Long Term Chronic Pain Treatment:

Focusing on Non-opioid Options

Robert G. Valentine, Jr., M.D.
Interventional Medical Associates, LLC
Gainesville, Florida

Background

- Anesthesiologist by training
  - Medical school and residency @ University of Arkansas for Medical Sciences
  - "Weird" guy who was interested in pain
    - Although anesthesiology was the only specialty at the time which required training in pain therapy in order to have an accredited program, those who were interested were a minority, to say the least
    - Even today, over 50% of physicians treating chronic pain are anesthesiologists (PM&R is coming on strong, and reasonably so)
  - Private practice treating pain patients since 1985
  - Founded Arkansas Pain Centers in 1988
    - First in Arkansas to dedicate full time practice to pain treatment
  - Sold APC and relocated to Florida in 2001
    - My wife wanted to move to Florida and I wanted to move to Wyoming so we compromised (she was right, as usual)

"Spring"

Alphonse Mucha 1896

Goals

- Theoretically
  - Improve function, minimize resource use and return to work
    - Makes me look good, makes you happy and is best for the patient
- Reality
  - *Sometimes* improve function, hope to return to, or continue, work in some capacity, optimize resource use
  - Often, especially with long term patients, the primary is to control (not eliminate) pain to *maintain functional status* as much as possible
  - Remember, response to treatment may be limited
    - "Despite the best of care and sequential trials of therapy, pain will remain unrelieved or inadequately relieved in 40-60% of patients with neuropathic pain." Pain 2007; 132: 325-6

"Pain Management"

- "Pain Management" = Opioid use
  - Such a common idea that patients and even physicians use the terms interchangeably (at least in Florida).
    - "My doctor referred me for pain management" too often means the patient was started on opioid(s), failed to improve over time and the physician became uncomfortable
    - What the patient hears (correctly or not) is, "I can't prescribe your medication any more, so I'm sending you to Dr. Whosis to do it."
    - Very difficult to make progress when patient is convinced, prior to ever being evaluated, that "Percocet is the only answer – unless maybe more Percocet is a better answer."
      - Reluctant to accept other approaches because opioids are "strong" pain medicine
      - Other approaches therefore viewed as taking patient's pain lightly
- ***False equation***
  - Numerous other options
- Opioids may at times be a *component* of "pain management" but they are *not* eqivalent terms

Non-opioid options

- Non-opioid Medication(s)
- Physiatric (Rehabilitation)
  - Including physical therapy
- Psychological/social
- Interventional
  - Minimally invasive
  - Surgical (no discussion)
- Alternative

Medication

- Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)
  - Primary action: inhibit cyclooxegenase
    - Enzyme which mediates conversion of arachidonic acid to prostaglandins and thromboxanes.
  - Isoenzymes exist
    - COX-1 (Multiple tissues in which COX-1 expressed constitutively)
      - Regulates renal autoregulation of blood flow, gastric cytoprotection, vascular homeostasis, platelet aggregation
    - COX-2 (Constitutively expressed in a few tissues, e.g. bone, CNS, kidney)
      - Primarily induced in inflammatory states
    - COX-3
      - RNA splice variant of COX-1, localized mostly in CNS but also present in heart
      - Clinical significance unclear
  - Potential for significant side effects
    - Renal toxicity, gastritis/gastric ulcer, cardiac events, etc.
      - Celebrex easist on gut, naproxen most GI risk but no cardiac, diclofenac most cardiac risk

Medication

- NSAIDs
  - Classes
    - Acetic Acids
      - Diclofenac (Cataflam, Voltaren, Zipsor)
      - Etodolac (Lodine)
      - Indomethacin (Indocin)
      - Ketorolac (Toradol)
      - Sulindac (Clinoril)
      - Tolmetin (Tolectin, Tolectin DS)
    - COX-2 inhibitor
      - Celocoxib (Celebrex) [previously: Vioxx, Bextra]
    - Fenamates
      - Meclofenamate
      - Mefenamic acid

Medication, cont.

- NSAIDs, cont.
  - Classes
    - Naphthylalkanones
      - Nabumetone (Relafen)
    - Oxicams
      - Meloxicam (Mobic)
      - Piroxicam (Feldene)
    - Propionic Acids
      - Fenoprofen (Nalfon)
      - Flurbiprofen (Ansaid)
      - Ibuprofen (Motrin)
      - Ketoprofen (Orudis, Oruvail)
      - Naproxen (Aleve,Anaprox, Naprelan, Naprosyn)
      - Oxaprozin (Daypro)

Medication

- NSAIDS, cont.
  - Classes
    - Salicylates, Acetylated
      - Aspirin
    - Salicylates, Nonacetylated
      - Diflunisal (Dolobid)
      - Salsalate (Disalcid, Salflex)
- Other:
  - Acetaminophen
    - Possible "COX-3" inhibitor
    - No actual anti-inflammatory effect
    - Recent reports suggest possible anxiolytic effect

Medication

- Tramadol
  - Weak mu-receptor (opioid) agonist
  - Enhanced neuronal serotonin release
  - Inhibits serotonin and norepinephrine reuptake
    - Similar to effect of tricyclic antidepressants
    - Should have increased efficacy in neuropathic pain
      - Clinical experience supports this
  - Possible anti-inflammatory activity that is independent of COX inhibition
  - Meta-analysis: better evidence for long term efficacy than typical opoids
  - Addiction risk lower than typical opiates
  - Physical dependence may occur
  - Potential for abuse but no one will rob and kill you for it

Medication

- Tricyclic Antidepressants
  - First antidepressants found to be effective for neuropathic pain
  - Analgesic effect is separate from antidepressant effect
    - Generally much lower dosage
      - e.g. up tp 35 mg amitriptyline for pain vs. +/- 300 mg for depression
  - Block reuptake of both serotonin and norepinephrine
    - Amitriptyline (Elavil)
      - Most anticholinergic effects (dry mucous membranes, etc.)
    - Nortriptyline and Desipramine
      - Least anticholinergic effects (e.g. dry mouth) and less sedating
    - Doxepin (Sinequan)
      - More sedating, anxiolytic effect equal to Valium, least cardiotoxic

Medication

- SNRIs (Serotonin-Norepinephrine Reuptake inhibitors)
  - All shown to have analgesic properties
  - All effective for neuropathic pain
    - Duloxetine (Cymbalta)
      - Multiple indications, including ***any chronic musculoskeletal pain***
    - Venlafaxine (Effexor)
      - No indications (older drug) but studies indicated effective for neuropathic pain
        - » More sexual side effects than duloxetine
    - Savella
      - Currently only specific indication in U.S. for fibromyalgia
      - Clinical experience has shown effective for other neuropathic pain conditions and possibly other types of chronic pain

Medication

- SSRIs (Selective Serotonin Reuptake Inhibitors)
  - Variable effects on pain
    - Fluoxetine (Prozac) ineffective for neuropathic pain
    - Citalopram (Celexa) and paroxetine (Paxil) shown to have *some* efficacy
  - *30-50% (some studies suggest up to 75%-90%) of pain patients become depressed*
  - SSRIs particularly effective for situational depression
    - Clinical effect fairly rapid compared to tricyclics
  - Depression may be physically painful
  - Treatment of depression not only may improve ability to effectively treat pain, it may lessen pain and improve overall level of function

Medication

- Anticonvulsants (or Anti-Epileptic Drugs – AEDs)
  - Effective for neuropathic pain by virtue of membrane stabilizing properties
    - Gabapentin (Neurontin) and Pregabalin (Lyrica)
      - Few drug interactions
      - Primarily excreted unchanged renally
    - Carbamazepine (Tegretol)
      - Older agent, still used for trigeminal neuralgia and occasionally in other refractory neuropathic pain states
      - Requires monitoring
      - Serious, potentially fatal, side effects (bone marrow suppression)
    - Oxcarbamazepine
      - Better tolerated but still has same potential side effects

Medication

- Anticonvulsants, cont.
  - Valproic acid
    - May cause thrombocytopenia
  - Topiramate (Topamax)
    - Often effective but significant side effects
      - Paresthesias
      - Kidney stones (1.5%)
      - Acute glaucoma (1 in 20,000)
      - Personality changes (often irritability)
      - Weight loss
  - Others:
    - Gabitril, Keppra, zonisamide, etc.

Medication

- Muscle Relaxants
  - Antispasmodics used to treat pain associated with muscle tension or spasm
    - FDA indications are generally for short term use but clinically often beneficial on prolonged basis (generics available so don't expect expensive studies to prove)
  - Baclofen
    - Spasticity (oral and intrathecal use)
    - Anecdotal evidence of analgesic properties
    - Effective for trigeminal neuralgia
  - Cyclobenzaprine (Flexeril)
    - Structurally similar to tricyclic antidepressants
    - Sedation often limits use (7.5 mg and long acting form Amrix at 6PM may be better tolerated)

Medication

- Muscle Relaxants
  - Tizanidine
    - Structurally similar to clonidine
    - FDA indication for spasticity from spinal cord injury or MS
    - Useful for sympathetically mediated pain, neuropathic pain, low back pain, myofascial pain
    - Monitor liver enzymes, low blood pressure
  - Mataxalone (Skelaxin)
    - Generally less sedating
  - Other:
    - Orphenadrine, methocarbamol, Lorzone (chlorzoxazone)

Medication

- Topical agents
  - Lidocaine (Lidoderm)
    - Useful for post-herpetic neuralgia (PHN), myofascial pain, peripheral neuropathies, myofascial pain
  - NSAID (Voltaren Gel, Pennsaid, Flector: diclofenac)
  - Capsaicin (Zostrix, etc.)
    - Useful for PHN, osteoarthritis, other neuralgias, possibly LBP
    - "Burning" sensation on application for 1st month or so may limit tolerability
  - Compounded formulas
    - Generally mixture of anticonvulsant, anti-inflammatory, muscle relaxer and local anesthetic (and others)
    - Often quite effective, especially for localized neuropathic pain, but applied 3-4 times a day

Medication

- NMDA Receptor Antagonists
  - Dextromethorphan (not controlled)
    - Most common use as cough suppressant
  - Ketamine (dissociative anesthetic) ("Lucy in the Sky with Diamonds")
  - Methadone
- NMDA involved in spinal "wind up"
  - Believed to be involved in generation of neuropathic pain and opioid tolerance
  - Inhibition of receptor can have potent analgesic effects

Medication

- α2-Agonists
  - Effects at spinal cord and peripherally
  - Sympatholytic activity
  - Clonidine
    - Antihypertensive
    - Useful in sympathetically driven pain such as CRPS/RSD
  - Tizanidine
    - Also useful as muscle relaxer and anti-spasticity agent as noted

Medication

- Corticosteroids
  - Potent anti-inflammatory agents
    - Decreasing inflammation reduces nociceptor sensitization
    - Reduce edema and neural compression
    - Decrease spontaneous firing of sodium channels (direct effect on nerve)
- Other OTC (non-herbal)
  - Examples
    - L-tryptophan (sleep, anxiety)
    - N-acetylcysteine (cold RSD/CRPS)

Medication

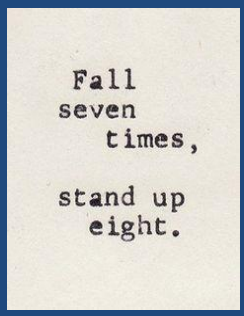
- "Medical Foods"
  - Substances occur in nature

Medication

- "Medical Foods"
  - Anti-inflammatory agent
    - Limbrel
      - Peroxidase
    - Less renal toxicity than NSAIDs
    - No known cardiac risk
    - Better GI tolerability
    - No effect on clotting
    - Long term efficacy comparable to naproxen

Medication

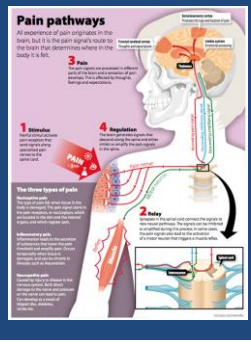
- "Medical Foods"
  - Neuropathy (neuropathic pain?)
    - MetanX
    - FDA indication for diabetic peripheral neuropathy
    - Clinically useful for other neuropathies
      - Possibly nerve injuries
    - Other off label uses



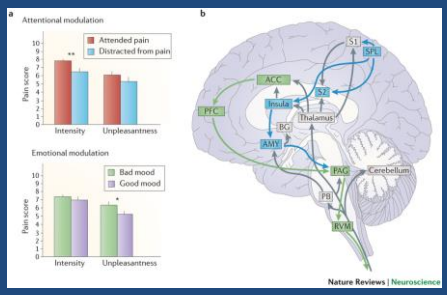
Psychological/behavioral/social

- Two of the three ascending pain pathways through the central nervous system terminate in affective, or emotional, centers in the brain
  - Not possible to discount and separate the emotional/psychological component of pain
    - Of course, we try to do just that every day
  - Psychological factors play a significant role in the experience, maintenance and exacerbation of pain
    - We were designed this way; part of being human
    - Each of us responds differently based on our own "wiring", social situation, past experiences, environment, etc.
    - Does not make the experience less real or less valid

Psychological/behavioral/social



Results of Psychological Modulation (Attentional and Emotional)



Goals of Psychological Therapy

- Increase perception of control over pain
  - Pain education
  - Psychophysiological interventions (e.g. biofeedback, hypnosis)
  - CBT (Cognitive Behavioral Therapy) to lower catastrophizing thinking around pain
- Lower secondary symptoms of psychiatric distress
  - Psychotherapy for depression and anxiety
  - Pharmacological management
  - Management of psychological trauma

Goals of Psychological Therapy

- Improve daily function
  - Improve sleep
  - Increase coping strategies (i.e. pacing, relaxation)
  - Goal setting
  - Return to work or other meaningful life activity
  - Minimze operant reinforcement of pain behavior
- Reduce negative health habits
  - Quit smoking
  - Lose weight
  - Increase exercise

Co-morbid Depression

- Most common psychological co-morbidity
  - Prevalence is 30%-50% in chronic pain patients
    - Some studies suggest up to 75%-90%
  - Cyclic relationship between pain and depression
  - Depression compromises pain threshold and tolerance
  - Serotonin levels are lower in pain patients
  - Result is lack of motivation/energy to participate in rehabilitation

Co-morbid Anxiety

- Prevalence 20%-40%
- Associated with prolonged diagnostic uncertainty
- Anxiety leads to increased sympathetic nervous system excitation which increases the experience of pain

Psychological/behavioral/social

- Psychological interventions
  - Cognitive Behavioral Therapy
    - Personalized but structured treatment with expectation of significant patient participation in treatment
    - Goals:
      - Reduction of pain intensity, frequency and duration of pain episodes, improved physical, social and psychological function, control of medication usage, reduce health care utilization, promote return to work
    - Important components:
      - Education
      - Rationale for treatment
      - Coping skills training (Relaxation and imagery techniques, diaphragmatic breathing to engage parasympathetic nervous system, Progressive muscle relaxation, Distraction, Imagery techniques, Hypnosis [or meditation, yoga], Pacing level of activity, Cognitive restructuring, Goal setting, Homework, Relapse prevention, Problem solving)

Psychological/behavioral/social

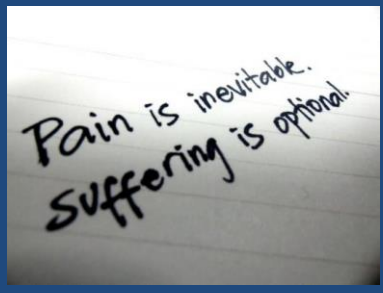
- One example
  - Coping skills training
    - Cognitive restructuring
      - Identify maladaptive thoughts during problematic situations (e.g. Pain exacerbations)
      - Introducing and practicing coping thoughts
      - Shifting from self-defeating to coping thoughts
      - Introducing and practicing positive or reinforcing thoughts
      - Finally, home practice and follow-up

Psychological/behavioral/social

- Another example ("Down and dirty" cognitive restructuring)
  - Patient with chronic low back pain following a work injury
  - Clearly improved with medication and minimally invasive techniques but not resolved
  - Anger issues over feelings that no one (e.g. employer, WC adjuster) cared about him and his situation
  - Seen in clinic one day with dramatic improvement in outlook ("Woe is me" was gone. "Suffering" component of pain was improved.)
  - Wife sat him down, explained that he had a family to support and basically told him it was time to get past his anger and self-pity and be a man. He thought about it and decided she was correct.
    - Unfortunately this doesn't work so easily for everyone and could have backfired

Psychological/behavioral/social

- Interdisciplinary Pain Rehabilitation Programs
  - Underlying concept is that people with complex pain problems are best treated using the collaborative efforts of a team of specialists which may include physicians, nurses, physical/occupational therapists, psychologists and vocational counselors.
    - Basically they don't only treat the pain. They attempt to treat the entire person.
    - Every patient I have had accepted into a program has improved.
    - Not every patient is candidate, nor does every patient need



Interventional Treatment

- Nerve blocks
  - Diagnostic, Therapeutic or both
  - Cranial nerve, spinal nerve *(selective or multiple)*, peripheral nerve
  - Autonomic ganglia *(Stellate ganglion, Lumbar sympathetic)*
- Soft tissue injections
  - Muscle, Tendon sheath, Bursa, Scar
- Joint injections
  - Spinal or peripheral
- Intradiscal injection or decompression
- Implantable
  - Spinal cord and/or peripheral nerve stimulation
  - Spinal infusion of medication (baclofen, Prialt, clondine, local anesthetic)
- Surgical

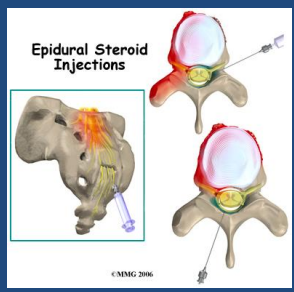
Interventional Treatment Options

- Nerve blocks
  - Cranial nerve
    - Trigeminal divisions and branches V
    - Spinal Accessory Nerve XI
      - Spasm of trapezius and/or sternocleidomastoid muscles
    - Other specific cranial nerves less likely in work injury
    - Superficial and/or deep cervical plexus (branches from I, II, III and IV)

Interventional Treatment Options

- Nerve blocks
  - Spinal
    - Selective transforaminal epidural block
      - Cervical, lumbar or sacral levels (thoracic can be done but difficult)
        - » Many do not perform cervical transforaminal injections
      - With (usually) or without steroid
    - Interlaminar epidural block
      - With (usually) or without steroid
        - » Can be used to perform sympathetic block in thoracic and lumbar regions, but is not very selective
    - Caudal epidural block
      - Access to sacral and lumbar nerve roots
      - Useful when desire to avoid placing needle at surgical site where dorsal epidural space may no longer exist

Epidural injections



Interventional Treatment Options

- Nerve blocks
  - Peripheral
    - Individual nerve(s)
      - Includes branches of paravertebral nerves to facet joints
        - » Usually diagnostic and may be followed by radiofrequency denervation
        - » Other peripheral nerves may be targets for radiofrequency lesioning also
    - Plexus
      - e.g. Lumbar plexus block to treat psoas muscle spasm/pain
    - May be therapeutic, esp. at surgical site(s)
      - Adjunctive medications (steroid, etc.)
      - Local anesthetic alone may be useful, as in sympathetic blockade
        - » Best analogy: rebooting your computer
  - Autonomic
    - Stellate ganglion (neck, arm, upper chest), lumbar sympathetic (lower extremity) most common
      - Initially diagnostic for RSD/CRPS and hopefully therapeutic as adjunctive therapy to support PT/OT
        - » Rebooting the computer again

Interventional Treatment Options

- Soft tissue injection
  - Muscle
    - Myofascial trigger point injection
      - TrP may be primary myofascial trigger pts or may be secondary to underlying disease (e.g. facet joint injury, disc herniation, etc.)
      - Mechanical disruption via needle tip and/or fluid injected
      - Improved blood flow via local vasodilitation from local anesthetic
    - Botulinum toxin may be useful when TrP injections helpful but fail to provide prolonged relief
  - Tendon sheath
  - Bursa

Interventional Treatment Options

- Joint injection
  - Spinal
    - Facet joint: cervical, thoracic, lumbar
    - Non-facet cervical: atlanto-occipital joint (AO), atlantoaxial joint (AA)
      - In practice treated as facet joint since they are spinal joints
      - More delicate and specialized techniques
    - Intra-articular inj. of facet joint often used as one of two diagnostic blocks preceding RF denervation if positive, but very temporary relief, but need at least one set of specific nerve blocks, as opposed to joint injection, prior to lesioning

Interventional Treatment Options

- Joint injection
  - Sacroiliac
    - Junction of spine and pelvis
      - Up 20%-25% of chronic adult back pain related to SI joint
      - Often difficult to differentiate from lower facet joint pain
      - 25%-30% of patients who continue who have low back pain after lumbar fusion have sacroiliac joint pain
      - Radiofrequency denervation of posterior joint capsule via sacral lateral branch lesioning (analogous to facet joint nerve lesioning at L5-S1, S1-2, S2-3)
        - » Requires ability to generate larger lesions required for adequate coverage
  - Peripheral
    - Shoulder, knee, hip, elbow, etc.
      - Generally therapeutic (with steroid) but may also provide diagnostic information

Interventional Treatment Options

- Intradiscal
  - Intradiscal injection
    - Diagnostic provocation discography
      - Patient blinded to level being injected and at least one normal control level inj.
      - Provoke pain
        - » Same (concordant) or different (discordant) quality
        - » Location
        - » Intensity
        - » Pressure required to produce pain (very important, as ANY disc will cause pain if enough pressure applied)
        - » Internal disc morphology
        - » Diagnostic value dependent to a degree on experience and judgement of discographer
      - Analgesic discography may be helpful in confirming result
      - Can't prove something hurts. *Can* prove pt complains of concordant pain in *abnormal* disc and *not* in normal disc
    - Intradiscal steroid
      - May be extremely helpful for acute HNP (disc herniation)
        - » Clinical experience is good but little evidence (I only perform on other physicians)

Interventional Treatment Options

- Intradiscal therapies
  - Decompression
    - Plasma decompression (coblation), Nucleotome, Dekompressor, IDET, Acutherm
      - Thermal energy used to shrink and modify collagen
      - Plasma decompression alters biochemisry of disc nucleus (may be important)
      - Mechanical removal of disc material
      - Can be very effective
  - Biacuplasty
    - Discogenic pain in presence of annular fissure/tear
      - RF energy used to create "strip" lesion in annulus to destroy nociceptors
  - Minimally Invasive Lumbar Decompression (MILD)
    - Intraspinal, not intradiscal
      - Percutaneous technique to debulk excess ligament and bone in cases of spinal stenosis thought to be symptomatic as means to avoid laminectomy and/or fusion

Interventional Treatment Options

- Implantable therapies
  - Stimulation analgesia
    - Spinal cord stimulation (SCS)
    - Peripheral nerve (individual or field) stimulation (PNS)
    - Combined SCS and PNS
    - Patient selection is of utmost importance
      - Appropriate diagnosis and place in treatment process
      - Psychological status
        - » Psychosis, severe depression, severe personality disorder (e.g. Borderline)
      - Work status less important
      - Successful trial yields positive results in ± 80% of cases
      - Just as other therapies, cannot produce "miracles"
        - » Won't suddenly be able to play piano, leap tall buildings, etc.

Interventional Treatment Options

- Spinal infusion
  - Non-opioid options
    - Baclofen for spasticity
    - Prialt for refractory neuropathic pain
    - Clonidine, esp. for neuropathic pain
    - Local anesthetic as adjuct to other medications
    - Neostigmine
  - Most are used in conjunction with an opioid but occasionally as monotherapy
  - Opioids
    - Morphine (PF) FDA indication
      - Others often used. Same adverse effect issues as oral opiods
      - "Micro-dosing" may provide better long term results

Alternative Treatments

- Alternative treatments
  - Chiropractic or other manipulation
    - Goal to restore joint mobility
    - Most often applied to vertebral joint but any peripheral joint may be treated
  - Acupuncture
    - Invasive or noninvasive
    - Scientific evidence of acupuncture analgesia
  - Herbal medicines
  - Energy Medicine
    - Biofield therapies (gi gong, reiki, therapeutic touch, acupuncture)
    - Bioeletromagnetic-based therapy (magnetic fields)
  - Mind-Body Medicine
    - Enhance the mind's capacity to affect bodily function and systems
      - I previously utilized hypnotherapy with great success in some RSD/CRPS patients

Opioids

- What is an opioid?
  - Any substance which primarily exerts an effect by binding to, and activating an opioid receptor
    - Includes synthetic and endogenous substances
    - "Opiate" specifically indicates derivation from opium
      - Does not include synthetic or endogenous molecules

- Why focus on non-opioid treatment?
  - Opioids have significant adverse effects
  - Opioids can be, and are, abused and misused.
  - Are opioids "bad" drugs (i.e. evil)?
    - No more so than automobiles, picture frames, baseball bats or any other inanimate object or substance.
    - Simply tools, but do have potential for significant drawbacks.

- Why focus on non-opioid treatment?
  - In my opinion, and that of many others, opioids, while they may be useful at times, are *grossly overused*.
  - Some reasons for "overuse"
    - *Patient (and referring physician) expectations*
      - Limited understanding of options available
      - Limited understanding of basic differences between acute and chronic pain
    - *"Easy" solution*
      - Attempting to educate patients about pain and preference for other treatments is very time consuming and often very frustrating – (new patient in my practice who presents on long term opioids takes me 90 minutes)
        - » Explain, at least every other vist, in some detail, that the concept of "can you give me something stronger" is not a valid concept
      - Contrast to: PA sees the patient, checks the latest urine test and provides a prescription for controlled medication to be signed - *easy*
    - *Limited treatment armamentarium of individual practitioner*
      - *" If all you have is a hammer, everything looks like a nail."*

Adverse effects of opioids

- Not innocuous substances
  - Push to increase use late 80's and early 90's
    - Major plus was "no end organ toxicity"
    - May have been incorrect
- Addiction and dependence
  - Addiction: continued use despite known negative effects on physical and/or social well-being
  - Dependence: withdrawal syndrome on discontinuation

Adverse effects, cont.

- Endocrine effects:
  - Central hypogonadism
    - ↓ hypothalamic gonadotropin-hormone releasing hormone
    - ↓ pituitary luteinizing-hormone releasing hormone
      - Possibly ↓ follicle-stimulating hormone
    - ↓ testicular testosterone: ovarian estradiol
    - ↓ testicular interstitial fluid
    - Loss of libido, impotence
    - Infertility (males and females)
    - Depression, anxiety, fatigue
    - Loss of muscle mass and strength
    - Amenorrhea, irregular menses
    - Osteoporosis and fractures
  - Cortisol and growth hormone deficiency

Adverse effects, cont.

- Sleep
  - Interferes with deep sleep
  - Literature suggests chronic use related to obstructive and central sleep apnea
- Hyperalgesia
  - Patient receiving opioids becomes more sensitive to certain types of pain
    - May be same as original underlying pain or different
  - Mechanism uncertain
    - Thought to be due to neuroplastic changes in CNS and PNS leading to sensitization of pronociceptive pathways
- Brain
  - Administration of morphine results in altered gray matter thickness in several brain structures
    - Implications uncertain, but changes remained five months following administration in initial study (2011)
    - May be altering risk/reward response

Adverse effects(?), cont.

- Efficacy
  - Opioid(s) have been known to humans for thousands of years
  - Still no good evidence of long term benefit
    - Do see some patients who clinically do well
    - Lack of evidence does not prove lack of efficacy

What I Actually Believe (and try to do)

- What do I believe?
  - A small subset of patients actually do well with opioid therapy
    - Fewer than 10% in my practice
- What do I do?
  - Attempt to utilize other treatments when able
  - Depends on multiple factors
    - Type of pain, previous treatment, individual patient
  - Generally try to utilize low doses of long acting forms or truly intermittent doses of short acting form
    - Newer options - e.g. Nucynta (tapentadol), BuTrans patch (transdermal buprenorphine) - may provide significant advantages over more typical opioid
    - The single thing I ***NEVER*** prescribe is 30 mg Roxicodone

Summary

- *Correct equation* is: Pain Management ≠ Opioids
  - Opioids may still be useful in some cases
  - Must be used appropriately
- Multiple other options which, in most cases, should be primary treatment
  - Interventional
  - Non-interventional
- Long term treatment is often aimed more at trying to maintain function rather than further improve function
- Always looking for something better for these patients, who are miserable and, at times, shattered beings

End

- "But pain... seems to me an insufficient reason not to embrace life. Being dead is quite painless. Pain, like time, is going to come on regardless. Question is, what glorious moments can you win from life in addition to the pain?"
- **Lois McMaster Bujold, *"Barrayar", 1991***
  US science fiction author