An Integrative Approach to Pain

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Pain

• >100 million Americans, more than heart disease, cancer, diabetes combined.
• 25.3 million adults suffer from daily chronic pain.
• 23.4 million report severe pain.
• Incidence of chronic low back pain, neck pain, and arthritic pain as high as 29%, 15.7%, and 28%, respectively, in adult population.

http://www.CDC.gov/DrLowDog.com


Chronic Pain

• Complex, severe and debilitating condition - considerable reduction in function & quality of life.
• Pain due to dysfunction of nerves, spinal cord or brain (neuropathic pain), or persistent pain caused by other non-malignant conditions, such as low-back pain, TMD, or pain due to inflammatory arthritic conditions.
**Neuropathic Pain**

- Direct consequence of lesion or disease of the somatosensory system (essentially all sensory experiences other than vision, hearing, taste and smell).
- Trauma, poorly controlled diabetes, side effects from drugs, infections (e.g., HIV, shingles), and autoimmune conditions (e.g., multiple sclerosis) can all lead to neuropathic pain.
- Treatment: antidepressants, anticonvulsants, opioids, and topical agents.
- Neuropathic pain can be particularly difficult to treat and is often accompanied by anxiety, depression, insomnia, and fibromyalgia.


**Central Sensitization**

- Heightened sensitivity to pain and sensation of touch (also to other senses like light or sound).
- Nervous system in persistent state of heightened reactivity - simple touch can be registered as painful or uncomfortable.
- Increases feelings of anxiety, emotional distress, malaise, and poor concentration.

**Opiates**

- Opioid industry more than $13 billion-a-year. Americans comprise ~4% of the world's population, we use > 30% of all opioids. US accounts for ~100% of hydrocodone (e.g., Vicodin), 81% for oxycodone (e.g., Percocet).
- 91 Americans die every day from opioid overdose; 50% from prescription opiates.
- Clinicians ill-prepared to deal with complex problems associated with chronic pain: creates easy atmosphere for prescribing pain meds.
- Pharmaceutical companies pumped millions of dollars into telling physicians and public that medications were safe and effective for chronic pain, claims now being challenged in courtrooms across the US.


“Drug Deaths in America Are Rising Faster Than Ever”

Josh Katz, NY Times June 5, 2017
The Down Side to Long-Term Use

- Opioids incredibly effective for short-term pain relief but risks often outweigh benefits for many people living with chronic pain.
- For chronic non-cancer pain: adverse events with opioids 78% with medium and long term use (average 6-16 weeks) compared to placebo.
- Tolerance (need more medication for same pain relief), increased sensitivity to pain, physical dependence, lower sex drive, confusion, constipation, dry mouth, nausea and vomiting, and an increased risk of new onset depression after 3 months of use.


Ibuprofen and Naproxen

- Prospective Randomized Evaluation of Celecoxib Integrated Safety vs Ibuprofen or Naproxen (PRECISION) trial and individual patient data of nearly 500,000 patients concluded “evidence would support avoidance of NSAID use, if possible, in patients with, or at high risk for, cardiovascular disease.
- If used, shortest-duration and lowest effective dose should be chosen, given evidence that risk is duration- and dose-dependent.
- Study found ibuprofen associated with significant increase in systolic blood pressure and higher incidence of newly diagnosed hypertension.


Ibuprofen and Heart Disease

- FDA warning about NSAID use in patients with cardiovascular disease released in 2005 and strengthened in July 2015, yet survey data shows that those with CVD are more than twice as likely to use NSAIDs than those without CVD.


Aspirin and GI Bleeding

- Systematic review: low dose aspirin associated with double the risk for upper GI bleeding and 80% increased risk for lower GI bleed.
- With increased risk from low-dose aspirin (81-85 mg per day), deeply concerning about long-term use of high dose aspirin (2-3 g/d) for pain.
- PPI can protect against bleed but comes with own risks.

Acetaminophen (Paracetamol)

• Acetaminophen has superior safety to ibuprofen, naproxen, and aspirin; commonly recommended as a first line therapy for pain.
• Maximum “safe” dose is 4000 mg per day but found in more than 600 OTC and prescription medications (e.g., Vicodin), dose can add up without realizing it.

Adverse Effects

• 2017 report found acetaminophen responsible for nearly half of acute liver failure cases in US - leading cause for liver transplantation.
• Study of 64,839 men and women (ages 50-76 years) followed up to 8 years found almost two-fold increased risk of blood cancers associated with high use of acetaminophen (≥ 4 days/week for ≥ 4 years).

Blunts Empathy?

• Ohio State University acetaminophen reduces user’s ability to feel empathy for another’s pain (healthy college students).
• This research must be confirmed by larger studies but hard not to find the researcher’s statement somewhat chilling.
  • “Because empathy regulates prosocial and antisocial behavior, these drug-induced reductions in empathy raise concerns about the broader social side effects of acetaminophen, which is taken by almost a quarter of adults in the United States each week.”


The Need for Alternatives

• Keen interest by researchers, clinicians and the public for additional/other options for managing chronic pain.
• Chronic pain is the leading indication for use of complementary and integrative medicine with 33% of adults and 12% of children in the US using it for this purpose.
• Although advances have been made in treatments for chronic pain, it remains inadequately controlled for many people.
Chronic Pain Cycle

Increased Pain

Depression

Anxiety

Sleep Disturbance

A Broader Approach

- Truly integrated approach would include treatments that address mind-body (e.g., meditation, yoga, tai-chi), nutrition (e.g., emphasis on plant based diet to reduce inflammation), manual medicine (e.g., massage, chiropractic), pain modulation (e.g., acupuncture, massage, botanicals, nutraceuticals), sleep and mood (e.g., cognitive behavioral therapy, guided imagery, botanicals, nutraceuticals).

IOM Report

- A cultural transformation is necessary to better prevent, assess, treat, and understand pain of all types.
- Healthcare providers should increasingly aim at tailoring pain care to each person’s experience and self-management of pain should be promoted


Think More Broadly

- An integrated approach will move beyond the pain and explore…..
  - Sleep and Rest
  - Work/Career
  - Diet and Food
  - Relationships
  - Mind-Body
  - Meaning and Purpose
The Role of Diet in Pain

- Diet can aggravate or improve numerous pain disorders.
- Inflammation often driven by eating a pro-inflammatory dietary pattern.
- Inflammatory mediators can impact pain, mood, heart disease, insulin sensitivity, and DNA repair.

Omega 3 Fatty Acids from Plants and Animals

- Dark green vegetables, walnuts, freshly ground flax seeds and other plant foods contain ALA.
- Converts to Intermediate Molecules.
- Cold water fish, fish oil, fresh seaweed, clean animal foods like free range chicken, eggs, and grass fed beef contain DHA and EPA.

Resolution Biology

- Resolution of inflammation is an active, programmed response. Omega 3s play crucial role.
- Increasing omega 3 fatty acids in the diet can help with mood, pain and promote overall health.

Omega 3 Index

- Omega-3 Index indicates % of EPA+DHA in red blood cell fatty acids.
- Canadian government found mean Omega-3 Index level of Canadians aged 20-79 was 4.5%. Fewer than 3% of adults had levels associated with low CHD risk; 43% had levels associated with high risk.
- What about chronic pain patients? Should we assess omega 3 fatty acid level to optimize their “anti-inflammatory” activity?
- I recommend 2-3 grams per day omega 3 fatty acids (concentrated triglyceride form. FDA has set 3 grams as safe level.)
Musculoskeletal Pain

- **Leading cause** of long-term pain and disability around the globe.
- Aging, obesity and lack of regular physical activity are major risk factors for arthritis and back pain.
- In US, 52 million American adults have arthritis and by 2040, that number will reach 78.4 million, or roughly 26% of all adults.


Body Weight

- For every 12 pounds of weight gain, there is a 36% increased risk for developing OA.
- Lumbar spine and knee two primary sites for pain in obese individuals. Reduction of body fat lowers mechanical and inflammatory stressors that contribute to OA.
- Weight loss strongly associated with a reduction in pain.

Menthol for Topical Analgesia

- Menthol long history as topical analgesic. Recent elucidation of TRPM8 channels as the “menthol receptor” provides evidence-based mechanism of analgesic action.
- Clinical studies report topical menthol as safe and effective in treating variety of painful conditions: musculoskeletal pain, sports injuries, neuropathic pain and migraine.


Essential Oil Ointments

- Vicks contains eucalyptus, cedar wood, camphor, and menthol, widely used for common cold and headache.
- Tiger-Balm contains peppermint, eucalyptus, clove and cinnamon oils, menthol and camphor, used for common cold, headache, rheumatic and muscular pains.
Anti-Inflammatory Herbs

- There are many, but some to consider include:
  - Salix containing plants, like willow (Salix spp)
  - Turmeric (Curcuma longa and other species)
  - Ginger (Zingiber officinale)
  - Boswellia (Boswellia serrata)
  - Cannabis (Cannabis sativa)
  - Devil’s Claw (Harpagophytum procumbens)
  - Licorice (Glycyrrhiza glabra, G. uralensis)

Turmeric (Curcuma longa)

- Family: Zingiberaceae (ginger family)
- Part Used: Rhizome
- Perennial plant grown in tropical areas, mostly India. Used in meat, fish and vegetable curries.
- Long history of medicinal use ~4,000 years.
- Curcuminoid pigments highly active; curcumin is main curcuminoid.
- Highly researched: more than 35,000 entries in the National Library of Medicine.

Turmeric for Arthritis

- Profound anti-inflammatory.
- Tuft's systematic review found curcumin significantly more effective than placebo and equivalent to NSAIDs for pain relief and functional improvement.
- Results suggest curcumin and boswellia formulations could be valuable addition to OA treatment regimens by relieving symptoms while reducing safety risks.

Turmeric + Boswellia (Boswellia serrata)

- 12 week randomized, double-blind, placebo controlled study in 201 people with osteoarthritis (40-70 years) found 350 mg curcumin + 150 mg boswellic acid taken three times daily led to statistically significant effect on physical performance tests and WOMAC joint pain index compared to placebo. Well tolerated, no significant adverse events.

References:

Depression and Pain

- Multiple studies suggest a link between inflammation, depression and pain.

- Danish study (>73,000 adults) showed that those with the highest levels of C-reactive protein (marker of inflammation) were twice as likely to have psychological distress and depression than those with normal levels.


Turmeric for Depression?

- Mini meta-analysis of 6 studies found curcumin reduced depression symptoms, particularly in middle-aged patients when given at higher doses for longer periods of time.

- Authors concluded, “there is supporting evidence that curcumin administration reduces depressive symptoms in patients with major depression.”

- Is it due to systemic reduction in inflammation?

- Is this modulated through the gut?


Absorption and Safety Issues

- Turmeric/curcumin not well absorbed into bloodstream from GI tract. Best to take turmeric/curcumin 2-3 times per day, rather than once per day, for best effects.

- Preparations bound to phosphatidycholine (Meriva) or piperine (3-5 mg) superior absorption.

- Dose 1000-1500 mg/d standardized extract (95% curcumin) used in most of the trials.

- Many ways to incorporate turmeric into daily diet as seen in my tips to the left.

- Many recipes for golden milk – this is the one we use the most at my home.
Cannabis sativa

- One of oldest cultivated crops. More than 20,000 uses: paper, fiber, rope, food, oil, textiles
- Hemp and marijuana are same plant with very different chemical profiles.
- Marijuana widely used as analgesic in 19th century US. Listed in USP and AMA opposed the Marijuana Tax Act in 1937.
- 1970 Controlled Substance Act listed Cannabis as Schedule 1 drug but many states have legalized for medicine and/or recreation.

Cannabis and THC

- One species of Cannabis with subspecies (e.g., C. indica)
- More than 540 compounds identified, 104 are cannabinoids.
- Major psychotropic component is Δ9-tetrahydrocannabinol (THC).
- When 26,145 samples of marijuana were analyzed covering the span of 1995-2014, testing showed average of 4% THC in 1995, which rose to approximately 12% in 2014. Far more euphoric and potent.


Cannabis and Pain

- Systematic review and meta-analysis of cannabinoids: 28 RCTs (2454 patients) with chronic pain found that, compared with placebo, cannabinoids associated with greater reduction in pain.
- Cannabis containing THC greater analgesia.
- Dosing remains confusing: most studies using CBD used 300 mg per day, far greater than what is commonly used.


Cannabis (Marijuana)

- Analgesia best supported use of Cannabis, and beneficial in sleep, mood, and anxiety.
- Benefit for peripheral neuropathy (pain reduction, better sleep, improved function) even in patients with symptoms refractory to standard therapies.
Cannabidiol (CBD)

- Cannabidiol (CBD) found in marijuana and hemp.
- Does not produce euphoric effects but has antipsychotic, anxiolytic, anti-seizure, analgesic, and anti-inflammatory properties.
- Epidiolex FDA approved for seizures refractive to treatment
- Research shows modest analgesic effects.


Back Pain

- Lower back pain highly disruptive, second leading cause of disability.
- It is acute if less than six weeks and chronic if persists > three months.
- Pain can be severe, making walking, standing and traveling long distances difficult, even though physical activity is effective for improving and preventing back pain.
- Back pain is frequently associated with anxiety, depression and irritability.
- Second major cause of short-term workplace absences; estimated 149 million days of work per year lost due to low back pain.

Clinical Practice Guidelines: Back Pain

- American College of Physicians provides treatment guidance based on efficacy, comparative effectiveness, and safety of noninvasive pharmacologic and nonpharmacologic treatments for acute (<4 weeks), subacute (4 to 12 weeks), and chronic (>12 weeks) low back pain in primary care.
- Recommendations on following slides.


Acute or Subacute Low Back Pain: Guidance

- Given that most patients with acute or subacute low back pain improve over time regardless of treatment, clinicians and patients should select nonpharmacologic treatment with superficial heat, massage, acupuncture, or spinal manipulation.
- If pharmacologic treatment is desired, clinicians and patients should select NSAID or skeletal muscle relaxants
  (Grade: strong recommendation)

Spinal Manipulation for Acute Back Pain

- 15 RCTS found spinal manipulation resulted in an improvement in pain of about 10 points on a 100-point scale.
- 12 RCTS found spinal manipulation resulted in improvements in function.


Chronic Low Back Pain Guidance

- Initially non-pharmacologic treatment with exercise, rehabilitation, acupuncture, mindfulness-based stress reduction, tai chi, yoga, progressive relaxation, electromyography biofeedback, cognitive behavioral therapy, or spinal manipulation
  (Grade: strong recommendation)
Headaches

- Migraines/headaches ~ 13% of US population.
- Headaches highest in women ages 18-44, where 3-month prevalence of migraine or severe headache is roughly 26%.
- Head pain is the third leading cause for emergency room visits.
- 70% say headaches caused problems in relationships, 59% have missed family and social events and 51% report that migraines cut their work and school productivity in half.


Acupuncture for Migraine

- Cochrane review 22 trials (n=4985) concluded that evidence suggests adding acupuncture to symptomatic treatment of attacks reduces frequency of headaches. Trials also suggest that acupuncture may be at least similarly effective as treatment with prophylactic drugs.
- “Acupuncture can be considered a treatment option for patients willing to undergo this treatment.”


Magnesium for Migraines

- Studies show migraineurs have low brain Mg during migraine attacks and may have systemic Mg deficiency.
- Canadian Headache Society: strong recommendation for prophylaxis with 600 mg magnesium citrate.
- Diarrhea most common side effect (magn glycinate and citrate less GI complaints than oxide). Caution in those with poor renal function.


Coenzyme Q10 for Migraines

- CHS guidelines gave a strong recommendation for prophylaxis of migraine: 300 mg/d.
- The AAN/AHS gave a Level C recommendation, stating it is possibly effective and may be considered for migraine prevention.
- 200-300 mg per day

Riboflavin for Migraines

- CHS guidelines gave strong recommendation for benefit, and minimal side effects.
- AAN/AHS give riboflavin Level B recommendation, probably effective and should be considered for migraine prevention. 200 mg BID
- Deficiency: increases light sensitivity


Peppermint: Headache

- Topical treatment with peppermint essential oil shown significantly more effective than placebo in controlled studies.
- Efficacy comparable to aspirin or acetaminophen. Peppermint oil in ethanol licensed for treatment of tension-type headache in adults and children above 6 years in Germany.

Temporomandibular Disorder

- Term used to group conditions in the masticatory muscles and the temporomandibular joint (TMJ), impaired movement capacity of the mandible, and TMJ symptoms such as clicking, grating and locking of the jaw.
- Most common cause of chronic orofacial pain.


TMD: Significant Cause of Pain

- 5-12% of population. Second most common musculoskeletal condition (after chronic low back pain) resulting in pain and disability.
- Arthralgia, local myalgia, myofascial pain, myofascial pain with referral, degenerative joint disease, subluxation, and headache.

TMP Pain Screening Tool

- For clinical use, responses from the screener can be used as part of the diagnostic process for a pain-related TMD diagnosis.
- Sensitivity 99.1% for both short (3 questions) and long questionnaire (6 questions); specificity was 95-98%.
- Radiographic imaging confirms TMD diagnosis.
- Patients are interested in treatment.


Care Option

- Ice or heat applications
- Soft foods when pain acute
- Self-care exercises
- Physical therapy
- Splint
- Anti-inflammatory diet
- Topical analgesics (e.g., capsaicin)
- Acupuncture

Splint Versus Self Exercise

- 52 people with anterior disc displacement without reduction randomly assigned to splint or a joint mobilization self-exercise treatment group.
- Warm-up, small mouth-opening and closing movements several times. Then mandibular downward pressure: 3 cycles of 30 seconds each were done 4 times per day.
- Participants in splint group wore a maxillary stabilization appliance while sleeping at night. Splint was adjusted to ensure occlusal contact of all mandibular teeth in centric relation and mandibular canine guidance in eccentric movement.
- All outcome variables significantly improved after 8 weeks of treatment in both groups (mouth opening range, maximum daily pain intensity, limitation of daily functions). Mouth opening range increased more in the exercise group than in the splint group.

Botox

- UCSF and VA Study: 71 patients with TMD with or without bruxism and refractory to conventional treatment (e.g. oral appliances, physiotherapy, etc.) received injections into temporalis and masseter muscles.
- 77% reported beneficial effects. Subjects with a concomitant bruxism diagnosis reported significant improvement over subjects without bruxism (87% vs. 67%).
- Note: injection in lateral pterygoid also beneficial.


Acupuncture and Dry Needling

- Small studies show dry needling or acupuncture of the lateral pterygoid and posterior, periarticular connective tissue, masseter and temporalis muscles improves pain and disability in patients with TMD.


Mood, Sleep and Pain

- Study 273,952 individuals/47 countries found depression significantly associated with severe pain (odds ratio 3.93).
- High prevalence of concomitant pain and sleep disturbance.
- Short sleep duration increases risk for developing chronic pain.
- Study in healthy young women found after just two nights of fragmented sleep: increased pain sensitivity in both superficial and deep tissues.


Cognitive Behavioral Therapy

- CBT has emerged as a recommended first-line therapy for insomnia. Scale can be an issue. Digital CBT has been shown to be effective for improving sleep, as well as mental health and well-being.
- CBT-I typically consists of:
  - Psychoeducation about sleep and insomnia
  - Stimulus control
  - Sleep restriction
  - Sleep hygiene
  - Relaxation training
  - Cognitive therapy
- Sleepio, CBT-I Coach (free)

Melatonin

- Melatonin maintains sleep-wake cycle, acts as an antioxidant, anti-inflammatory, pain reliever, and mood regulator, making it ideal for many with chronic pain.
- Systematic review of 19 studies: melatonin significantly decreases pain intensity, as evidenced by pain scores, regardless of the type of pain.
- Plays important role in GI physiology: regulation of gastrointestinal motility, local anti-inflammatory reaction and moderation of visceral sensation. Studies show it can improve symptoms and quality of life in people living with IBS.


Melatonin Sleep and Safety

- Meta-analysis of 12 randomized, placebo-controlled trials found convincing evidence melatonin reduces the time it takes to fall asleep in primary insomnia (p = 0.002) and delayed sleep phase syndrome (when it takes 2 or more hours to fall asleep past conventional bedtime) (p < 0.0001).
- Studies have failed to show any serious adverse effects with melatonin, even at extreme doses (100 mg) in adults. Taking melatonin doesn’t suppress the endogenous production of melatonin and there is no rebound insomnia when it is discontinued. Dose generally 2-3 mg 2 hours before bed.


California Poppy

- Official state flower California. Native Americans used as food and medicine for millennia.
- Aerial plant used to relieve tooth pain, headache, and promote sleep.
- Basic science shows it acts on GABA-A receptors in the brain, similar to a benzodiazepine, but without habit-forming tendency of the drug. Has anxiolytic, analgesic, sedative activity.


European Union monograph recognizes traditional use for relief of mild symptoms of mental stress and to aid sleep.
- It also discusses research that indicates that a "standardized extract of California poppy can be used in the management of chronic pain and as a hypnotic-mild-sedative for the management of pain-related insomnia."
- Dose: 300-600 mg 1-2 times per day.

Mindfulness Meditation

- Mindfulness meditation excellent as it can decrease pain intensity and stress levels.
- Long-time meditators have greater activation of areas responsible for sustaining attention, processing empathy, integrating emotion and cognition.
- Review of 47 trials found meditation improves:
  • Anxiety
  • Depression
  • Pain


Meditation Resources

- Obviously a local class is the very best option.
- Insight Timer - ~4,000 guided meditations from more than 1,000 teachers (self-compassion, nature, stress, podcasts and more). More than 750 meditation music tracks. Free.
- Headspace - very good for beginners with 10 minute meditations. Free.
- The Mindfulness App - nice 5 days guided mediation program to get you started. Can be personalized and integrated into other health apps. Free.
- Aura - multiple teachers, from 3-10 minute daily meditations. Customizable. $29 for 6 months.

Meaning and Purpose

- What truly gives a person a sense of meaning and purpose in life?
- How can someone discover her life purpose to focus on the essence of who she is? Her being.
- How can one live from a "deep place" despite his or her pain?
- So important to explore..... it is often the key to less suffering.....