Could Cannabis and / or Hemp *Really* Solve the Opioid Epidemic?

What are the Patient Options

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Past-President;

American Osteopathic Academy of Sports Medicine

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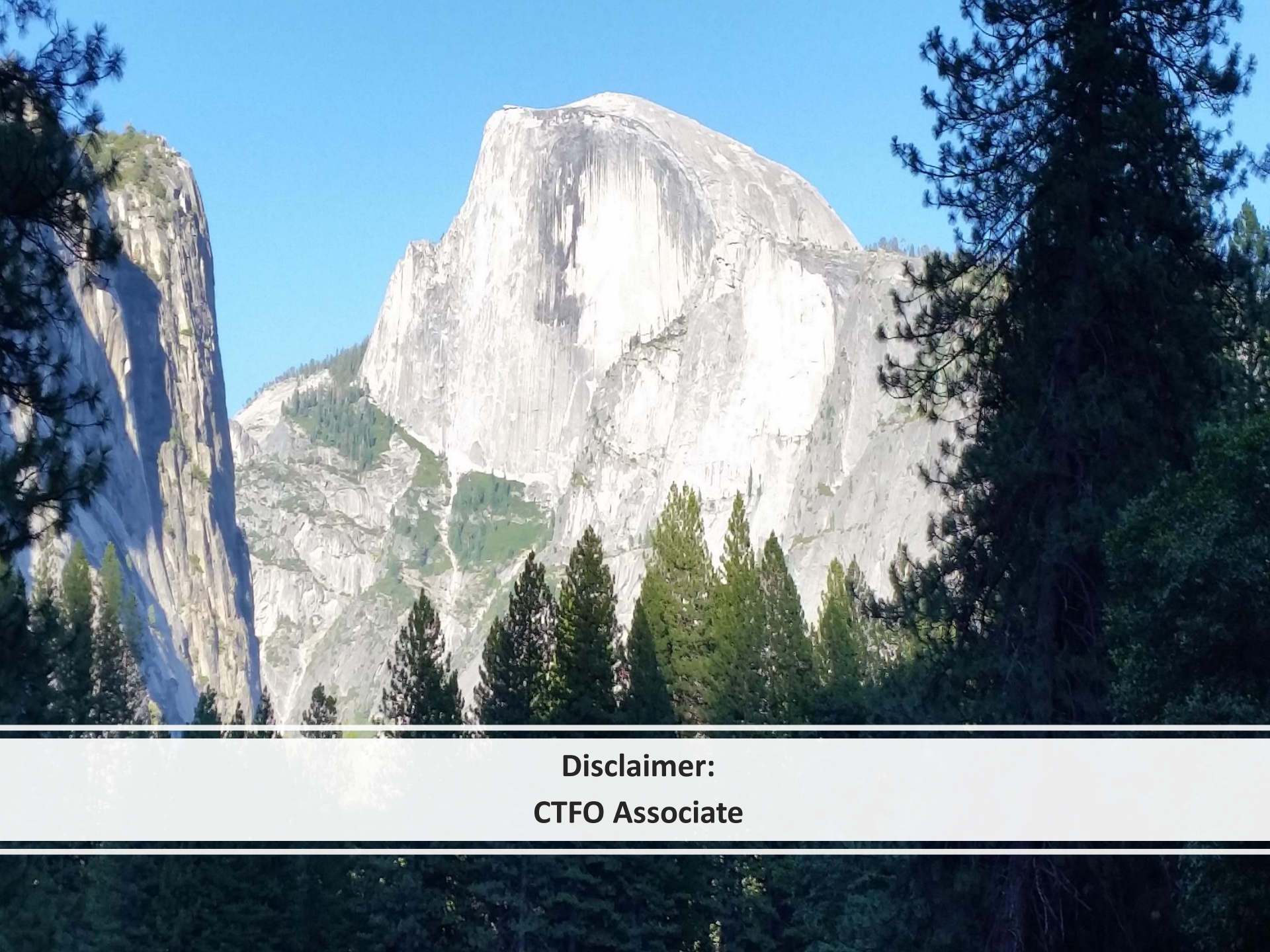

Disclaimer:

CTFO Associate

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3) **Review the current use of Opioids for Pain**
4) **Learn what drove patients to seek alternative pain control**
5) **Learn the efficacy and safety of CBD**

What Causes Musculoskeletal Pain?

Rapid Onset

- Trauma
  - Falls
  - Injuries
  - MVA

Insidious Onset

- Overuse / Repetitive motion
- Postural imbalance / strain
- Poor Lifestyle

Symptoms & Types of Pain

Symptoms

- Sharp
- Severe
- Ache
- Burn
- Dull

Types

- Acute
- Chronic

Types of Pain

Acute

- Falls
  - Fractures
  - Dislocations
- Injuries
  - Work Related / Hobby
  - Strain / Sprain
- MVA

Chronic

- Overuse / Repetitive motion
  - Inflammatory
    - OA / Arthritis
    - Bursitis
    - Tendonitis
  - Non-Inflammatory
    - Tendinosis
- Postural imbalance / strain
  - Kyphosis
  - Lordosis

Chronic Pain

- **MSK Conditions**
  - **Prevalence**
    - **Estimated 127M Americans (one in two adults)**
      - **comparable to total % Americans w/chronic lung or heart condition**
      - **Estimated $213B annual treatment, care and lost wages**
      - **Arthritis and related conditions (66%)**
      - **Back and neck pain; injuries from falls, work, military service and sports (33%)**

AAOS-2016

Chronic Pain

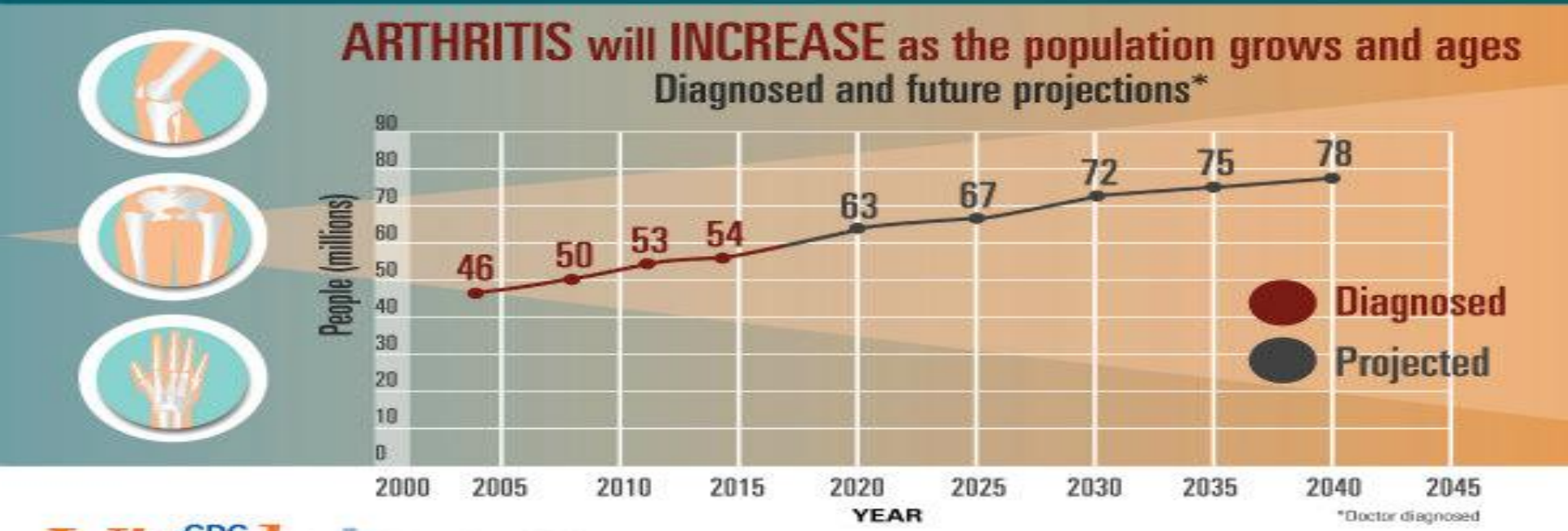
Related data/costs of musculoskeletal diseases & injuries:

- **Arthritis and rheumatoid conditions resulted in an estimated 6.7 million annual hospitalizations.**
- **Average annual cost per person for treatment of a musculoskeletal condition is $7,800.**
- **Estimated annual cost for medical care to treat all forms of arthritis and joint pain was $580.9 billion, which represented a 131 percent increase (in 2011 dollars) over 2000.**
- **In 2012, 25.5 million people lost an average of 11.4 days of work due to back or neck pain, for a total of 290.8 million lost workdays in 2012 alone.**

AAOS-2016

Chronic Pain

- Osteoarthritis / Arthritis
  - Prevalence
    - Arthritis most common joint disorder US
    - Knee OA 10% men & 13% women > 60 y/o



CDC Vitalsigns™
www.cdc.gov/vitalsigns/arthritis

SOURCE: National Health Interview Survey, 2013-2015.

50% Population =/> 65 y/o
36% Pop. 18 - 64 y/o

CDC

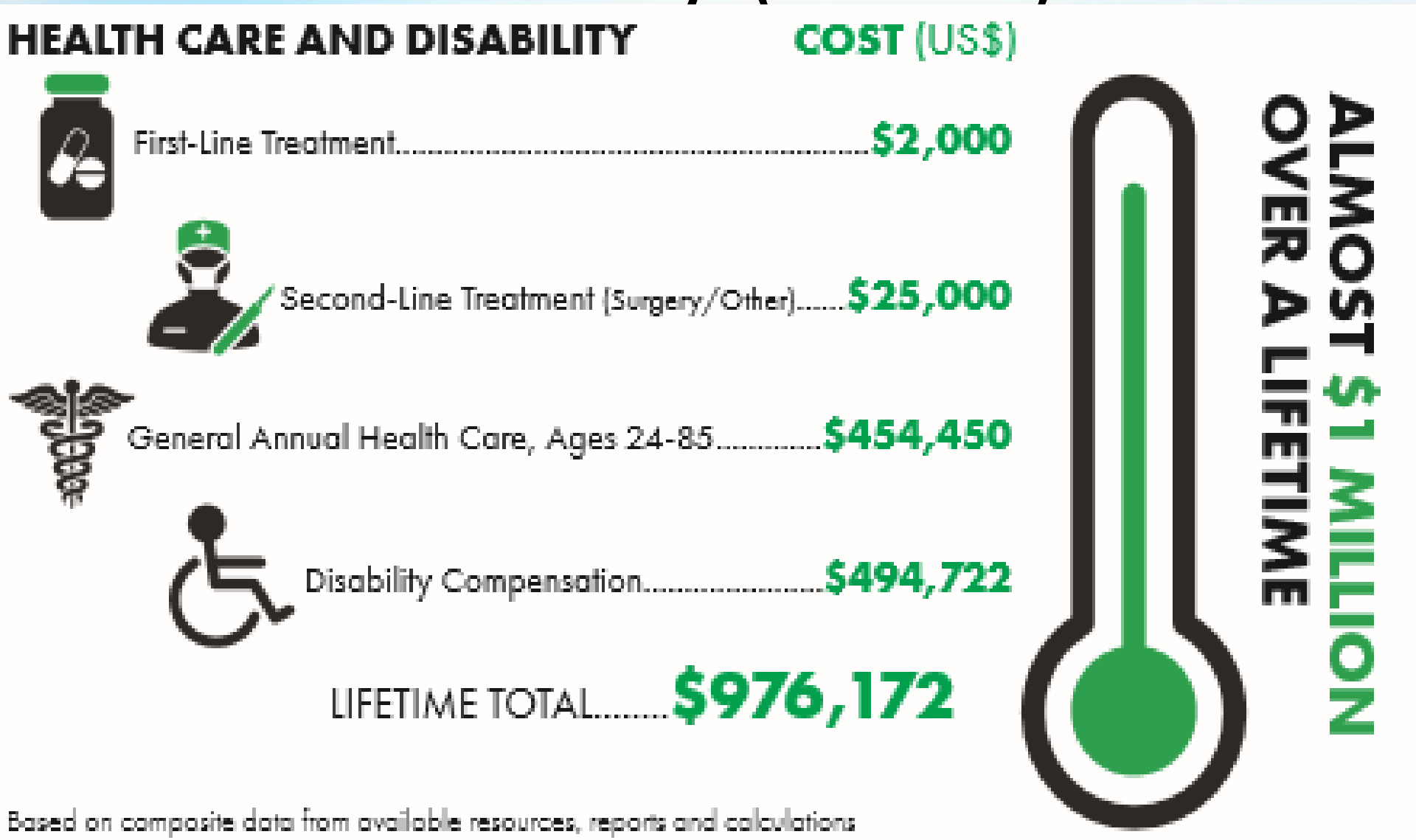
Chronic Pain

Consider "Arthritis in the Military"

- A Lifetime Of Disability for the rest of his or her life, require arthritis-related health care, paid for by U.S. taxpayers, in the form of doctor visits, medications, procedures and physical therapy.
- Average annual health care expenditures for a disabled veteran are $7,450.
- Cost Example Based on a U.S. Army soldier diagnosed with post-traumatic OA at age 24 (two years after a traumatic injury), who is discharged and requires knee replacement surgery in his or her thirties. (Amounts will vary in individual situations, including the kind of treatment, surgery required, number of dependents, etc.)

Chronic Pain

"Arthritis in the Military" (continued)



Pain Management: Pharmaceuticals

Analgesia / Anti-Inflammatory

- Acetaminophens
- NSAIDS
  - Oral
    - Increased GI Side Effects
  - Topical
    - Decreased GI Side Effects

Sedative / Other

- zolpidem (Ambien)
- amitriptyline
- trazodone
- gabapentin (Neurontin)

Pain Management: Pharmaceuticals

Anti-Inflammatory

- **NSAIDS**
  - **Topical Studies of diclofenac, ibuprofen & ketoprofen**
  - **Less Plasma concentrations**
  - **Increased Meniscus and Cartilage concentrations**
    - **Do NOT want this**

1. ***C Rolf*** et al. Intra-articular absorption and distribution of ketoprofen after topical plaster application and oral intake in 100 patients undergoing knee arthroscopy. **Rheumatology** 1999 38: 564-567.
2. ***CA Heyneman*** et al. Oral versus topical NSAIDs in rheumatic diseases. A comparison. **Drugs** 2000 60: 555-574.
3. ***J Radermacher*** et al. Diclofenac concentrations in synovial fluid and plasma after cutaneous application in inflammatory and degenerative joint disease. **British Journal of Clinical Pharmacology** 1991 31: 537-541.

What are Treatment Options for Musculoskeletal Pain?

Traditional

- Pharmaceutical
- Manipulation
- Physical Therapy

Complementary and Alternative

- Acupuncture
- Body Alignment Therapy
- Dietary
- Herbal
- Homeopathic
- Laser/Light
- Massage
- Mind-Body Therapy
- Viscosupplementation Inj
- Prolotherapy
- PRP
- Stem Cell

Biologic Therapy

The Ultimate Massage……

Pain Management: Pharmaceuticals

#1) What about Steroid Injections?

- ✓ Steroids if individual will NOT out live their joint or body part (PZ).

- ✓ Jüni P Intra-articular corticosteroid for knee osteoarthritis. Cochrane Database Syst Rev. Oct. 2015

Unclear if clinically important benefits of intra-articular corticosteroids after one to six weeks, effects decrease over time, and no evidence that an effect remains six months after a corticosteroid injection.

- ✓ Wernecke C, The Effect of Intra-articular Corticosteroids on Articular Cartilage: A Systematic Review. Orthop J Sports Med. Apr. 2015

Corticosteroids have a time- and dose-dependent effect on articular cartilage, with detrimental effects at high doses and durations.

- ✓ Bellamy N IA corticosteroid for treatment of osteoarthritis of the knee. Cochrane Database Syst Rev. Apr. 2006

Longer term benefits have not been confirmed based on the RevMan analysis. The response to HA products appears more durable.

Pain Management: Pharmaceuticals

#2) What about Viscosupplementation Injection? (AMSSM Position Statement)

- **Knee OA with viscosupplementation injection [hyaluronic acid (HA)] vs. steroid [intra-articular corticosteroid (IAS)] vs. placebo [intra-articular placebo (IAP)] treatment effect using Outcome Measures in Rheumatoid Arthritis Clinical Trials–Osteoarthritis Research Society International (OMERACT-OARSI) criteria.**
- **Systematic literature search relevant articles 1960 to August 2014 in the MEDLINE, EMBASE, and Cochrane CENTRAL using a network meta-analysis (NMA) of relevant literature determine a benefit from HA vs. IAS vs. IAP.**
- **11 articles met inclusion criteria from the search strategy.**
  - ✓ **Subjects receiving HA were 15% and 11% more likely to respond to treatment by the OMERACT-OARSI criteria than those receiving IAS or IAP, respectively ($P < 0.05$ for both).**
- ***Recommends HA for the appropriate patients with knee OA.***

Pain Management: Regenerative Medicine

#3) What is Prolotherapy?

- Nonsurgical treatment
- Strengthen and tighten the ligaments and tendons that hold bones and muscles in place.
- Series of injections stimulate body's natural healing response
- Restores proper joint alignment and relieves pressure on sensitive tissues.
- Dramatic and lasting pain relief.

Pain Management: Regenerative Medicine

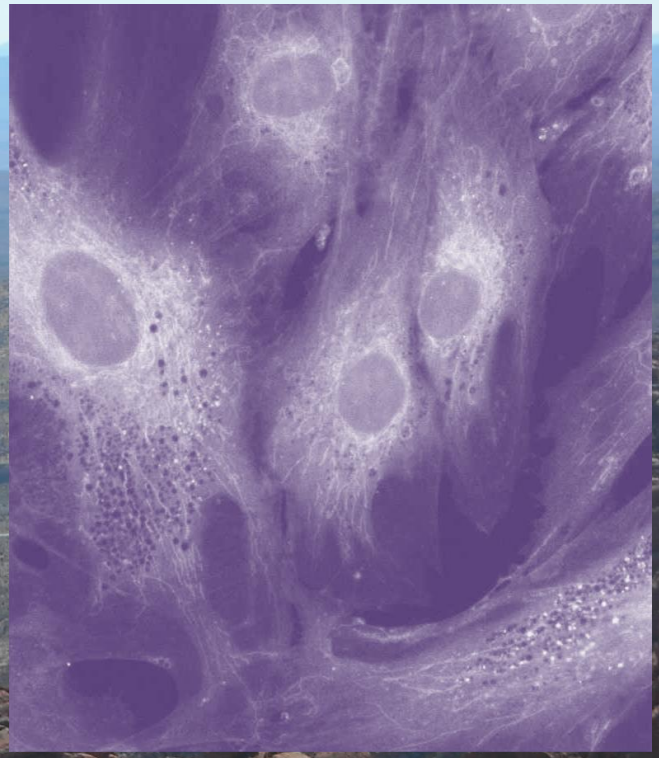
#4) PRP (Concentrated Platelets) = Platelet Rich Plasma

How Does PRP Injection Work?

- Injections of concentrated platelets with growth factors and low or high leukocyte concentrations into the damaged area.
- Triggers and provides the body's natural healing response and causes the proliferation of new tissue of ligaments, tendons or chondral surface.
- Tissue growth continues, the ligaments and tendons become thicker and stronger, regaining their ability to stabilize the joint and take the pressure off sensitive nerve endings.
- Pain subsides, range of motion returns, and cartilage degeneration slows down, halts or reverses.
- Sometimes one treatment is enough to achieve complete pain relief, but it usually takes 3 treatments, administered at 3-5 weeks apart, to produce sufficient tissue growth to relieve pain and restore normal function.

Pain Management: Regenerative Medicine
#5) What's an MSC?

- Mesenchymal stem cell
- Present in adipose and orthopedic tissues like bone, periosteum, synovial tissue, cartilage, bone marrow, muscle, ligaments, and tendon
- Can differentiate into all orthopedic tissues and orchestrate repair of same



Could Cannabis &/or Hemp *Really* Solve the Opioid Epidemic?

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- *Abnormal forces,*
- *environment / lifestyle.*

2) Review legislation that reduced/controlled narcotic prescriptions
3) Review the current use of Opioids for Pain
4) Learn what drove patients to seek alternative pain control
5) Learn the efficacy and safety of CBD

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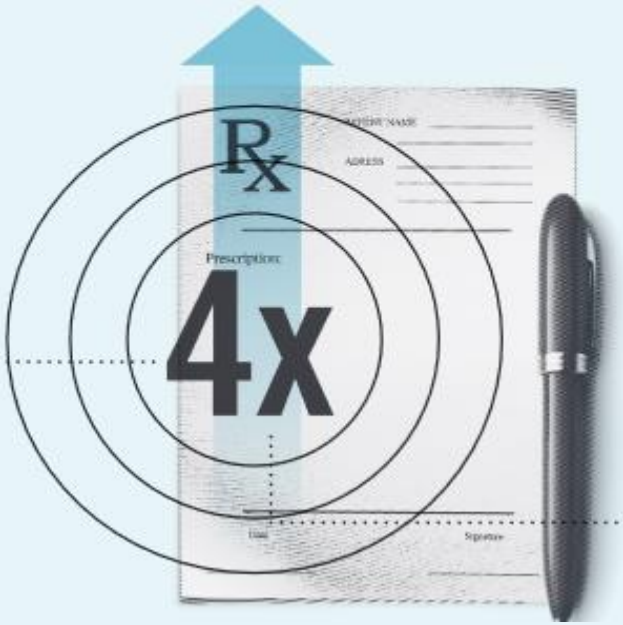
CDC cares about the health, safety, and well-being of patients with chronic pain. CDC is committed to ensuring that these patients get the best possible care. There is not enough science to know whether opioids control chronic pain long term, but it is clear that they have very serious risks and side effects.

The Epidemic

The amount of opioid prescriptions dispensed has

QUADRUPLED

since 1999



but the amount of pain that Americans report remains

UNCHANGED

Since 1999, more than

165,000

PEOPLE HAVE DIED FROM OVERDOSE

related to prescription opioids.

Nearly

2M

PEOPLE

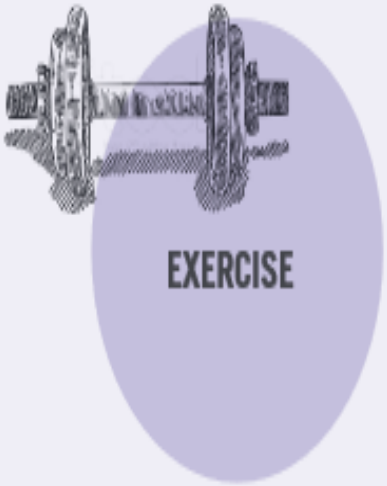
either abused or were dependent on prescription opioids in 2014

CDC Recommendations to Manage Pain

Consider ways to manage chronic pain without prescription opioids.
Some options may work better and have fewer risks and side effects:

Nonopioid pain relievers such as Tylenol, Motrin, or Naprosyn

Certain medications that also have benefits for depression and seizures



Physical therapy and exercise

Changing thoughts and behaviors related to pain

Another Satisfied Massage Client!!

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The current use of Opioids for Pain

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

Chronic pain = lasts >3 months or past the time of normal tissue healing (*5*).

- **1999–2002 National Health and Nutrition Examination Survey 14.6% adults widespread or localized pain lasting at least 3 months.**
- **2001–2003 Survey: Overall prevalence of common, predominantly musculoskeletal pain conditions (e.g., arthritis, rheumatism, chronic back or neck problems, and frequent severe headaches) estimated 43% adults in the US,**
- **2012 National Health Interview: 11.2% adults report daily pain.**
- **Evidence supports short-term efficacy of opioids for reducing pain and improving function in noncancer nociceptive and neuropathic pain in randomized clinical trials lasting primarily ≤12 weeks.**
- **Few studies conducted to rigorously assess the long-term benefits of opioids for chronic pain (pain lasting >3 months) with outcomes examined at least 1 year later.**

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What drove patients to seek alternative pain control

PCP Perspective

1) Onerous guidelines
   a) PMP Monitoring
   b) Drug Testing
   c) Paperwork
2) Threat of losing license
   a) Regulations and guidelines contribute to the paranoia
3) Increased referral rate to Pain Management
   a) Bottle neck / delay to be seen
4) 2018 Farm Bill, according to FDA made any cannabis or cannabis derivates with less than 0.3 percent THC no longer a “controlled substance.” This applies to most CBD products.

Patients seek alternative pain control

Survey data from patrons of Michigan medical marijuana dispensary suggesting that medical cannabis use in pain patients was associated with a 64% reduction in opioid use (Boehnke et al., 2016).

Prescription data from Medicare Part D enrollees in states with medical access to cannabis suggest a significant reduction in the prescription of conventional pain medications (Bradford and Bradford, 2016).

Pain is one of the primary reasons for the use of medical cannabis, suggest a number of pain patients are replacing the use of opioids with cannabis, despite the fact that cannabis has not been approved by the FDA for chronic pain.

Ch. 4 Therapeutic Effects of Cannabis and Cannabinoids
https://www.ncbi.nlm.nih.gov/books/NBK425767/

Patients seek alternative pain control

“CBD may be able to treat addiction through reduced activation of the amygdala during negative emotional processing and has been found to reduce heroin-seeking behavior, likely through its modulation of dopamine and serotonin.” [43, 44, 85, 86]

“An attractive option in chronic pain treatment, particularly in the context of opioid abuse, not only because of its potential efficacy but also because of its limited misuse and diversion potential as well as safety profile.” [86]

https://www.mayoclinicproceedings.org/article/S0025-6196(19)30007-2/fulltext

Patients seek alternative pain control

"More research will be needed because these were pilot human studies with small sample sizes, but they represent potential future areas of cannabinoid use in the clinical treatment of pain relief and opioid abuse."

"More reflection on the right political and industrial means to go about expanding access to CBD is needed in the context of controversial evidence supporting expanding access to medical marijuana as a pain control option." 6, 86

https://www.mayoclinicproceedings.org/article/S0025-6196(19)30007-2/fulltext

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Pain Management: CBD

- Blake DR "Preliminary assessment of the efficacy, tolerability and safety of a cannabis-based medicine - nabiximols in the treatment of pain caused by rheumatoid arthritis." Rheumatology (Oxford) 2006 NIH Database.

"The 1st ever controlled trial of a CBM (Cannabis Based Medicine) in RA, a significant analgesic effect was observed and disease activity was significantly suppressed following nabiximols (Sativex) treatment. While the differences are small and variable across the population, they represent benefits of clinical relevance and show the need for more detailed investigation in this indication."

Pain Management: CBD

CBDA as a selective cyclooxygenase-2 inhibitory component in cannabis - 2008

Takeda S[1], Misawa K, Yamamoto I, Watanabe K.

Organization for Frontier Research in Preventive Pharmaceutical Sciences, Hokuriku University, Kanazawa, Japan.

- Cannabidiolic acid (CBDA) selectively inhibited cyclooxygenase (COX)-2 activity having 9-fold higher selectivity than COX-1 inhibition.
- The carboxylic acid moiety in CBDA is a key determinant for the inhibition.
- The crude extract of cannabis containing mainly CBDA was shown to have a selective inhibitory effect on COX-2.
- This study suggest that naturally occurring CBDA in cannabis is a selective inhibitor for COX-2.

Pain Management: CBD

Cannabinoids in the management of difficult to treat pain

Ther Clin Risk Manag. 2008 Ethan B Russo

“Given (cannabinoids) multi-modality effects upon various nociceptive pathways, their adjunctive side benefits, the efficacy and safety profiles to date of specific preparations in advanced clinical trials, and the complementary mechanisms and advantages of their combination with opioid therapy, the future for cannabinoid therapeutics appears very bright, indeed.”

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2503660/

Pain Management: CBD

Cannabinoids in the management of difficult to treat pain - CONTINUED

Referencing studies back to the 1970s, a "newcomer" CBG exhibits GABA uptake inhibition to a greater extent than THC or CBD, suggesting possible utilization as a muscle relaxant in spasticity. GABA uptake inhibitors can be used for a number of conditions including seizures, anxiety disorders (generalized anxiety disorder, social phobia, social anxiety disorder, panic disorder, etc.), insomnia, as muscle relaxants, and for chronic pain as analgesics.

Again, while these studies, anecdotal reports, and online discussion boards show promise for CBG's use as a pain reliever, robust long-term medical research in humans is needed."

Pain Management: CBD

Cannabinoids as novel anti-inflammatory drugs

- **Executive summary – 2009**
- **Cannabinoids, mediate their effects through activation of specific cannabinoid receptors known as cannabinoid receptor 1 and 2 (CB1 and CB2).**
- **Cannabinoid system has been shown both *in vivo* and *in vitro* to be involved in regulating the immune system through its immunomodulatory properties.**
- **Cannabinoids suppress inflammatory response and subsequently attenuate disease symptoms. This property of cannabinoids is mediated through multiple pathways such as suppression of cytokines and chemokines at inflammatory sites.**
- **Cannabinoids have been tested in several experimental models of autoimmune disorders such as rheumatoid arthritis and have been shown to protect the host from the pathogenesis through induction of multiple anti-inflammatory pathways.**

Prakash Nagarkatti; Future Med Chem. 2009 Oct; 1(7): 1333–1349.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2828614/

Pain Management: CBD

CBDa, a major cannabinoid in fiber-type cannabis, is an inhibitor of MDA-MB-231 breast cancer cell migration, Takeda,et.al., 2012

- **"These results indicate that COX-2 activity is not an essential factor for the migration of MDA-MB-231 cells, and that other pathway(s) are likely to be involved in the anti-migration effects of CBDA."**
- ***How relates to MSK Pain?***

CBDa activity does NOT affect regenerative pathways of tissue growth and repair factors (PRP, MSC)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4009504/

Pain Management: CBD

Involvement of the endocannabinoid system in osteoarthritis pain La Porta C, et.al., 2014

"The ubiquitous distribution of cannabinoid receptors, together with the physiological role of the endocannabinoid system in the regulation of pain, inflammation and even joint function further support the therapeutic interest of cannabinoids for osteoarthritis… This review summarizes the promising results that have been recently obtained in support of the therapeutic value of cannabinoids for osteoarthritis management."

https://www.ncbi.nlm.nih.gov/pubmed/24494687

Pain Management: CBD

- Few contraindications – similar as CYP450 enzyme pathway.
- Philpott "Attenuation of early phase inflammation by cannabidiol prevents pain and nerve damage in rat osteoarthritis" Pain, 2017 Dec, NIH Database

"Showed 1st time local CBD administration inhibited pain & peripheral sensitization in established OA. Topical treatment with CBD reduced leukocyte trafficking and joint hyperemia during the early stages of MIA *(Joint irritant)*. By attenuating this initial inflammatory response with CBD, end-stage OA pain and peripheral neuropathy were abrogated. Thus, CBD may be a safe therapeutic to treat OA pain locally as well as block the acute inflammatory flares that drive disease progression and joint neuropathy."

- Hammell "Transdermal cannabidiol reduces inflammation and pain-related behaviors in a rat model of arthritis" Eur J Pain. 2016 NIH Database

"These studies demonstrate topical applied CBD has long-lasting therapeutic effects w/o psychoactive side-effects. Thus, topical CBD has potential as effective treatment of arthritic symptomatology. At present, one in five (21%) adults worldwide are diagnosed with some form of arthritis by their physicians (Helmick et al., 2008). The data presented suggest transdermal CBD is a good candidate for developing improved therapies for these debilitating disease."

Pain Management: CBD

- **The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research - 2017**
  - ✓ **The committee reached nearly 100 research conclusions based on consideration of more than 10,000 research articles**
  - ✓ **The committee found three medical applications for cannabis use supported by conclusive evidence:**

1. In adults with chemotherapy induced nausea and vomiting, oral cannabinoids are effective antiemetics.

2. *In adults with chronic pain, patients who were treated with cannabis or cannabinoids are more likely to experience a clinically significant reduction in pain symptoms*

3. In adults with multiple sclerosis (MS) related spasticity, short term use of oral cannabinoids improves patient-reported spasticity symptoms.

- ✓ ***For these conditions the effects of cannabinoids are modest; for all other conditions evaluated there is inadequate information to assess their effects.***

http://www.nationalacademies.org/hmd/~/media/Files/Report%20Files/2017/Cannabis-Health-Effects/Cannabis-public-release-slides.pdf

Pain Management: CBD

Cannabis and joints: scientific evidence for the alleviation of osteoarthritis pain by cannabinoids MelissaO'Brien , 2018

- ✓ **Cannabis used for millennia to treat a multitude of medical conditions including chronic pain.**
- ✓ **OA pain one of most common types pain and patients turning cannabis to manage their symptoms.**
- ✓ **Growing body of scientific evidence supporting analgesic potential of cannabinoids to treat OA pain.**
- ✓ **An endocannabinoid system identified in OA joints.**
- ✓ **Animal studies show cannabinoids reduce OA pain, inflammation and nerve damage.**
- ✓ **Few clinical trials tested efficacy/safety medical cannabis.**
- ✓ **Endocannabinoid system looks promising for OA pain, but more research is required.**

https://www.sciencedirect.com/science/article/pii/S147148921830043?via%3Dihub

Pain Management: CBD

Joint Problems Arising From Lack of Repair Mechanisms: Can Cannabinoids help? Malek and Starowicz, 2018

- ✓ **Review *in vitro, in vivo – animal and human* studies.**
- ✓ **Potential role of the endocannabinoid system in the modulation of the mechanism underlying structural pathology of cartilage surface, subchondral bone and synovial fibroblasts during OA**
- ✓ **Potential role of the endocannabinoid system in the repair mechanism of the structural pathology of OA**
  - ✓ **Chondroprotective activity – inhibitory on proteoglycan breakdown**
  - ✓ **Enhances bone cell differentiation, survival and function.**
  - ✓ **Reduces cytokine activity of the synovial fibroblasts**
- ✓ **"CBD can be an effective oral anti-arthritic therapy" Malfait, 2000.**

https://bpspubs.onlinelibrary.wiley.com/doi/full/10.1111/bph.14204

Pain Management: CBD

CBD Oil

Should You Try It for Arthritis Symptoms? - 2019

Daniel Clauw, MD, Professor University of Michigan, an expert in chronic pain, doesn't write off CBD's potential benefits and recommends it to some of his patients.

"A recent trial showed CBD alone was effective in [the treatment of] knee OA, and it appears as though it is very safe," he says. "Nearly all potential side effects of cannabinoids are from THC, not CBD."

https://www.arthritis.org/living-with-arthritis/treatments/natural/supplements-herbs/cannabidiol-oil.php

Myorelaxant Effect of Transdermal Cannabidiol Application in Patients with TMD: A Randomized, Double-Blind Trial – 2019

Methods: Polish version Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) was used.

- **60 pts enrolled, randomly divided, Ave. age Group1 - 23.2 yrs (SD) & Group2 - 22.6 yrs, parallel & double-blind trial.**
- **Grp1 CBD formulation, (Hemp Extract CBD concentration 7.3% (66.97 mg CBD/mL, 0.461 mg CBDA/mL, & 0.28 mg CBDV/mL). Ea. pt applied pea size & rubbed gently into skin surface (approx. 4×4 cm) on both sides, BID for 2 wks.**
- **Grp2 received placebo formulation for topical use. (same cholesterol carrier vehicle)**
- **Masseter muscle activity measured days 0 & 14, with surface electromyography (sEMG).**
- **Pain intensity VAS (Visual Analogue Scale) measured days 0 & 14.**

JCM | Free Full-Text | Myorelaxant Effect of Transdermal Cannabidiol Application in Patients with TMD: A Randomized, Double-Blind Trial | HTML (mdpi.com)

Myorelaxant Effect of Transdermal Cannabidiol Application in Patients with TMD: A Randomized, Double-Blind Trial – 2019

Results:

- **Grp1 sEMG masseter activity significantly decreased (11% RT & 12.6% LT). Pain intensity VAS scale similarly significantly decreased 70.2% (5.6 to 1.6)**
- **Grp2 sEMG masseter activity not significantly decreased (0.23% RT & 3.3% LT). Pain intensity VAS scale similarly was not significantly decreased at 9.81%. (5.1 to 4.6)**

Conclusion:

Application of CBD formulation over masseter muscle reduced the activity of masseter muscles and improved the condition of masticatory muscles in patients with myofascial pain.

JCM | Free Full-Text | Myorelaxant Effect of Transdermal Cannabidiol Application in Patients with TMD: A Randomized, Double-Blind Trial | HTML (mdpi.com)

Pain Management: CBD

Cannabidiol (CBD)
what we know and what we don't - 2020

Peter Grinspoon, MD – Harvard Health

"**CBD may offer an option for treating different types of chronic pain. …*European Journal of Pain* showed, animal model, CBD applied on the skin could help lower pain and inflammation due to arthritis. Another study demonstrated the mechanism by which CBD inhibits inflammatory and neuropathic pain, two of the most difficult types of chronic pain to treat.** More study in humans is needed in this area to substantiate the claims of CBD proponents about pain control."

Cannabidiol (CBD) — what we know and what we don't - Harvard Health Blog - Harvard Health Publishing

Effectiveness Topical CBD Oil Symptomatic Relief of Peripheral Neuropathy the Lower Extremities-2020

- 29 pts, 15 randomized CBD group (250 mg CBD/3 fl. Oz) & 14 to placebo group, 62% M & 38% F, mean age 68 years.
- After four weeks, the placebo group was allowed to crossover into the treatment group.
- Neuropathic Pain Scale (NPS – 0 to 10) statistically significant reduction in intense pain (4.6 to 3.3).

"Our findings demonstrate that the transdermal application of CBD oil can achieve significant improvement in pain and other disturbing sensations in patients with peripheral neuropathy. The treatment product was well tolerated and may provide a more effective alternative compared to other current therapies in the treatment of peripheral neuropathy."

The Effectiveness of Topical Cannabidiol Oil in Symptomatic Relief of Peripheral Neuropathy of the Lower Extremities - PubMed (nih.gov)

The Effectiveness of Topical Cannabidiol Oil in Symptomatic Relief of Peripheral Neuropathy of the Lower Extremities | Bentham Science (eurekaselect.com)

Pain Management: CBD

Summaries from the NFL/NFLPA Committee on Pain Management: 1) Alternatives to Opioids for Chronic Pain and 2) Cannabidiol and Cannabis – 2/2021

ALT-O: Alternatives to Opioids for Chronic Pain

State of the Science: Cannabidiol (CBD) and Cannabis

Players see CBD & medical cannabis as possible solutions to their medical issues— especially pain-related issues— but the state of the science is unclear.

Players may opt for CBD as a medical treatment in lieu of treatments with more scientific evidence supporting them.

While Marijuana is still banned the threshold needed to trigger a *positive test was raised fourfold*.

ClinicalTrials.com – 1/21/2021

- There were 276 clinical studies for CBD trials and research that started in 2020.
- One example, 11/2/20, a clinical trial took place at the University of Virginia, testing the effectiveness of CBD shea butter on hand osteoarthritis patients.

CBD: Background and Lit Review of Potential Treatments

- 15 year Lit Review, 75 citations
- Availability, Interest Use of CBD grown exponentially as represented by internet search's; btw 2017-2018 160%, 6.4M/month surpassing previous leaders of veganism, exercise and acupuncture.
- 2019 Gallup poll found 14% Americans used CBD, highest concentration in the West, 18-29 y/o most common and 30-49 y/o next.
- 2018 cross-sectional study of CBD users found majority treating specific conditions, most commonly pain (musculoskeletal), anxiety, depression and autoimmune.

Osteopathic Family Physician, Volume 13, No.2, March/April 2021

CBD: Background and Lit Review of Potential Treatments - Continued

- Evidence supports CBD for analgesic, anticonvulsant, antiemetic, antinociceptive, antipsychotic, anxiolytic, immunomodulatory and neuroprotective properties.
- Possible explanatory models include anti-inflammatory properties, suppression of lymphocyte proliferation, blockade of reactive oxygen burst by granulocytes, regulation of pain reception and inhibition of the lipopolysaccharide-induced increase in serum tumor necrosis factor.
- Because of the shift to Non-Opioid pain management this area of CBD research needs more attention.

Osteopathic Family Physician, Volume 13, No.2, March/April 2021

CBD: Background and Lit Review of Potential Treatments - Continued

SAFETY CONCERNS

- CBD does inhibit Cytochrome P450 both in vitro and animals. (Last Slide for Reference)

Osteopathic Family Physician, Volume 13, No.2, March/April 2021

The Effect of Cytochrome P450 Metabolism on Drug Response, Interactions, and Adverse Effects

Table 1
Significant Cytochrome P450 Enzymes and Their Inhibitors, Inducers, and Substrates

Enzyme	*Potent inhibitors**	*Potent inducers†*	*Substrates*
CYP1A2	Amiodarone (Cordarone), cimetidine (Tagamet), ciprofloxacin (Cipro), fluvoxamine (Luvox‡)	Carbamazepine (Tegretol), phenobarbital, rifampin (Rifadin), tobacco	Caffeine, clozapine (Clozaril), theophylline
CYP2C9	Amiodarone, fluconazole (Diflucan), fluoxetine (Prozac), metronidazole (Flagyl), ritonavir (Norvir), trimethoprim/sulfamethoxazole (Bactrim, Septra)	Carbamazepine, phenobarbital, phenytoin (Dilantin), rifampin	Carvedilol (Coreg), celecoxib (Celebrex), glipizide (Glucotrol), ibuprofen (Motrin), irbesartan (Avapro), losartan (Cozaar)
CYP2C19	Fluvoxamine, isoniazid (INH), ritonavir	Carbamazepine, phenytoin, rifampin	Omeprazole (Prilosec), phenobarbital, phenytoin
CYP2D6	Amiodarone, cimetidine, diphenhydramine (Benadryl), fluoxetine, paroxetine (Paxil), quinidine, ritonavir, terbinafine (Lamisil)	No significant inducers	Amitriptyline, carvedilol, codeine, donepezil (Aricept), haloperidol (Haldol), metoprolol (Lopressor), paroxetine, risperidone (Risperdal), tramadol (Ultram)
CYP3A4 and CYP3A5	Clarithromycin (Biaxin), diltiazem (Cardizem), erythromycin, grapefruit juice, itraconazole (Sporanox), ketoconazole (Nizoral), nefazodone (Serzone‡), ritonavir, telithromycin (Ketek), verapamil (Calan)	Carbamazepine, *Hypericum perforatum* (St. John's wort), phenobarbital, phenytoin, rifampin	Alprazolam (Xanax), amlodipine (Norvasc), atorvastatin (Lipitor), cyclosporine (Sandimmune), diazepam (Valium), estradiol (Estrace), simvastatin (Zocor), sildenafil (Viagra), verapamil, zolpidem (Ambien)

CYP=cytochrome P.

**—These will slow down substrate drug metabolism and increase drug effect.*

†—These will speed up substrate drug metabolism and decrease drug effect.

‡—Brand not available in the United States.

Information from references 10 and 14 through 16

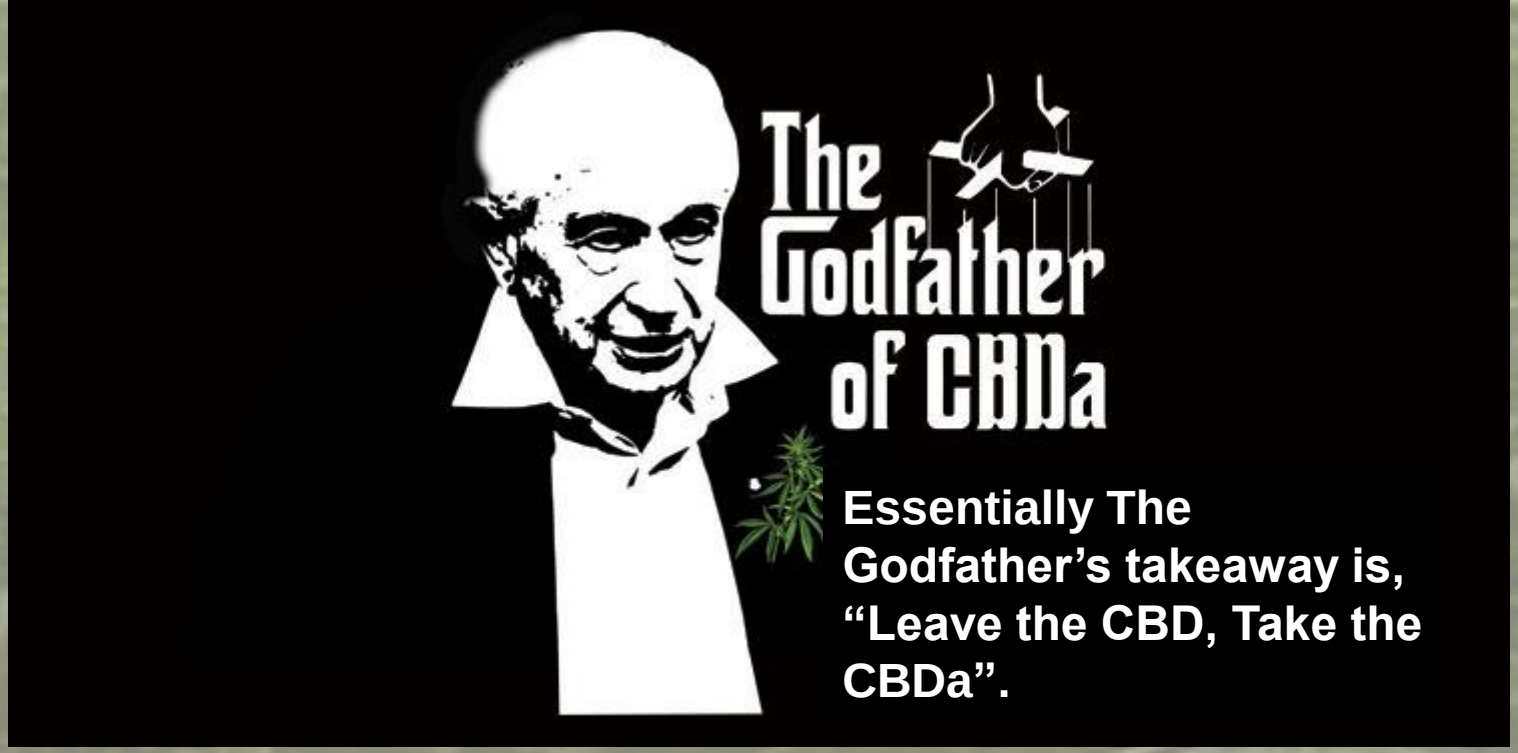
Pain Management: CBD

Raphael Mechoulam, Ph.D., Professor
Hebrew University of Jerusalem
Head, Medicinal Chemistry Lab
President, Multidisciplinary Center for Cannabinoid Research
Head of Research for EPM

The Chemistry Behind Cannabinoid Acid – 2019

“CBDA, it is naturally occurring but very unstable, and is much stronger than CBD with no side effects……the activities of these acids and they seem to be important and very important particularly in a variety of fields.”

https://www.healtheuropa.eu/raphael-mechoulam-latest-findings-93683-2/93683/



While Americans were getting high, groovin' to the Beatles and winning the space race to the moon, a research scientist on the other side of the world, in Israel, discovered and literally named the compounds known as cannabinoids.
Today the most known are THC and CBD.

But, according to this doctor, Dr. Mechoulam, there is a parent cannabinoid of CBD that is about to grab all the headlines – CBDa.

Pain Management: CBD

What is a good starting dose?

***Start low and go slow! (I don't Rx THC)**

***Usual starting dose of CBD**

0.1-0.6 mg/kg in 1-2 divided doses, up to 10-20mg/kg.

150 lb – 7 to 12 mg up to 78 to 156 mg

180 lb – 17mg ie 5mg/kg

***Different delivery methods have different onset and duration times – be aware (oral ingested delayed vs. sublingual faster acting) – unsure on transdermal**


Yosemite National Park
Hiking to Half Dome?
HALF DOME
PERMIT REQUIRED
7 days a week
Yosemite National Park
Travel on Subdome and Half Dome is
DANGEROUS
during and after lightning and rainstorms
SERIOUS INJURY AND DEATH have resulted from:
Falls on wet, slick rock
Lightning strikes to hikers on exposed terrain
EVALUATE THE WEATHER BEFORE PROCEEDING PAST THIS POINT

Thank you for your time and care of patients!

Phillip Zinni III, DO, FAOASM, MS, ATC

Past-President
American Osteopathic Academy of Sports Medicine

National Medical Director
The Industrial Athlete

209-324-2255
JockOccDoc@Hotmail.com

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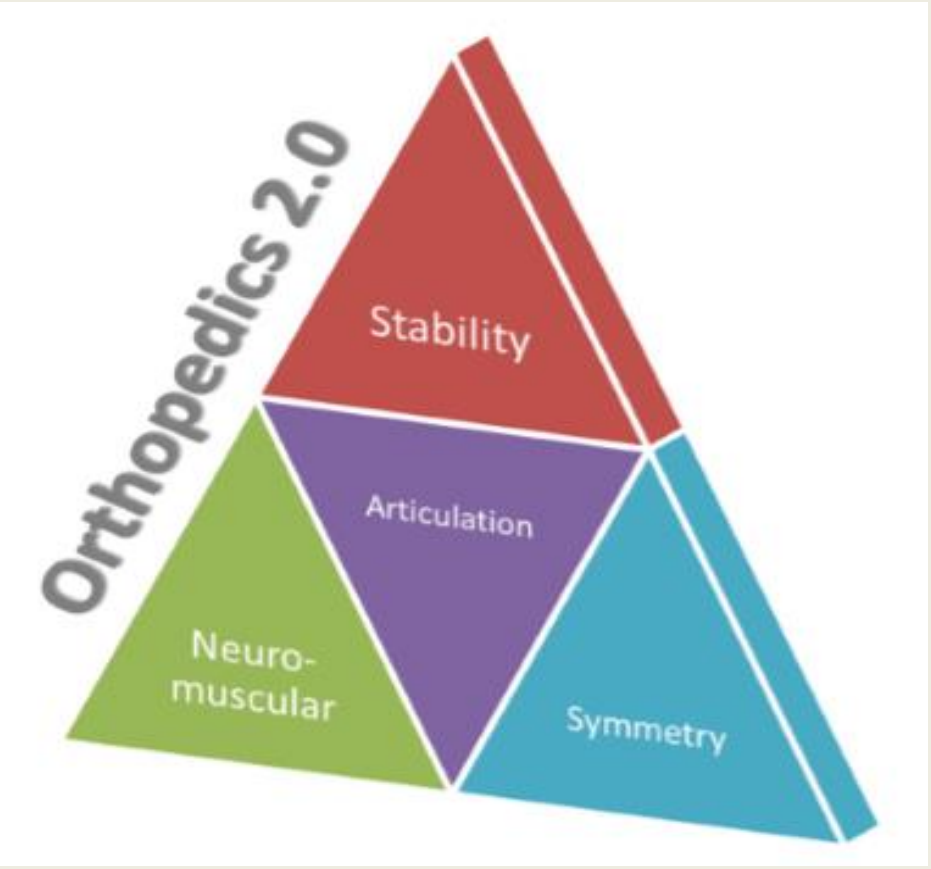
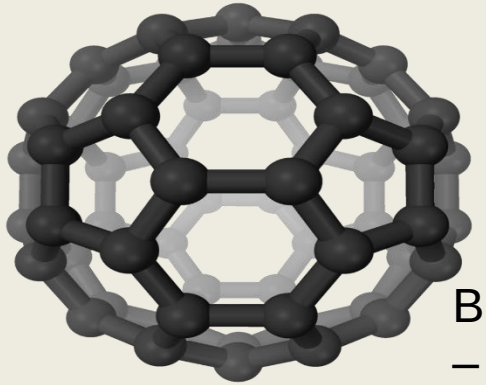
Form Follows Function or Deformity Delineates Dysfunction

SANS – Christopher Centeno MD

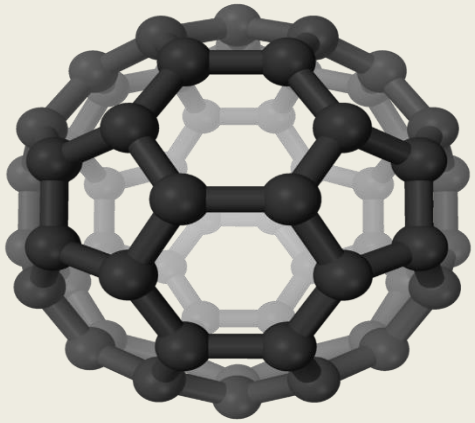


Tensegrity



Biotensegrity – Buckyball

Form Follows Function or Deformity Delineates Dysfunction



BIOTENSEGRITY

Buckyball / Buckminsterfullerene

Organism approach states everything is in balance even at the cellular level.

Pain Management: Herbal

Daily Doses

- **Boswellia Serrata Extract: 1200 mg**
- **Curcumin Extract (Turmeric): 1200 mg**
- **Cayenne: 360-2400 mg**
- **Devil's Claw: 1530 mg**
- **Feverfew 85-125 mg**
- **Ginger: 1200 mg**
- **White Willow Bark (Salicin): 360-720 mg**