SS scale score ≥ 5 or WPI 3 - 6 and SS scale score ≥ 9.</td>
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<td>2. Symptoms have been present at a similar level for at least 3 months.</td>
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<td>3. The patient does not have a disorder that would otherwise explain the pain.</td>
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<thead>
<tr>
<th>Ascertainment</th>
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<tbody>
<tr>
<td><strong>WPI:</strong> Note the number of areas in which the patient has had pain over the past week (score will be between 0 and 10): left shoulder girdle, right shoulder girdle, left hip (buttock, trochanter), right hip (buttock, trochanter), left jaw, right jaw, upper back, lower back, left upper arm, right upper arm, left lower arm, right lower arm, left upper leg, right upper leg, left lower leg, right lower leg, neck, chest, abdomen.</td>
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<thead>
<tr>
<th>SS scale score:</th>
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<tr>
<td>A. Fatigue, waking unrefreshed, cognitive symptoms. For each of the 3 symptoms above, indicate the level of severity over the past week using the following scale: 0, no problem; 1, slight or mild problems, generally mild or intermittent; 2, moderate, considerable problems, often present or at a moderate level or both; 3, severe, pervasive, continuous, life-disturbing problems.</td>
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<td>B. Considering somatic symptoms in general, indicate whether the patient has 0, no symptoms; 1, few symptoms; 2, a moderate number of symptoms; or 3, many symptoms.</td>
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<td>The SS scale score is the sum of the severity of the 3 symptoms (fatigue, waking unrefreshed, cognitive symptoms) plus the extent of somatic symptoms in general. The final SS score is between 0 and 12.</td>
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FMS, fibromyalgia syndrome; WPI, widespread pain index; SS, symptom severity.
Myofascial Pain Syndrome

→ Often occurs after repetitive injury or result of poor posture

→ Pathogenesis = poorly understood
Myofascial Pain Syndrome

Presentation:
- Local or referred pain
- Tightness, tenderness and stiffness
- Classic signs: trigger points
  - Referred pain in a characteristic pattern
  - Restricted range of motion
  - Visible/plapable twitch response

Associated Symptoms
- Stiffness
- Sleep disturbance
- Functional impairment
Chronic Low Back Pain

- 28% of patients with chronic pain in US
- Leading cause of disability
- 72% of chronic pain costs ($34 billion)
Causes of Low Back Pain

- Difficult to determine
- Often previous repetitive injury from sports or heavy physical activities at work
- Also have arthritis, disk changes or prior surgery

N.B.: NO clear association between radiologic changes on MRI and chronic low back pain
Inflammatory Pain

→ Type of nociceptive pain resulting from activation of central and peripheral nervous systems by inflammatory mediators

→ Manifested as heat, swelling, erythema and pain
Osteoarthritis

- Most common chronic joint disease
- Increased incidence because of rises in obesity and elderly population
- Presents with pain, deformity and loss of function
- Treatment:
  - Exercise
  - Non-pharmacologic
  - Pharmacologic
  - Surgery
Chronic Pain and Comorbid Conditions

- Insomnia – 17% of adults with chronic pain
- Psychologic distress - >90% of patients with chronic pain
  - Depression
  - Anxiety
  - PTSD
  - Personality disorders
  - Substance abuse

[These patients have significantly greater functional limitations and pain intensity than those without these co-morbidities]
Formal Assessment Tools

Ensure that these issues are considered and addressed

Examples:

- Opioid Risk Tool (ORT)
- Patient health Questionnaire-9 (PHQ-9)
- Patient Catastrophizing Scale (PCS)
- Patient Reported Outcomes Measurement Information System (PROMIS)
## ORT (Opioid Risk Tool)

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
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<tr>
<td><strong>1. Family History of Substance Abuse</strong></td>
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<tr>
<td>Alcohol</td>
<td>[ ] 1</td>
<td>[ ] 3</td>
</tr>
<tr>
<td>Illegal Drugs</td>
<td>[ ] 2</td>
<td>[ ] 3</td>
</tr>
<tr>
<td>Other</td>
<td>[ ] 4</td>
<td>[ ] 4</td>
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<tr>
<td><strong>2. Personal History of Substance Abuse</strong></td>
<td></td>
<td></td>
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<tr>
<td>Alcohol</td>
<td>[ ] 3</td>
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<tr>
<td>Illegal Drugs</td>
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<tr>
<td>Prescription Drugs</td>
<td>[ ] 5</td>
<td>[ ] 5</td>
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<tr>
<td><strong>3. Age (if between 16-45)</strong></td>
<td>[ ] 1</td>
<td>[ ] 1</td>
</tr>
<tr>
<td><strong>4. History of Preadolescent Sexual Abuse</strong></td>
<td>[ ] 3</td>
<td>[ ] 0</td>
</tr>
<tr>
<td><strong>5. Psychological Disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADD, OCD, Bipolar, Schizophrenia Depression</td>
<td>[ ] 2</td>
<td>[ ] 2</td>
</tr>
<tr>
<td>Depression</td>
<td>[ ] 1</td>
<td>[ ] 1</td>
</tr>
<tr>
<td><strong>Low (0-3) Moderate (4-7) High (8+)</strong></td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td><strong>Total</strong></td>
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Other Comorbid Considerations

- Vitamin D deficiency may be a contributing factor in patients with chronic pain.

- Consider for patients with nonspecific symptoms:
  - Musculoskeletal pain
  - Headaches
  - Fatigue
Malingering and Drug-Seeking

Potential Aberrant Behaviors

• Stealing
• Trading prescriptions
• Prescription forgery
• Obtaining prescriptions (from nonmedical sources)
• Repeated dose escalation
• Resistance to change in therapy despite adverse effects
• Repeated visits to other physicians or ER visits
• Injecting oral drugs
• Drug-related deterioration in function in work, social or family settings
Essentials of Management

- Comprehensive history
- Focused physical exam
- Prior records
- Assessment
- Treatment Plan
- Consult subspecialists
- DOCUMENT
- Assess risk of abuse/misuse (before initiating long-term opioid therapy)
Chronic Pain Conundrum

→ Believe patients
→ Treat appropriately

BUT

→ Be aware of potential aberrant behaviors
Evaluation

→ Determine etiology, intensity and influence (effects) of chronic pain
→ May need extended visit times
→ Use patient self-report whenever possible
→ Apply 7 A’s at each visit:
  → Analgesia
  → Affect
  → ADL’s
  → Add up pills
  → Adjunct therapy
  → Adverse reactions
  → Aberrant drug-related behavior
Evaluation

- Utilize various pain assessment tools
  - PROMIS – patient-reported of physical, mental and social health status
  - Chronic Pain Grade Questionnaire
  - Brief Pain Inventory (BPI) – helps to differentiate neuropathic from nociceptive pain; has long and short forms (use long for initial visit and short for follow-ups)
Physical Examination

- Focused physical

- Consider provocative maneuvers, e.g.
  - Straight-leg raise
  - Spurling’s test
  - Patrick’s test, aka FABER

- Assess for signs of drug addiction (injection/needle marks, nasal septum holes, conjunctivitis)
Final Assessment

Most chronic pain patients have several pain diagnoses and co-morbidities

Choose treatment modalities to type of pain and etiology
Overall Management of Chronic Pain Patient

- Multimodal
- Multi-disciplinary

[patient education, physical medicine, drugs, psychologic and spiritual counseling, relaxation techniques, interventional procedures, surgery and integrative medicine]
Core Principles

→ Explain nature of their chronic pain condition
→ Set appropriate goals
→ Develop comprehensive treatment approach
→ Develop a plan for adherence
Goal of Therapy

- Relieve pain as much as possible while enhancing patient function and quality of life

N.B.: Achieving a pain-free state is most often not a realistic goal

- Help patients learn how to live with their pain but not become their pain
Follow the 5 R’s and 2 E’s:

- Be Reasonable
- Be Reachable
- Include Record keeping
- Revisit and Revise
- Use Electronic state prescription drug monitoring programs
- Have an Exit strategy (for patients with CP taking opioids)
Documentation

- Patient self-reports
- Behavioral indicators of pain
- Physical exam results
- Clinical and assessment findings
- Treatment strategies
- Responses to interventions
Treatment Modalities for Musculoskeletal Pain (Non-pharmacologic)

- Physical activity
- Weight loss, physical therapy, aquatherapy, yoga, Pilates
- Gait, balance and posture retraining
- Psychologic modalities (e.g., CBT)
- Pain coping skills
- Interventional pain modalities
- Facet joint, sacroiliac joint, disk treatment
- Back bracing
- Kyphoplasty
- Surgical interventions
- Consults (for fibromyalgia w/uncertain dx)
Non-pharmacologic Therapies for Chronic Pain

Key: Multimodal therapy

- Behavioral
- Cognitive
- Integrative
- Physical
Behavioral Therapy

Among patients with chronic low back pain, short-term behavioral therapy is more effective than usual care for pain relief [?!]
Cognitive Behavioral Therapy

→ Addresses maladaptive thinking that can contribute to increased pain and disability, in addition to changing maladaptive behaviors

→ CBT was found to be effective in improving pain immediately post-treatment, improving mood, and decreasing catastrophizing outcomes and disabilities over 6 months

→ Shown to be effective for improving psychologic and physical function, with modest improvements in pain
- **Cognitive Behavioral Therapy**: Yes (‘A’, Cochrane)
  
  “Cortical plasticity related to chronic pain can be modified by behavioral interventions that provide feedback to the brain areas that were altered by somatosensory pain memories.”

  H. Flor, 2002 & 03

  “Individuals can gain voluntary control over ... specific brain region... these effects were powerful enough to impact severe, chronic clinical pain.”

  de Charms, 2005, Nat’l Acad Sci
Hypnosis

→ Shown to be effective in pain reduction
NON-PHARMACOLOGIC

- **Music Therapy:** Yes (‘A’, Cochrane)

- **Meditation:** Yes (‘A’, Cochrane)
  - Strong evidence for the use of relaxation & hypnosis in reducing pain in a variety of medical conditions
Guided imagery, Diaphragmatic Breathing and Muscle Relaxation

➔ All 3 potentially helpful in reducing pain/pain perception
Mindfulness-Based Stress Reduction

→ Shown to improve physical and emotional functioning in patients with chronic low back pain
Integrative Medicine Therapies

- Acupuncture/acupressure
- Chiropractic/osteopathic manipulation
- Superficial heat or cold
- Massage
- Touch therapy
Physical Therapies: Rehabilitation and Exercise Programs

All major guidelines recommend exercise as a part of a multimodal approach to patients with chronic pain.

In particular, exercise has been shown to benefit joint tissue in patients with osteoarthritis.
Chronic Low Back Pain

Good evidence that multidisciplinary rehab, including exercise, CBT, spinal manipulation, produces greater decreases in pain and disability than usual care or physical treatment for chronic low back pain.
Herbal Dietary Supplements

- Glucosamine and Chondroitin
  - Not shown to produce a clinically-significant improvement in pain or function when compared to placebo (according to GAIT trial)

- S-Adenosyl-L-Methionine
  - A dosage of 1,200 mg/day has been shown to be as effective as celecoxib in relieving joint pain (although it has a slower onset of action and may take up to 2 months to produce an effect)
Interventional Techniques

→ Minimally-invasive techniques for management of chronic musculoskeletal pain
Interventional Techniques

- **Facet joint pain**
  - Facet joint corticosteroid/medial branch injection (poor to good)
  - Radiofrequency denervation of medial branch (good)

- **Sacroiliac joint pain**
  - Sacroiliac joint injection (good for short term)
  - Radiofrequency denervation of sacral medial branches (good for select patients)
Interventional Techniques

- Axial low back pain
  - Epidural steroid injections
  - Prolotherapy (repeated injections of irritant solutions to strengthen lumbosacral ligaments)

- Spinal stenosis pain
  - Epidural steroid injections (poor to fair)

- Myofascial pain
  - Trigger point injections (fair)
  - Acupuncture (fair)
Interventional Techniques

- Herniated lumbar disk (moderate to good in the short term)

- Shoulder/knee/hip pain
  - Steroid injections
  - Viscosupplements
Interventional Techniques

- **Spinal fusion**
  - Used to decrease pain in patients with chronic low back pain with documented vertebral instability.
  - Most useful in patients with moderate to high-grade spondylolisthesis, but not as effective for patients with degenerative disk disease.
Pharmacotherapy for Chronic Pain

- Most chronic pain patients are treated with a combination of non-pharmacologic and pharmacologic therapies.

- Useful to employ the World Health Organizations’ 3-Step Analgesic Ladder.
Step 1
Nonopioid ± Adjuvant

Pain persisting or increasing

Step 2
Opioid for mild to moderate pain ± Nonopioid ± Adjuvant

Pain persisting or increasing

Step 3
Opioid for moderate to severe pain ± Nonopioid ± Adjuvant

Pain persisting or increasing

Invasive treatments

Quality of Life

Proposed 4th Step

The WHO Ladder

Pain Severity

1 - 3

4 - 7

8 - 10

Deer, et al., 1999
Treatment Modalities for Musculoskeletal Pain (Pharmacologic)

I. First-line Therapy:
   • Acetaminophen
   • NSAID
   • Muscle relaxant

II. Second-line Therapy:
   • SNRI

III. Third-line Therapy:
   • Opioid, low-dose
   • Anticonvulsant (second generation)
   • Weak anti-spasmodic
Step 1: Mild Pain

- Non-opioid analgesics
  - Acetaminophen
  - NSAID
  - Salicylates – ASA, choline magnesium trisalicylate, diflunisal, salsalate
  - Others – diclofenac, etodolac, fenoprofen, ibuprofen, meloxicam, nabumetone, naproxen, etc.
  - Cyclooxygenase-2 inhibitor (celecoxib)

- +/- Adjuvant
USING ACETAMINOPHEN EFFECTIVELY

- First-line agent for OA
- Safe alternative to NSAID’s for non-inflammatory pain
- Safe given q4H to max 4000 mg/day
- Caution with Liver Disease or Heavy EtOH
- Rapid onset (20-30 mins)
Do not exceed:

- 4 gm / day > 10 days in healthy patients
- 3.2 gm / day for chronic use in healthy pts.
- 2.6 gm / day for chronic use in non-healthy pts.
NSAID’S: GUIDELINES FOR USE

- 40-60% of NSAID use is by older people.
- In many circumstances can be replaced by an analgesic.
- Avoid chronic use in high risk patients.
- Not for use in chronic background analgesia.
Step 2: Moderate Pain

• Opioid
  • Acetaminophen-codeine
  • Acetaminophen-dihydrocodeine
  • Acetaminophen-oxycodone
  • Tramadol
• +/- Adjuvant
• +/- Non-opioid
Step 3: Severe Pain

- **Opioid**
  - Morphine
  - Hydrocodone
  - Hydromorphone
  - Levorphanol
  - Fentanyl
  - Oxycodone
  - Oxymorphone
  - +/- Adjuvant
  - +/- Nonopioid
MYOFASCIAL - FIBROMYALGIA MEDICATIONS

- **Strong evidence**: ‘A’ Rec

- Amitriptyline, 25-50 mg at bedtime
- Cyclobenzaprine, 10-30 mgs at bedtime
- Pregabalin, 450 mg/day
- Gabepentin, 1600-2400 mg/day
- Duloxetine, 60-120 mg/day
- Milnacipran, 100-200 mg/day
MYOFASCIAL FIBROMYALGIA MEDICATIONS

- **Modest evidence**: ‘B’ Rec
  - Tramadol, 200-300 mg/day
  - SSRIs (fluoxetine, sertraline)

- **Weak evidence**: pramipexole, gamma hydroxybutyrate, growth hormone, 5-hydroxytryptamine, tropisetron, s-adenosyl-methionine
MYOFASCIAL FIBROMYALGIA MEDICATIONS

No evidence:
- Opioids
- Benzodiazepines
- Hypnotics
- Melatonin
Opioids

→ Long-term opioid therapy for chronic pain is controversial given the limited evidence of long-term effectiveness and the well-documented adverse effects

→ Average pain reduction of only 2-3 points (on a 0-10 pain scale)
Conundrum:

Chronic pain is common among patients undergoing treatment for addiction

-- for example, in one study, 37% of patients receiving methadone maintenance and 24% of those in inpatient addiction facilities had severe chronic pain.
Indications and Treatment Initiation

- A trial of opioids is indicated for chronic pain if pain is:
  - moderate or severe
  - has an adverse effect on quality of life or function
  - potential benefits outweigh harms
  - other treatment modalities have been ineffective
Treatment Initiation

- Assess the 7 A’s (Table 12)
- Start low and go slow
  - 1\textsuperscript{st} – short-acting
  - 2\textsuperscript{nd} – change to long-acting after effective dosing achieved, using same short-acting for breakthrough pain

- Avoid long-acting opioids in opioid-naïve patients (secondary to sedative and respiratory effects)
7 A’s:

→ Analgesia
→ Affect
→ ADL’s
→ Add up pills
→ Adjunct therapy
→ Adverse reactions
→ Aberrant drug-related behavior
Adverse Effects and Complications

- Counsel patients on possible transient or lasting cognitive effects that may affect driving and work safety.
- Advise of possible respiratory depression (most common cause of mortality from opioid overdose).
Addiction and Tolerance: Opioids

- Highly addictive
- One of the most abused substances among young adults between 18-25 y.o.
- Need to be able to distinguish between physical dependence, tolerance and addiction
Physical Dependence

Patients develop physical dependence after taking opioids daily for several weeks (and abrupt discontinuation can lead to withdrawal symptoms).
Tolerance

- Can occur within 1 week of starting an opioid
- When switching to another opioid, start with half of the equivalent dose
Opioid-Induced Hyperalgesia (OIH)

- If despite increasing the dosage, pain is still not controlled or pain worsens, consider OIH.
- If so, opioid therapy should be discontinued.
Monitoring Treatment and Discontinuation

→ Use a validated risk stratification tool for aberrant behavior, such as Opioid Risk Tool (ORT)
Monitoring Treatment

- Routinely screen for aberrant behavior
- Inquire about pain level
- Assess adherence (pill counts and UDS)
- Decreased drug dosages when appropriate
- Document your plan and expectations (opioid agreement)
Opioid Agreement

• Address indications
• Goals
• Alternatives
• Risks and benefits
• Proper storage and disposal of opioids
• Expectations [one prescriber, no early refills, use of a single pharmacy]
• Plans for violations/aberrant behavior
• Follow-up
• Monitoring systems
Discontinuation

✓ Adverse reactions
✓ Lack of progress toward therapeutic goals
✓ Inappropriate drug use
✓ Part of an exit strategy
Discontinuation

→ Opioids should not be stopped abruptly, because severe withdrawal symptoms may occur

→ Clonidine has been used off-label to offset some withdrawal symptoms
Detoxification

- Special license or qualifications
- Typically in-patient
- Simplified out-patient treatment with buprenorphine (need special DEA number)
Methadone

- Moderate to severe chronic pain that does not improve with other opioids
- Initiated and monitored by clinicians familiar with its usage
- Advantages: excellent bioavailability and potency at a low cost
- Duration of analgesic effect: 4-8 hours
- Elimination half-life: 8-59 hours
- Peak respiratory effect typically occurs later and persists longer than peak analgesic effect.
Methadone

- Perform EKG to identify patients at high risk of methadone-associated arrhythmias, particularly QTc prolongation, which can lead to torsades de pointes
- Necessitates diligent monitoring and follow-up
Necessary Additional Office Data

- Pill counts
- Random urine drug screens
- Prescription drug monitoring program

[Occasionally, clinicians have difficulty interpreting urine drug screening results, and consulting with a toxicology subspecialist can be helpful]
Adjuvant Pharmacotherapy

- Antidepressants
  - TCAs
  - SNRIs
  - SSRIs
  - Bupropion

N.B.: All antidepressants have a black-box warning regarding suicidality
Anticonvulsants

→ often used in chronic pain, especially for concomitant nerve pain
Muscle Relaxants

- Most common adverse effects = drowsiness and nausea
- Newer long-acting formulations mitigate these side effects
Muscle Relaxants

- Cyclobenzaprine
- Tizanidine
- Baclofen – more centrally-acting; treatment of spasticity
Other Adjuvants

- **Botox/Myobloc** – blocks Ach release at NMJ [Evidence supports possible benefit in treatment of piriformis syndrome]

- **Clonidine** – relieves hyperalgesia in patients with sympathetically-mediated pain syndromes

- **Corticosteroids**
Conclusion

- Multimodal
- Multidisciplinary
SAFE PRESCRIBING

- Remember basic principles:
  - Use WHO pain ladder
  - Take a careful drug history
  - Know the pharmacology of the Rx
  - “Start low, go slow”
  - Regularly review the regimen
  - Remember that drugs may cause illness
- Non-Opiates 1st
  - Acetaminophen
  - NSAID’s

- Then Adjuvants
  - Muscle Relaxants
  - Anticonvulsants

- Opioids Last
Interventional Techniques – Forefront

PRP/Stem cell injections

- Joints (shoulder, knee, hip)
- Muscle
- Disks