

Rational Opioid Prescribing: What Doctors and Nurses Need to Know



Brian S. Kahan, DO
The Kahan Center for Pain Management

Objectives

1. Describe the incidence, effects and costs of chronic pain
2. Discuss attitudes towards management of non-malignant pain
3. Summarize key facts regarding current litigation in chronic pain
4. Articulate a rational approach to treatment of chronic pain

Objectives

- Describe the effects of THC on humans
- Describe the human endocannabinoid System
- Describe the effects of cannabidiol on humans
- Review Maryland law on recommending medical cannabis
- Briefly review current medical research on medical cannabis

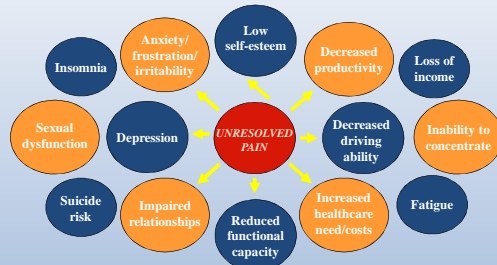
Many Americans Suffer from Chronic Pain

- CDC (2018) found over 20% of Americans have chronic pain
- 34% have recurrent pain
- 66 million are partially or totally disabled
- 8 million are permanently disabled by back pain
- At least 50 million Americans suffer from chronic, recurrent headaches and spend \$4 billion annually on medication.
- An estimated 31 million people in the U.S. experience chronic facial and neck pain.
- There are 65,000 new cases of permanent disability diagnosed each year

Psychosocial Effects of Chronic Pain

- Loss of employment / income
- Depression, fear, anxiety
- Isolation
- Sleep disorders
- Marital and family dysfunction

Impact of Unrelieved Pain



Chronic Pain is Expensive

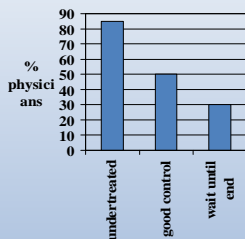
- Chronic pain disables more people than cancer or heart disease and costs the American people more than both combined.
- 2012, Pain problems cost \$635 billion a year in medical costs, lost working days, and workers' compensation

J. Borica, International Association for the Study of Pain (IASP)

Pain Presents Dual Health Problems

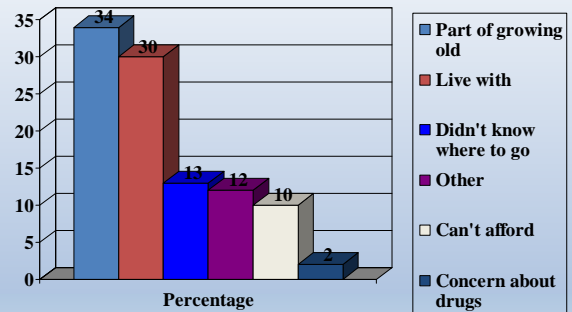
- Pain is now part of vitals signs and required to be below 5/10 for discharge in most hospitals
- Pain is in the media-
- Lawsuits have arisen from inadequate pain control
- Prescription drug use among teenagers and college students is increasing
- DAWN data reveals increased ER visits for non-medicinal use of opioids
- Lawsuits have arisen for overtreatment of pain

Pain is Under Treated: The Physician Perspective



- Most patients are under medicated
- Pain control in my practice is good or very good
- I would wait until patient's prognosis is 6 months or less before maximizing treatment

Healthcare's Perception of Pain



Physicians Beliefs Regarding Opioids

Belief Regarding Opioid analgesics	Overall % agreeing or strongly agreeing	OR _{adj} Specialty Geriatrics	OR _{adj} level of training Attending
For chronic pain, giving opioids on a regular schedule is preferred over as needed dosing	90%	1.00 (p=0.995)	1.48 (P=0.664)
Patients hesitate to ask for pain medications because of fear of addiction to opioids	78%	9.92 (p=0.030)	0.91 (p=0.348)
Patients accurately judge their intensity of pain	76%	8.37 (p=0.044)	2.40 (p=0.110)
Patients with chronic pain often require higher doses of pain medication than patients with acute pain	57%	0.81 (p=0.644)	0.85 (p=0.672)
25% of all patients receiving chronic opioids become addicted	16%	0.51 (p=0.404)	0.34 (p=0.111)
Increasing analgesic requirements is a sign that the patient is becoming addicted	8%	0.83 (p=0.826)	1.48 (p=0.584)
Sedation is a common side effect of chronic opioid use	30%	0.30 (p=0.048)	1.39 (p=0.448)

Physician Attitudes Toward Opioid Prescribing for Patients With Persistent Noncancer Pain.
Lin, Jenny; Alford, David; Moore, Carlton
Clinical Journal of Pain. 23(9):799-803, November/December 2007.

Physicians Beliefs Regarding Opioids, cont.

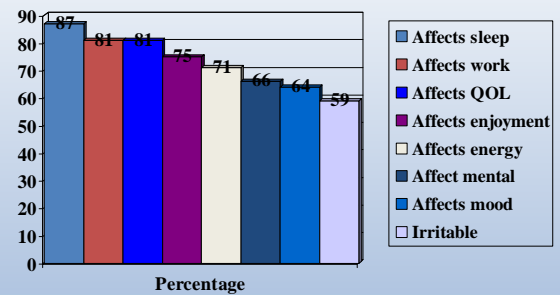
Physician Belief	Overall % agreeing or strongly agreeing	OR _{adj} Specialty Geriatrics	OR _{adj} level of training Attending
I hesitate to prescribe opioids for my patients because			
I am concerned about side effects	58%	0.44 (p=0.080)	0.83 (P=0.634)
I am concerned about diversion for illegal use	37%	0.10 (p=0.004)	0.82 (p=0.660)
I am concerned about causing addiction	31%		0.50 (p=0.167)
I do not know how to prescribe the correct dose	27%	0.09 (p=0.020)	0.77 (p=0.596)
I am concerned about regulatory scrutiny	21%	0.17 (p=0.095)	0.27 (p=0.046)

Physician Attitudes Toward Opioid Prescribing for Patients With Persistent Noncancer Pain.
Lin, Jenny; Alford, David; Moore, Carlton
Clinical Journal of Pain. 23(9):799-803, November/December 2007.

Patients' Perceptions of Pain



Individual Perception of Pain



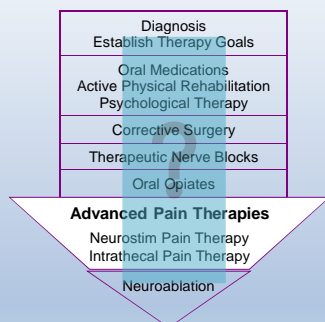
Awareness of Pain Treatment

- 86% of patients stated they were taken seriously
- 80% thought they were assessed properly
- 27% stated their pain relief was ineffective
- 78% were never referred to a pain specialist
- 65% were not aware of pain specialists

Obstacles to Treatment

- Physicians knowledge
- Physician fear
 - The fear of iatrogenic addiction is a primary impediment to prescribing opioids for the treatment of pain. Bloodworth AJPMR 2005
- Understanding how pain occurs
- Lack of trust / disbelief
- Cookbook treatment plans
- Medical certification

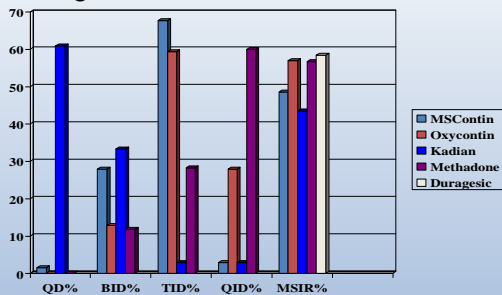
Pain Treatment Continuum



Opioids

- Work by blocking mu-receptors in the periphery and central nervous system
- Good for moderate to severe pain
- Should be used in combination with Tylenol or NSAID's if possible but not in one pill
- Side effects

Retrospective Assessment of Frequency of Dosing in Chronic Pain



Royal, M., Jenson, M. Oklahoma Univ. of Med.

Pain: Facts and Fiction

- Facts
 - Acute and chronic pain are serious problems for 20 to 30% of the U.S. Population
 - At any one point, 50% of Americans have experienced some kind of pain within the past 2 weeks
 - Over 65 million people in America have disabling chronic pain

Pain: Facts and Fiction, cont.

- Fiction
 - Pain is inevitable
 - Pain will not kill you
 - Taking pain medication early- when the pain appears to be most bearable leads to:
 - Development of tolerance
 - Less effective pain relief later when the pain is severe

Current State

Are We Just Creating Addicts?

YES

- Substance abuse and Mental Health Services (SAMHSA) survey
- Center on Addiction and Substance Abuse (CASA)
- USA survey 7/20/06
- Drug Abuse Warning Network (DAWN)

NO

- Formation of patient advocacy groups
- State Medical board guidelines
- Federal guidelines
- Litigation for under treatment of pain
- Hippocratic Oath

Substance Abuse and Mental Health Services

- SAMSHA survey revealed 7.9% of 12 or older currently used illicit drugs
- 2.4 million persons used pain relievers for non-medicinal purpose
- Marijuana use still #1 illicit drug used followed by opioids

Center on Addiction and Substance Abuse

- CASA found 212% increase in teenagers trying illicit drugs from 1992-2003
- 15.1 million people abusing prescription drugs
- 212% increase in the number of 12 to 17 y/o using controlled substances for the first time

USA Today

- 1 in 5 adults have a relative addicted to drugs or alcohol

Drug Abuse Warning Network

- Increased ED visits associated with drug misuse/abuse
- ½ million of these ED visits were due to non medicinal use of medication
- Misuse of opioids accounted for more deaths in the US than heroin or cocaine

JAMA April 6, 2011 vol. 305 vol. 13 pp.1315

- Association between opioid prescribing patterns and opioid overdose-related deaths
- Conclusion
 - Patients who were receiving higher than 50 mg/d of morphine equivalent for non malignant pain had a higher rate of overdose compared to those < 50 mg/d

TABLE 4 Federation of State Medical Boards (FSMB) model policy for the use of controlled substances for the treatment of pain¹⁰

Criteria when evaluating the physician's treatment of pain, including the use of controlled substances¹⁰

Evaluation of the patient. A medical history and physical examination must be obtained, evaluated, and documented in the medical record. The medical record should document the nature and intensity of the pain, current and past treatments for pain, underlying or coexisting disease or conditions, the effect of the pain on physical and psychological function, and history of substance abuse. The medical record also should document the presence of one or more recognized medical indications for the use of a controlled substance.

Treatment plan. The written treatment plan should state objectives that will be used to determine treatment success, such as pain relief and improved physical and psychological function, and should indicate if any further diagnostic evaluations or other treatments are planned. After treatment begins, the physician should adjust drug therapy to the individual medical needs of each patient. Other treatment modalities or a rehabilitation program may be necessary, depending on the etiology of the pain and the extent to which the pain is amenable to physical and psychological treatment.

Informed consent and agreement for treatment. The physician should discuss the risks and benefits of the use of controlled substances with the patient, as well as the risks and benefits of the patient's nonparticipation in the treatment if the patient is without medical decision-making capacity. The patient should receive prescriptions from one physician and one pharmacy whenever possible. If the patient is at high risk for medication abuse or has a history of substance abuse, the physician should consider the use of a written agreement between physician and patient outlining patient responsibilities, including:

- Urine/toxicology medication levels screening when requested
- Number and frequency of all prescription refills
- Reasons for which drug therapy may be discontinued (eg, violation of agreement)

Periodic review. The physician should periodically review the course of pain treatment and any new information about the etiology of the pain or the patient's state of health. Continuation or modification of controlled substances for pain management therapy depends on the physician's evaluation of progress toward treatment objectives. Inadequate response to treatment may be indicated by the patient's decreased pain, increased level of function, or improved QOL. Objective evidence of improved or diminished function should be monitored, and information from family members or other caregivers should be considered in determining the patient's response to treatment. If the patient's progress is unsatisfactory, the physician should assess the appropriateness of continued use of the current treatment plan and consider the use of other therapeutic modalities.

Continuation. The physician should be willing to refer the patient as necessary for additional evaluation and treatment or to refer the patient to another treatment modality. Special attention should be given to those patients with a history of substance abuse or with a controlled substance disorder who may require extra care, monitoring, documentation, and consultation with or referral to an expert in the management of such patients.

Medical records. The physician should keep accurate and complete records to include:

1. Medical history and physical examination
2. Diagnostic, therapeutic, and laboratory results
3. Evaluation and consultations
4. Treatment objectives
5. Discussion of risks and benefits
6. Informed consent
7. Treatments
8. Medications (including date, type, dosage, and quantity prescribed)
9. Instructions and agreements
10. Periodic review

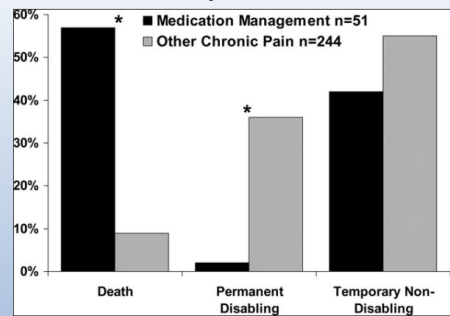
Records should remain current, be maintained in an accessible manner, and be readily available for review.

Compliance with controlled substances laws and regulations. To prescribe, dispense, or administer controlled substances, the physician must be licensed in the state and comply with applicable federal and state regulations. Physicians are referred to the Practitioner's Manual of the FSMB¹⁰ and any relevant documents issued by state medical boards for specific rules governing controlled substances as well as applicable state regulations.

10. DEA Drug Enforcement Administration QOL, quality of life; 1207, urine drug testing.
Federation of State Medical Boards of the United States, Inc. Model policy for the use of controlled substances for the treatment of pain, 2008.

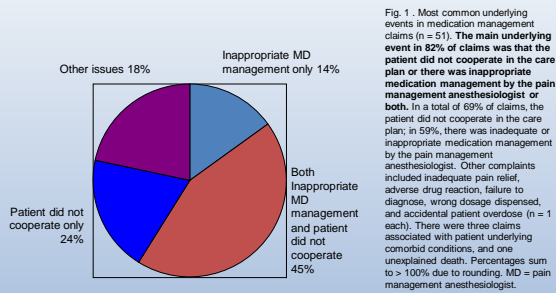
What Do the Regulatory Committees Want?

Who's Really to Blame?



Severity of injury. Death was the outcome in 57% of medication management claims.

Who's Really to Blame? cont.



Malpractice Claims Associated with Medication Management for Chronic Pain. Fitzgibbon, Dermot; Rahmell, James; Michna, Edward; Stephens, Linda; Posner, Karen; Domino, Karen

Who's Really to Blame? cont.

Table 2. Sites of Pain in Medication Management Claims (n = 51)

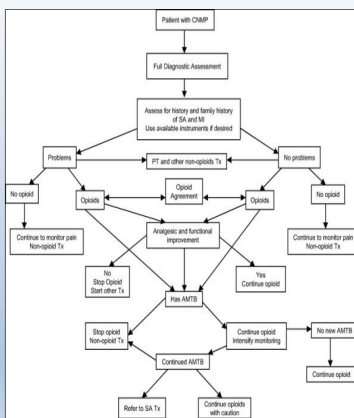
Site of pain*	n	% of 51
Back	27	53
Neck	12	24
Lower extremity/hip	9	18
Headache	6	12
Pelvic/bladder/urinary tract	4	8
Shoulder	3	6
Upper extremity	3	6
Multiple sites	3	6
Other unspecified sites	2	4
No. pain sites		
Single site	35	69
Two sites	9	18
Three sites	3	6
Multiple sites unspecified	4	8

Table 2. Sites of Pain in Medication Management Claims (n = 51)

* Percentages sum to more than 100% because some patients had multiple sites. Shoulder pain was never the sole site of pain in a claim. Pain in both upper extremities or in both lower extremities was classified as a single site.

Malpractice Claims Associated with Medication Management for Chronic Pain. Fitzgibbon, Dermot; Rahmell, James; Michna, Edward; Stephens, Linda; Posner, Karen; Domino, Karen

Schematic Treatment Plan For Nonmalignant Pain



How Do I Prescribe Opioids?

- Treat pain the same way you treat other non-curable diseases
 - HTN
 - Chronic angina
 - Diabetes
 - Rheumatological
 - Cancer

Step I: Comprehensive Initial Evaluation

History and Physical

- Extensive history
- Try and get medical records prior to appointment
- Review social history and abuse of non-illicit agents. e.g. tobacco
- Complete physical attention to pain behavior findings
- Complete pharmacological history

Screening tools

- Opioid risk tool
- CAGE questionnaire
- Urine drug screen
- Genetic history
- Smoking history
 - When is your first cigarette?
 - inc incidence if within 1 hour of waking

Table 3. Patient Factors Commonly Associated with Medication Misuse or Addiction

Factor*	No. Claims	% of 51
Patient medical history		
Depression	23	45
Suicide attempt†	3	6
Drug or alcohol problems	18	35
Aberrant behaviors		
Getting medications from multiple providers	18	35
Concurrent use of illicit drugs or alcohol	10	20
Escalating dosages without permission	7	14
Losing prescriptions	2	4
Taking medications prescribed to others	2	4
Failed screening tests	2	4
Asking for early refills	2	4
Number of factors‡		
None	10	20
One	13	25
Two	16	31
Three	8	16
Four	3	6
Five	1	2

* Factors sum to more than 100% due to multiple factors in some claims. † All also had a history of depression. ‡ Each factor was counted only once for each patient, even if the behavior (e.g., losing prescriptions) occurred multiple times.

Red Flags

TABLE 5 Suggestive physical findings for suspicion of drug abuse^{67,140,145}

- Evidence of current intoxication (drowsiness, nodding, slurred speech, impaired attention/memory)
- Spider angiomas
- Hepatomegaly
- Red facies
- Palms erythema ("liver palms")
- Salivary gland enlargement
- Cigarette burns
- Unexplained bruises/frequent falls
- Diabetes/blood pressure/ulcers not responsive to treatment
- Signs of hypogonadism
- Inflamed/eroded nasal septum
- Dilated pupils
- Track marks/injection sites
- Gunshot/knife wounds
- Poor hygiene
- Nutritional deficits
- Frequent hospitalizations
- Alcohol withdrawal signs (eg, flushing, sweating, hyperreflexia, hypertension, tremor)
- Opioid withdrawal signs (eg, mydriasis, sweating, irritability, rhinorrhea, nausea, cramps, vomiting, diarrhea, muscle aches, piloerection, yawning)

Adapted from Fishbain DA: Chronic pain and addiction. In: Bony TZ, Cole BE, eds. *Weiner's Pain Management: A Practical Guide for Clinicians*, 7th ed. Boca Raton, FL: CRC Press; 2006. Weaver MF, et al: *Arch Intern Med* 1999;159:913-24. O'Brien CP: Drug Addiction and Drug Abuse. In: Brunton LL, Lazo JS, Parker KL, eds. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*, 11th ed. New York, NY: McGraw-Hill, 2005.

Suggestive Findings of Abuse

Aberrant Behaviors

TABLE 8 Examples of aberrant drug-related behaviors^{67,228}

More Indicative of Addiction	Less Indicative of Addiction
<ul style="list-style-type: none"> • Selling prescription drugs • Prescription forgery • Stealing or "borrowing" another patient's drugs • Injecting oral formulations • Obtaining prescription drugs from nonmedical sources • Concurrent abuse of alcohol or illicit drugs • Multiple dose escalations or other nonadherence despite warnings • Multiple episodes of prescription "loss" • Repeatedly seeking prescriptions from other clinicians or from emergency rooms without informing prescriber, or after warnings to desist • Evidence of deterioration in ability to function at work, in the family, or socially that appears to be related to drug use • Repeated resistance to changes in therapy despite clear evidence of adverse physical or psychologic effects from the drug 	<ul style="list-style-type: none"> • Aggressive complaining about the need for more drug • Drug hoarding during periods of reduced symptoms • Requesting specific drugs • Openly acquiring similar drugs from other medical sources • Unsanctioned dose escalation or other nonadherence with therapy on 1 or 2 occasions • Unapproved use of the drug to treat another symptom • Reporting psychic effects not intended by the clinician • Resistance to change in therapy associated with "tolerable" adverse effects with expressions of anxiety related to the return of severe symptoms

Adapted from: Fishbain DA: Chronic pain and addiction. In: Bony TZ, Cole BE, eds. *Weiner's Pain Management: A Practical Guide for Clinicians*, 7th ed. Boca Raton, FL: CRC Press; 2006. Kirsh RL, Whitcomb LA, et al: *Clin J Pain* 2002;18:S52-60.

Step II: Establish Diagnosis

- X-rays, MRI, CT, neuropsychological studies
 - Use technology and don't be afraid of cost containment. Remember they can sue you for more
- Psychological evaluation
- Precision diagnostic interventions

Step III: Establish Medical Necessity

- Physical diagnosis
- Therapeutic interventional pain management
- Physical modalities
- Behavior therapy

Step IV: Assess Risk Benefit Ratio

- Treatment is beneficial
- Sleep apnea
- Respiratory dysfunction
- Addiction tendencies for legal and illegal substances

Step V: Establish Treatment Goals

- 4 weeks, 8 weeks, 3 months, 6 months, 12 months
- Be realistic
 - Never pain free
- Make patient do it
- Stick to it
- Determine baseline function
 - Distance walking, transfers, ADL's, pain level

Step VI: Obtain Informed Consent

- Opioid consent to treat
- Opioid contract
- Rules and regulations
- Contact me at bkahan@thekahancenter.com for copies

Step VII: Initial Dose Adjustment Phase (8-12 weeks)

- Start low dose
- Utilize opioids, NSAID's, and adjuvants
- Discontinue due to:
 - Lack of analgesia
 - Side effects
 - Lack of functional improvement

Step VIII: Stable Phase (stable-moderate doses)

- Monthly refills
- Assess for 4 A's
 - Analgesia
 - Activity
 - Aberrant behavior
 - Adverse effect
 - Manage side effects

Step IX: Adherence Monitoring

- Prescription monitoring program
 - Utilize free electronic prescribing software that is web based
- Random urine drug screens
- Pill counts

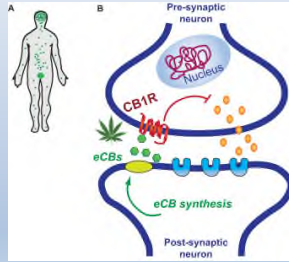
Step X: Outcomes

- | | |
|--|--|
| <ul style="list-style-type: none">• Success – continue if:<ul style="list-style-type: none">– Stable doses– Analgesia, activity– No abuse, side effect | <ul style="list-style-type: none">• Failed – discontinue if:<ul style="list-style-type: none">– Dose escalation– No analgesia– No activity– Abuse– Side effects– Non-compliance |
|--|--|

Human Endocannabinoid System

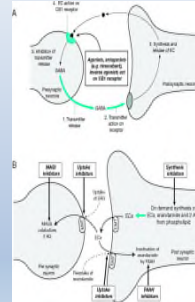
- Endocannabinoids play an important role in cell signaling but are limited to paracrine (cell to cell) or autocrine(same cell)
- Characteristics of ECS
 - lipophilic
 - hydrophobic
 - retrograde transmission in CNS) post synaptic to presynaptic)
 - synthesized on demand
 - short half life
- two main receptors
 - CBD1-R
 - CBD2-R
- Cannabinoid receptors are found throughout the human body

Human Endocannabinoid System



- Retrograde action
- Endogenous release of anandamide binds to CBD1-R

Human Endocannabinoid System



- A simplified diagram of the function of CB1 receptors and the action of the endocannabinoid (EC) system at a neuronal synapse in the central nervous system. (A) The retrograde action of ECs. γ -Aminobutyric acid (GABA) release and action is shown with thick arrows, EC release and action with thin arrows. (B) Synthesis, release, uptake and inactivation of the ECs, anandamide and 2-arachidonyl glycerol (2 AG). The potential sites at which the EC system can be manipulated therapeutically are shown in boxes. FAAH, fatty acid amide hydrolase; MAGL, monoacyl glycerol lipase; EMT, endocannabinoid membrane transporter.
- Cannabinoids and the endocannabinoid system
- Dale, M.M., MB BCh PhD, Pharmacology Condensed, Chapter 15, 40-42
- Copyright © 2009 © 2009, Elsevier Limited. All rights reserved

Human Endocannabinoid System

CBD1-Receptor

- Predominantly found in CNS and PNS
- Concentrated on GABA releasing neurons (inhibitory) and glutaminergic releasing neurons (excitatory)
- Activation of CBD1-R suppresses neurotransmitter release pre synaptically
- this could result in an excitatory response or inhibitory response depending on location
- endogenous ligand
 - anandamide
 - 2-arachidonolglycerol
- exogenous ligand
 - THC partial agonist



CBD2-Receptors

- predominantly found in immune system
- thought to have protective effect on autoimmunity and inflammation
- endogenous ligand
 - 2-arachidonolglycerol
- Exogenous ligand
 - CBD
- THC

Pharmacology of Cannabis

- Marijuana is comprised of more than 60 pharmacologically active cannabinoids.
- Cannabinoid receptors are found throughout the human body
- CBD1 receptors- CNS and PNS
- CBD2 receptors-immune system
- The exogenous ligands such as cannabidiol (CBD) and tetrahydrocannabinol (THC)

Pharmacology of Cannabis

THC

- THC is the most bioactive substance and 95-99% bound to plasma lipoproteins
- Metabolized by the CYP2C9 and CYP3A4 to active metabolite 11-OH-THC which crosses the blood brain barrier
- Oral administration peak serum concentration
 - 30-190 minutes
- Inhalation peak concentration
 - 3-10 minutes



CBD

- CBD is second most bioactive substance
- Metabolized by liver but is it's own active metabolite
- Substrate of CYP2C9 and CYP3A4. Inhibits CYP2C
- Oral administration peak serum concentration
 - 30-120 minutes
- Inhalation
 - Unknown

Current US Medical Research on Efficacy of Medical Cannabis

- A Randomized, Placebo-Controlled, Crossover Trial of Cannabis Cigarettes in Neuropathic Pain. Journal of Pain, 2008-06-01, Volume 9, Issue 6, Pages 506-521, Copyright © 2008 American Pain Society
 - 38 patients total
 - Conclusion smoking high 34 mg THC and concentrations (7%), low dose 19 mg THC (3%) placebo had a mixed linear analgesic response on neuropathic pain.
 - Higher concentrations had greater impairment in attention, learning and memory as well as psychomotor speed.
 - Serum levels of CBD, THC and CBN did not correlate with analgesic effect but cognitive impairment did with THC levels

Current cannabis levels available on market

- Harlequin 8-16% THC
- GDP 17-23% THC
- Blue Dream 17-24% THC
- Sour Diesel 19-25% THC
- Girl Scout Cookies 17-28% THC

Current Medical Research on Efficacy of Medical Cannabis

- Sativex
 - Spasticity- only approved in Europe. Ratio of thc to cbd 1:1 oral form
- Cesamet
 - Chemo induced nausea
- Drobinolol- Marinol

Why is it legal?

– MONEY

Does it have potential?

- Neuropathic pain control
- Spasticity
- Obesity
- Brain diseases
- Psychiatric diseases

How can we be sure it works?

☞ Only if it becomes schedule II to allow proper human research.

- Need Federal government involvement
- The cannabis calculator.

Side effects?

- Sedation
- Psychosis
- Anxiety
- Overdose

What are some of the advantages?

- Better than opioids?
- Non habit forming?
- Less chance of overdose?
- Organic?
- Low drug drug interaction?

What are the disadvantages?

- Cancer?
- Altered motor function?
- Impaired cognitive thinking?
- Decreased sperm count

Summary

Why Do We Bother?

- Pain is a real problem with real complications.
- The Hippocratic Oath states "I will keep them from harm ..." and its modern equivalent, the Declaration of Geneva, states "the health of my patient will be my first consideration."
- The American Medical Association states that "physicians have an obligation to relieve pain and suffering."
- the American Nurses Association's position is that "nursing encompasses ... the alleviation of suffering ..."

Is It Worth the Risk?

Only you can answer that question.



How Do We Protect Ourselves?

- Treat pain like other non-curable diseases
- Be systematic in your approach
- Utilize diagnostic studies in combination with interventional treatment to come to a conclusive diagnosis
- Don't just prescribe, prescribe for an effect
- Document success and failures

Who Is Really Watching?

- Everyone
- We are all waiting to find the answer to this question:
Is chronic opioid analgesic therapy effective in management of non-malignant pain?

References

- American Pain Society 1999
- Opioid guidelines in the management of chronic non-cancer pain. *Pain Physician* 2006; 9:1-40
- DAWN report Issue 19, 2006
- Behavioral monitoring and urine toxicology testing in patients receiving long term opioid therapy. *Anesth Analg* 2003;97:1097-1102
- Issues in opioid management. *Am J Phys Med Rehabil* 2005;84:S42-55
- Opioid therapy for chronic pain. *N Engl J Med* 2003;349:1943-1953
- Use of opioid medications for chronic non-cancer pain syndromes in primary care. *J Gen Intern Med* 2002;17:173-179
- Prescription drug abuse....*Pain Physician* 2006;9:287-321
- JAMA April 6, 2011
- Stanos, SP, et al. Pain management with opioid analgesics. *Am J of PMR* 2009
- Nicholson, Bruce. Management of Chronic Noncancer Pain in a Primary Care Setting. *The Southern medical Association* 3/20/2007
- **Malpractice Claims Associated with Medication Management for Chronic Pain.** Fitzgibbon, Dermot; Rathmell, James; Michna, Edward; Stephens, Linda; Posner, Karen; Domino, Karen *Anesthesiology*. 112(4):948-956, April 2010.

References

- Therapeutic potential of cannabinoid medicines. (full – 2013) <http://onlinelibrary.wiley.com/doi/10.1002/dta.1529/full>
- The endocannabinoid system in normal and pathological brain aging (full – 2012) <http://rstb.royalsocietypublishing.org/content/367/1607/3326.full>
- Cannabinoids for medical Use: a systematic review and meta-analysis. *JAMA* 2015;313(24) 2456-2473
- Endocannabinoids Griffing, George *Emedicine/Medscape* 2-5-2015/1361971
- PubMed search randomized controlled trials for medical marijuana or medical cannabis
- ClinicalKey search randomized controlled trials for medical marijuana or medical cannabis or cannabis.

Question and Answer Session

