

Medical Marijuana: The Risks, Benefits And Medical Implications

Andrea Efre, DNP, ARNP, FNP-C



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

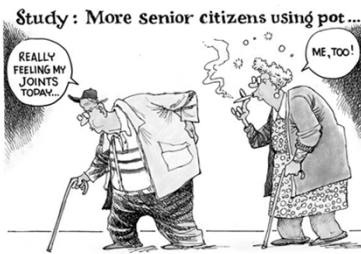
Objectives

By the end of this session the participant will be able to:

- Describe medical reasons for using marijuana
- Consider the short term and long term side effects of marijuana
- Discuss the accessibility of medical and recreational marijuana, including the legal and social implications of the drug

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Do you already have an image of a Marijuana User



DAVE GRANLIND © www.davegranlind.com

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabis (Marijuana) The Plant

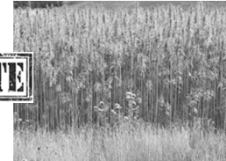
- Cannabis: 3 sub-species - C. sativa, C. indica and C. ruderalis
- Cannabis sativa (most common) varieties produce marijuana and hemp
- Difference between marijuana and hemp plants = Resin

Marijuana (grown for "high")

- High resin (rich in trichomes) = High in THC
- Usually grown indoors hydroponically

Hemp for industrial use (No high)

- Low resin = Low in THC
- Grown outside



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabis (Marijuana)

What's in a name?

- The international agreed term is 'cannabis'
- Marijuana is a term used in USA
- Also known as Marijuana, Marihuana, Mariguana:
 - Terms were associated with the Mexican immigrant population (after 1910 Mexican Revolution).
 - Its suggested that the first marijuana laws were aimed at placing social controls on the immigrant population
- Marijuana was spelled marihuana in the Marihuana Tax Act of 1937 and in the Industrial Hemp Farming Act of 2005
 - The Marihuana Tax Act of 1937 criminalized pot possession throughout the United State
 - This tax law passed under the name of Marijuana - medical community did not realize it was cannabis

Street names:

- ☺ Doobie/Dubie
- ☺ Dope
- ☺ Ganga
- ☺ Grass
- ☺ Green
- ☺ Hash
- ☺ Herb
- ☺ Hooch
- ☺ Hydro
- ☺ Joints
- ☺ Marijuana
- ☺ Mary Jane
- ☺ Pot
- ☺ Reefers
- ☺ Smoke
- ☺ Weed

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabis in History

- 8,000-7,000 B.C. the earliest woven fabric apparently was made of hemp fibers
- 2,700 B.C. China ~ used flowers and resin to medically treat menstrual disorders, gout, rheumatism, malaria, constipation, and absent-mindedness
- 1000-2000 B.C. Hemp was used for fiber throughout the world for fabrics
- 1213 B.C. Egyptians used cannabis for treating glaucoma, inflammation and enemas
- 1000 B.C., India and Middle East used a mixture of milk and cannabis (named bhang) as an anesthetic and anti-phlegmatic



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabis in History

- 1840's to 1900's: Cannabis extracts, tinctures and elixirs were 2nd and 3rd most used medicines in America. scientific journals wrote of therapeutic benefits
- 1851: U.S. Pharmacopoeia of Medicines stated cannabis could be used to treat asthma, neuralgia, glaucoma, nausea, epilepsy, depression, rheumatism, arthritis, alcoholism and others.
- Late 1800s British neurologist used cannabis for epilepsy
- 1911: New Orleans ban marijuana (one of the first in US)
- 1937: Banned The Marihuana Tax Act
- 1940's the war effort legalized hemp again (needed hemp ropes and parachutes), but made illegal again post war – when Hemp was imported from India
- 1960's: Rock and Roll – called for legalization again
- 1970's: CBD used for seizures - success but the studies small and not well blinded
- 1996: California legalized marijuana for medical use



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabis - Hemp

- Hemp is bred specifically
 - Fiber- paper, fabric, rope, and Construction
 - Seeds – feed, beer, and hemp flour (confections, baking additive)
 - Oil - cooking, nutritional supplements, fuel, paint
- Benefits of Hemp: Typically richer in CBD - Without intoxication
- International Standard:
 - limit of TCH = 0.3% as the official limit for legal hemp
- U.S. law defines hemp as all parts of any *Cannabis Sativa* plant containing no psychoactive properties, except for defined exceptions
- Canadian plant scientists Ernest Small and Arthur Cronquist, wrote 1976 taxonomic report to include hemp and other forms of cannabis
- Of Note: Farm Bill: 2014: President Obama Signed Farm Bill with Amendment to Allow Industrial Hemp Research (adding to legislative/legal confusion)

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabis - Hemp

- 9th century: monks wrote manuscripts, on hemp paper using hemp oil to burn the lamp light
- Medieval times, Islamic physicians used cannabis to treat nausea and vomiting, epilepsy, inflammation, pain, and fever
- Christopher Columbus brought with him gifts of hemp fabrics
- 1620 Mayflower: hemp seeds were brought to USA by pilgrims
- It is said that Thomas Jefferson used hemp paper to draft both
 - The Constitution
 - Declaration of Independence
 - Final documents were written on parchment
- Hemp paper was widely used in that time period
- No evidence has been found/proven regarding the smoking of hemp or marijuana during that time
- Prison uniforms given to slaves from Africa were made from hemp fabric



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Politics Vs Science



- Federal law currently prohibits the use, sale, and possession of marijuana
 - Schedule I – No medical use and not able to be prescribed
- However, 28 states have legalized marijuana for "medical" use - with an Rx
 - This makes the prescribers responsible for the Rx
 - big responsibility
 - Prescribing a drug that is Schedule I
- Schedule I - Marijuana, heroin, ecstasy and LSD
- Schedule II - cocaine, methamphetamine, opium and morphine

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Politics Vs Science

- Its important to separate the legalization of:

- Medical marijuana
 - CBD Only
 - Recreational marijuana
- Some states agree to recreational use:
- Legalized use without a prescription
 - EG: Colorado, Oregon and Washington State

28 Legal Medical Marijuana States and DC
Laws, Fees, and Possession Limits

28 LEGAL MEDICAL MARIJUANA STATES AND DC



http://medicalmarijuana.procon.org/view_resource.php?resourceID=000881 – researched and copied March 2017

Note: on 4/6/17 West Virginia passed a bill making some forms of medical cannabis acceptable, making it the 29th state

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Research Trials



Why is research so limited?

- Lack of Phase 3 clinical trials
- The schedule I
 - Schedule I status makes it very difficult to use in clinical trials
 - Illegal status scares the research investigators
- Bias may make publication of the work more difficult
- Will trials ever be approved if it includes "smoked" marijuana?
- Until re-scheduled large scale research trials will probably not take place
- Medical and research communities base their opinions on limited studies, possible side effects, and "opinions" on personal or anecdotal patient experiences

Cartoon from: <http://www.marijuana.com/blog/news/2014/10/novelist-patricia-cornwell-donates-500k-for-harvard-marijuana-research/>

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabinoids

Endocannabinoids – refer to natural cannabinoids in the body

- Intercellular lipid messengers that activate the cannabinoid receptors - similar to neurotransmitters like acetylcholine or dopamine
- Endocannabinoids are lipophilic molecules and not very soluble in water
- Receptors - CB₁ (brain) and CB₂ (immune system). These receptors exist in the parts of the brain that control N/V, chronic pain and seizures

Synthetic cannabinoids - are those which have been man-made (Rx or chemical)

- Manufactured artificially to mimic the effects of natural cannabinoids
- Medications: Dronabinol (Marinol) and Nabilone (Cesamet)
- K2 and Spice

Phytocannabinoids – refer to the molecules derived from the cannabis plant

- Naturally found in varieties of cannabis plants - concentrated in the resin
- Produced in structures known as glandular trichomes
- Cannabis contains multiple cannabinoids (60-80), but little is known about most
- The most studied cannabinoids are: Tetrahydrocannabinol (THC) and cannabidiol (CBD)

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabinoids

Phytocannabinoids

Tetrahydrocannabinol (THC) - psychoactive "high" effect (Δ^8 THC and Δ^9 THC)

- Mostly associated with Marijuana (flower/bud)

- Positive effects: analgesic, anti-spasmodic, anti-tremor, anti-inflammatory, appetite stimulant and anti-emetic properties,

Cannabidiol (CBD) - medical effects without making the subject "high"

- CBC is mostly associated with hemp, but is best sourced from CBD-rich cannabis plants

- Positive effects: anti-inflammatory, anti-convulsant, anti-psychotic, anti-oxidant, neuroprotective and immunomodulatory effects

Cannabinol (CBN) – trace amounts - psychoactive, sedative and analgesic

- Both **THC and CBD** are used in "medical marijuana"

- Separately or combined "**Ratio is important**"

- Choices of cannabinoid depends on individual needs, the medical marijuana laws, and the prescribing provider

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabis (Marijuana) The Plant

Cannabis: 3 sub-species –

- Cannabis Sativa
 - Most popular for smoking
 - Used for industrial hemp
 - Tall – up to 15 feet
 - Usually dried
 - High ratio of THC to CBD
- Cannabis Indica
 - 3-6 feet tall and able to be grown indoors
 - Flowers are stickier and resin makes hashish
 - More sedative
 - Higher in CBN than other varieties
- Cannabis Ruderalis
 - Small/short plant (20-25 inches)
 - Not very psychotropic
 - Mostly used by breeders and cultivators



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Medical Marijuana

- American Academy of Neurology (represents over 27,000 neurologists) became one of the first medical organizations in the U.S. to endorse the use of medical marijuana
- They issued guidelines saying that oral cannabis, medical marijuana pills and medical marijuana spray may help ease pain and other symptoms caused by MS
- They do not yet endorse smoked marijuana
- Difference between current Rx "marijuana" pharmaceutical and medical marijuana
 - Rx approved in USA uses synthetic THC
 - Medical marijuana is natural but not FDA approved.
 - There are no safety/purity standards, limited clinical trials and remains Schedule I – sometimes leaving the prescriber with questions
- FDA approved THC in the USA
 - Dronabinol (Marinol) – Schedule III
 - Nabilone (Cesamet) – Schedule II

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Prescription Cannabinoid

Dronabinol (Marinol) - Schedule III

- Synthetic delta-9- tetrahydrocannabinol (delta-9-THC)
 - Anorexia associated with weight loss in with HIV/AIDS
 - Dose is 2.5mg-10mg PO BID
 - Chemotherapy-induced nausea and vomiting (failed conventional antiemetics)
 - 5mg PO Q2-4 hours (max 15mg/day)
- Onset of action: 0.5 to 1 hours and peak effect at 2 to 4 hours.
- Duration of action: psychoactive effects is 4 to 6 hours, but the appetite stimulant effect may continue for ≥ 24 hours



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Prescription Cannabinoid

Dronabinol (Marinol) -

- Side effects:
 - CNS (reported by 33% of patients)
 - Tachycardia, palpitations, orthostatic hypotension,
 - Nausea, Vomiting and diarrhea
 - Conjunctival injection (red eyes)
 - Confusion, dizziness, drowsiness, depression, hallucinations
 - Warned not to drive, operate machinery,
- Caution in: seizures, cardiac disorders, mania, schizophrenia, vulnerable populations
- In pain patients, oral dronabinol has similar psychoactive effects to smoking marijuana



There have been some additional studies for use in multiple sclerosis, Parkinson's and Huntington's disease, and disturbed behavior in Alzheimer's disease and Tourette syndrome, but not FDA indicated

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Prescription Cannabinoid

Nabilone (Cesamet)

- Synthetic delta-9- tetrahydrocannabinol (delta-9-THC)
- Indication: Nausea and vomiting related to chemotherapy
 - 1-2mg PO BID – Give 1-3 hours prior and during Chemotherapy treatment – usually 5 day course
 - Effects: vomit less and eat more
- Side Effects: most common drowsiness, spinning sensation, dry mouth, feeling "high", lack of coordination, difficulties concentrating, headache, mood changes, tachycardia and hypotension.
 - Avoid alcohol, driving, operating machinery
 - Mental side effects may last 2-3 days
 - Adverse psychiatric reactions can persist for 48 to 72 hours following cessation of treatment



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Prescription Cannabinoid

New medication; On the Fast Track for FDA approval – but the spray is not currently approved for use in the U.S. for any condition

GW Pharmaceuticals is collaborating with Otsuka Pharmaceutical on Phase III clinical trials for cancer pain - but no regulatory application has been made for MS spasticity

Approved in 25 countries – including Canada, Europe, Scandinavia and UK

Nabiximols (Sativex) – vaporizer/Spray

- Composed primarily of two cannabinoids: CBD (cannabidiol) and THC (Δ^9 tetrahydrocannabinol), which are administered in an oromucosal spray
- Moderate to severe multiple sclerosis spasticity (MSS)
- Canada also allows Sativex to be used for relief of neuropathic pain and advanced cancer pain



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

FDA Approved Vs Legislative Approved

Currently Two approved Rx medications in the USA

What if they are not the best option for your patient, what options do you have?

Depends on the State



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Marijuana - Cannabinoids

Δ^9 -Tetrahydrocannabinol (THC)

- Psychoactive ingredient
- Anticonvulsant, but can also be pro-convulsant
- The psychotropic effects of Δ^9 -THC limit tolerability, and are the reason many use it for recreation

Cannabidiol (CBD)

- Non-psychoactive ingredient
- Neuroprotective and anti-inflammatory and anticonvulsant
- Well tolerated (Devinsky, et al 2014)

- Marijuana's therapeutic effects (versus side effects) depend on the concentration of THC
- Cannabidiol (CBD) has an ability to mitigate the psychoactive effects of THC. As a result, the THC-CBD ratio for many strains of marijuana has been engineered to achieve desired effects (Hill, 2015)

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabis Classification and THC

United Nations Office on Drugs and Crime (UNODC) states:

- Cannabis flower often contains 5% THC
- Cannabis resin can contain up to 20% THC content
- Cannabis oil may contain more than 60% THC content

Cannabis is more potent now than ever

- THC content in marijuana had increased worldwide from 1970 to 2009 (Cascini, Aiello, & Di Tanna, March 2012)
- Change raw THCA to THC = through heat

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabis Preparations Containing THC

- **Herbal** - Marijuana describe the dried flowers, leaves and stems of the female cannabis plant, which are usually smoked and are least potent of the preparations. Usually 3%-20% THC and considered recreational more than medicinal.
 - Industrial hemp plants contain less than 1% THC and are thus not valued for recreational use
- **Hashish** - made from the resin (a secreted gum) of the cannabis plant. It is dried and pressed into small blocks, and smoked (eg: crumbled into tobacco) or added to food. consumed orally or smoked, and is also vaporized
- **Hash oil** - most potent cannabis product, is a thick oil obtained from hashish and is usually smoked. Produced by solvent extraction-Cannabinoids: THC (~ 30%) and THCA (~ 60%)
 - New trend in street drug use known as Dab, Wax and butane honey oil.



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabis (Marijuana) Preparations

- Tincture** - dried flowers of the female cannabis plant are soaked in ethanol to create a solvent. The THC and other cannabinoids dissolve into the alcohol. Consumed sublingually, orally, sublingual spray, or topically (eg: Green Dragon)
- Kief** - is a powder, rich in resin trichomes (high THC concentration) and usually consumed as a powder or compressed to produce cakes of hashish. From the colloquial Arabic كيف *kēf/kif*, meaning pleasure or intoxication.
- Infusion** – mixed with non-volatile solvents such as butter or cooking oil
- Cannabis preparations are more bioavailable when prepared or infused in an oil, such as butter



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabis (Marijuana) Preparations

- Cannabis Liquor** - Liquor may be infused with cannabinoids. Best to cook stems and leaves into brandy or rum. Can be added to coffee and other beverages.
- Cannabis Topicals (applied to the skin)** - Cannabinoids combined with a penetrating topical cream can enter the skin and body tissues and allow for direct application to affected areas (e.g. allergic skin reactions, post-herpes neuralgia, muscle strain, inflammation, swelling, etc.). Less or limited psychoactive affect



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabis (CBD) Preparations

- CBD Oil is the most common preparation**
 - Oral or sub-lingual
 - Intranasal
 - Transdermal (patches) and balm or lotion
 - Capsules (made from oil)
- Non-psychoactive
- Past centuries (especially 1800's) was used for gout, rheumatism, malaria, pain, and fever.
- CBD is not psychoactive, but as a component of the cannabis/marijuana plant it is a Schedule I substance under the federal Controlled Substances Act (CSA)
- Most well known use is Charlotte's Webb – used for Refractory epilepsy—especially in children with Dravet syndrome



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Charlotte's Web

- Charlotte's web - marketed as dietary supplements and claim efficacy against Dravet Syndrome
- Charlotte's Web was developed in 2011 by the Stanley brothers – through crossbreeding a strain of marijuana with industrial hemp
 - Less THC and more CBD – in 2014 THC content was 0.3%
 - Sometimes referred to as "Realm Oil"
- A number of high profile and anecdotal reports have sparked debate
- Dravet syndrome (rare) catastrophic form of intractable epilepsy that begins in infancy.
- GW Pharmaceuticals is seeking FDA approval to market a formulation of CBD, under the tradename Epidiolex, as a treatment for Dravet syndrome
 - Epidiolex was granted fast-track status and is in late stage trials following positive early results from the drug



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

16 States with Laws Specifically about Legal Cannabidiol (CBD)

- | | |
|--|---|
| <ul style="list-style-type: none"> Alabama (2014) Delaware (2015) Florida (2014) Georgia (2015) Iowa (2014) Kentucky (2014) Mississippi (2014) Missouri (2014) | <ul style="list-style-type: none"> North Carolina (2014) Oklahoma (2015) South Carolina (2014) Tennessee (2014) Texas (2015) Utah (2014) Virginia (2015) Wisconsin (2014) |
|--|---|

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabidiol (CBD) Indications

- Epilepsy/Seizures – reduced frequency
 - Especially in treatment-resistant epilepsy in children and young adults
- Huntington's disease
- Cancer – of multiple types and multiple symptoms
- Neuropsychiatric disorders
 - Anxiety
 - Post traumatic stress disorder
 - Schizophrenia or schizophreniform disorder
 - Autism and mental health conditions
 - Psychosis - May have anti-psychotic effects – insufficient evidence - inconclusive
- Neonatal hypoxic-ischemic encephalopathy

Many studies, including Devinsky 2014 & 2016

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabidiol (CBD) Indications

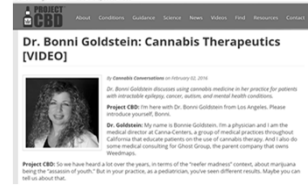
- HIV-associated neuropathic pain
- Spasms and pain
- Spasms associated with multiple sclerosis
- Dystonia
- Dystonia in Parkinson's disease
- Parkinson's disease with psychotic symptoms
- Anti-inflammatory effects
- Dependency and withdrawal of cannabis
 - May be used BID to treat marijuana withdrawal symptoms – reduce or eliminate anxiety or dissociative symptoms
 - Studies are limited
- Not enough basic pharmacologic data on the role of CBD, especially in the treatment of refractory epilepsy. (Welty, 2014)



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

CBD and THC Combination

- THC to CBD Ratio:
 - Balance is the Key
- Studies are limited
 - Most have used whole cannabis - not measured or broken down into THC or CBD
- It appears that CBD may protect against some of the psychological effects of TCH
- Studies using a combination of CBD and THC for Multiple sclerosis have little to no adverse effects on cognition or mood – other than those observed with similar psychoactive drugs



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Indications of Cannabis

- Nausea and vomiting
- Appetite loss and weight loss
 - Usually HIV/AIDS – anorexia and wasting syndrome
- GI inflammation and maybe Crohn's
- Hiccups
- Chronic Pain
- Neuropathic pain
 - Pain associated with MS, HIV and traumatic or spinal injury
- Multiple sclerosis
 - Reduced pain
 - Reduced spasticity
 - May improve urinary symptoms
- Epilepsy
 - Mixed results. Pediatrics seem to reduce seizures by 50% (Press et al, 2015)
 - Adults may not (Hamerle et al 2014)
- Headaches

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

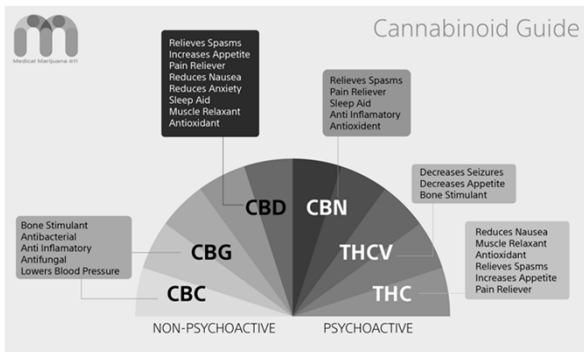
Indications of Cannabis

- Inflammation
- Psychiatric:
 - Bipolar disorders PTSD
 - Anxiety
- Glaucoma – IOC reduced - most likely THC rather than CBD (studies are old 1970-80's)
 - New studies needed.
 - Effective dose is frequent and high = ↑ side effects
- May assist with:
 - Reduced alcohol use
 - Reduced opioid consumption
 - Assisting in opiate withdrawal symptoms
 - Quit cocaine
 - Cannabis may be addictive – But CBD may assist in cannabis withdrawal

Spontaneous regression of benign brain tumor may have been associated with cannabis use (Foroughi et al, 2011)

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Balancing Cannabinoid with Indication for Use



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Multiple sclerosis, epilepsy, and movement disorders

A systematic review of medical marijuana by an AAN subcommittee

- **Spasticity:** oral cannabis extract (OCE) tetrahydrocannabinol (THC) is effective, and nabiximols appear to be effective
- **Central pain or painful spasms:** OCE, THC and nabiximols are probably effective
- **Urinary dysfunction:** nabiximols is probably effective for reducing bladder voids/day; THC and OCE are probably not
- **Tremor:** THC, OCE and nabiximols are probably ineffective at treating tremors, or levodopa-induced dyskinesias in patients with Parkinson disease.
- Unknown efficacy in epilepsy or other movement disorders: non-chorea-related symptoms of Huntington disease, Tourette syndrome, and cervical dystonia
- Risk of serious adverse psychopathologic effects was nearly 1%
- Smoked marijuana is of unclear efficacy for reducing pain (Koppel, et al 2014)

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Analgesic - Marijuana vs Dronabinol

- Study: Cooper, Comer & Haney, 2013
- Compared the analgesic effectiveness of smoked marijuana vs oral dronabinol
- Used healthy male (N = 15) and healthy female (N = 15) in NY State
 - Comparable doses: marijuana (0.00, 1.98, or 3.56% THC) to dronabinol (0, 10, or 20 mg)
 - Pain response assessed: immersed their left hand in cold water (4 °C)
 - Pain sensitivity (time to report pain) and pain tolerance (withdraw the hand from the water)
- Both decreased pain sensitivity and increased pain tolerance more than placebo, but no difference between marijuana and dronabinol
- Dronabinol analgesia effect was of a longer duration

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cannabigerol (CBG) Cannabinol may help Prevent or Cure Colorectal Cancer

- Colon carcinogenesis may be inhibited by Cannabigerol (CBG)
- Cannabigerol (CBG) is a cannabis-derived non-psychoactive cannabinoid
- Interacts with specific targets involved in carcinogenesis
- Cannabigerol (CBG) hampers colon cancer progression
- Selectively inhibits the growth of colorectal cancer cells
- Cannabigerol (CBG) is a promising agent for the prevention and cure of colorectal cancer

Borrelli, F., et al (2014)

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

American Academy of Neurology

- The AAN: concluded that certain forms of medical marijuana (only in pill or oral spray form) can help treat some symptoms of MS
- These include spasticity, certain types of pain (pain related to spasticity, including painful spasms, and painful burning and numbness) and overactive bladder.
- Most of the MS studies examined pill or oral spray forms of medical marijuana.
- The AAN caution that medical marijuana can worsen thinking and memory problems which many many people with MS suffer from these problems already due to the disease itself

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

American Academy of Neurology

- The American Academy of Neurology concluded that there is not enough information to show if medical marijuana (smoked or medical marijuana) is safe or effective in these neurologic diseases:
 - Motor symptoms in Huntington's disease
 - Tics in Tourette syndrome
 - Cervical dystonia (abnormal neck movements)
 - Seizures in epilepsy
- Parkinson's disease: medical marijuana does not help relieve abnormal movements that can develop in the late stages of the disease from the drug levodopa, which is the main drug used to treat shaking, stiffness and slowness of movements.

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Dosing

- Dosing difficult – Limited studies (anecdotal)
- Start low – Go slow -
Titrate to effect and side effects
 - 5-10mg 2-4 times a day
 - 1 to 3 g/day when smoked or vaporized
- 25 mg of pharmaceutical-grade cannabis with a THC (content 9.4%) was effective in reducing intensity of pain, improved sleep and was well tolerated when smoked as a single inhalation 3x/day for five days (Ware, 2010)
- To treat eating disorders, 7.5-30 milligrams of THC has been taken by mouth daily for four weeks
- A dose of 15-30 milligrams of cannabis extract capsules has been taken by mouth in five-milligram increments, based on tolerance, for 14 days
- Multiple sclerosis symptoms: Cannabis plant extracts containing 2.5-120 milligrams of a THC-CBD combination by mouth daily for 2-15 weeks

| Strength of Cannabis (assuming negligible cannabidiol) | Daily dosage of cannabis corresponding to 2.5 - 90 mg of THC |
|--|--|
| 10% THC | .15 g - 5.55g |
| 15% THC | .12 g - 3.69g |
| 20% THC | .08 g - 2.79g |
| 25% THC | .04 g - 2.25g |
| 30% THC | .01 g - 1.86g |

Donald Abrams, MD, Professor of Clinical Medicine at the University of California, San Francisco, et al (2004)

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Dosing

- Titrate to effect, but may take 3-4 weeks
- Increasing dosage every 3-4 weeks by 5-25mg until symptom relief
- Sleep disorders, 40-160 milligrams of CBD has been taken by mouth
- Chronic pain: 2.5-20 mg CBD by mouth for an average of 25 days
- Epilepsy: 200-300 mg of CBD by mouth daily for up to 4.5 months
- Huntington's disease: 10 mg per kilogram of CBD by mouth daily for six weeks
- Schizophrenia: 40-1,280 mg CBD by mouth daily for up to four weeks
- CBD is well tolerated in humans with doses up to 600 mg and Does not result in psychotic symptoms (Mechoulam, 1978)



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Dosing

- Acceptable dose:
 - Most recommend serving size is 10mg of THC per serving
- Edibles are easily over dosed
 - Eg: Chocolate bars and cookies

- Example: These Kief chips
 - Small print on the bottom 120mg
 - 12 chips per bag
 - No instruction to just eat one
 - No website, 800 number or warnings on the bag



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Pharmacokinetics Cannabis (THC)

- Oral and inhalation route of cannabis produce different results
- Smoked THC bioavailability averages 30%
- Pulmonary assimilation of inhaled THC = maximum plasma concentration within minutes, psychotropic effects start within seconds to a few minutes, reach a maximum after 15–30 minutes, and taper off within 2–3 hours.
- Following oral ingestion, psychotropic effects set in with a delay of 30–90 minutes, reach their maximum after 2–3 hours and last for about 4–12 hours, depending on dose and specific effect.
- Oral THC bioavailability approximately 4-12%
- Oral absorption is highly variable
- The onset of action is delayed and titration of dosing is more difficult
- THC is widely distributed, particularly to fatty tissues. The spleen and body fat are long-term storage sites.
- The elimination of THC and its many metabolites (from all routes) occurs via the feces and urine. Metabolites persist in the urine and feces for several weeks.

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Pharmacokinetics of CBD

- Bioavailability varies greatly depending on route of administration of CBD
 - 34%–46% for intranasal administration (Paudel et al, 2010)
 - 40% for vaporization (Solowij et al, 2014)
 - Oral CBD may be as low as 6%, owing to significant first-pass metabolism (Hawksworth et al, 2004)
- Orally administered cannabidiol (CBD) has shown a relatively high incidence of somnolence in a pediatric population in recent studies. The acidic environment during normal gastrointestinal fluid converts CBD into the psychoactive components Δ^9 -THC and Δ^8 -THC (Merrick et al, 2016)
- Cannabidiol can both inactivate and enhance various cytochrome P450 enzymes
- CBD is a more potent inhibitor of cytochrome P450 enzymes than grapefruit
 - CBD reduces the enzymatic degradation of warfarin, thereby increasing its duration of action and effect.
 - A person taking a CBD-rich product may have changes in INR, and warfarin dose may be difficult to stabilize

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

General Side Effects

- Nausea, vomiting
- Dizziness or fainting symptoms
- Seizure
- Increased weakness, fatigue and feelings of intoxication (Koppel, 2014)
- Increased risk of ischemic stroke (Singh, 2012)
 - Mixed information about strokes, appear to be \uparrow risk with \uparrow THC and \uparrow reports with synthetic cannabinoid (Spice)
- There may be increased risk of testicular cancer (Huang, 2015)
- Marijuana smokers over 40yrs have higher odds of a clinical diagnosis of glaucoma, rather than self-reported glaucoma in order to gain Rx. Possible explanation is that marijuana use actually may increase glaucomatous optic nerve damage (Baker et al 2015)

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Behavioral Side Effects

- Behavioral or mood changes
- Anxiety, panic, and attentional abnormalities
- Cognitive impairment
- Psychosis
- Suicidal thoughts or hallucinations
- Mood changes and suicidal thoughts are of concern in MS, who are at an increased risk for depression or suicide (1% of population)
- Psychosis, dysphoria, and anxiety are associated with higher concentrations of THC (Koppel, 2014)
- 5 Year follow-up of cannabis users had higher level of psychotic symptoms and lower level of functioning (Clausen, et al, 2014)
- Cannabis may induce paranoia and disorientation in novice users
- Sexual behavior: small amounts may increase desire and arousal in both genders. Large amounts cause ED in males (Agabio et al, 2016)

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Cardiovascular Side Effects

- Tachycardia and increased cardiac output
- THC = vasoconstrictor effect and cardiac ischemia due to \uparrow cardiac workload and postural hypotension (Karabag et al, 2015)
- Increased blood carboxyhemoglobin levels = inadequate myocardial blood supply (Karabag et al, 2015)
- Vasovagal Syncope, increased vagal tone, sinus bradycardia, hypotension, sinus arrest and asystole (Brancheau, et al, 2016)
- Trigger acute coronary syndromes (ACS), cardiac arrhythmias, sudden death, atrial fibrillation, asystole, and may \uparrow risk of strokes (Rezkaia, 2016) – however, many times marijuana was used with tobacco, so effects may be related to tobacco
- Case studies
 - 26yr male - ACS and acute renal failure (Karabag et al, 2015)
 - 33yr male - MI (Renard et al, 2012)
 - 40yr male - ACS related to multivessel coronary artery (Filali et al, 2013)
 - 18yr male - Prolonged atrial fibrillation with normal heart structure precipitated by new-onset seizures (Singh, et al 2014)

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Pulmonary Side Effects

- Lung function abnormalities are different from those of tobacco smoking
- Large airway inflammation, bronchitis and effects bronchial mucosa
- Increased large airways resistance
- Lung Hyperinflation
- Reports of bullous emphysema
- No convincing evidence that it causes COPD or emphysema
- Risk of lung cancer – debatable – evidence is mixed, some say ↑ 2-fold
- Methods of inhaling cannabis (joint, bong, pipe or vaporizer) are still unknown
- Cannabis has acute bronchodilator effects but there is no evidence that this is clinically useful
- Difficult to separate tobacco and marijuana as the causation



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Table 1. Adverse Effects of Short-Term Use and Long-Term or Heavy Use of Marijuana.

| | |
|--|---|
| <p>Effects of short-term use</p> <p>Impaired short-term memory, making it difficult to learn and to retain information</p> <p>Impaired motor coordination, interfering with driving skills and increasing the risk of injuries</p> <p>Altered judgment, increasing the risk of sexual behaviors that facilitate the transmission of sexually transmitted diseases</p> <p>In high doses, paranoia and psychosis</p> <p>Effects of long-term or heavy use</p> <p>Addiction (in about 9% of users overall, 17% of those who begin use in adolescence, and 25 to 50% of those who are daily users)*</p> <p>Altered brain development*</p> <p>Poor educational outcome, with increased likelihood of dropping out of school*</p> <p>Cognitive impairment, with lower IQ among those who were frequent users during adolescence*</p> <p>Diminished life satisfaction and achievement (determined on the basis of subjective and objective measures as compared with such ratings in the general population)*</p> <p>Symptoms of chronic bronchitis</p> <p>Increased risk of chronic psychosis disorders (including schizophrenia) in persons with a predisposition to such disorders</p> | <p>Adverse effects related to regular use of marijuana during adolescence</p> <p>Volkow et al, 2014</p> |
|--|---|

* The effect is strongly associated with initial marijuana use early in adolescence.

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Side Effects of Cannabidiol (CBD)

- Most studies report CBD is well tolerated
- **No** psychomotor or psychoactive effects
- **No** changes in HR, BP or temperature, NO EKG or EEG changes
- **No** GI effects
- Chronic use and high doses up to 1,500 mg/day of CBD are reportedly well tolerated in humans
- Immune system - effects may be generally positive.
- **May** worsen HIV infection, tumor genesis, metastases or allergic inflammation in the lungs

However: May alter drug pharmacokinetics and pharmacodynamics

- Inhibition of hepatic drug metabolism - Inactivate human P450 3A4
 - Opiates, benzodiazepines, macrolide antibiotics, CCB some statins, and more
- Decreased activities of p-glycoprotein and other drug transporters
 - Bergamaschi, 2011

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Ongoing CBD Research

- The NIH recognizes the need for additional research on the therapeutic effects of CBD and other cannabinoids, and supports ongoing efforts to reduce barriers to research in this area.
- NIH is currently supporting a number of studies on the therapeutic effects as well as the health risks of cannabinoids.
- These include studies of the therapeutic value of CBD for:
 - Treatment of substance use disorders (opioids, alcohol, cannabis, methamphetamine)
 - Attenuation of the cognitive deficits caused by THC
 - Neuropathic pain due to spinal cord injury
 - Mitigating the impact of cannabis use on risk for schizophrenia
 - Examination of the potential of CBD as an antiepileptic treatment

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Withdrawal from Cannabis (THC)

- Sleep disturbances and insomnia and trouble falling asleep
- Unpleasant dreams
- Loss of appetite
- Increased anxiety
- Feeling bored
- Feeling sad or depressed
- Migraine
- Irritability and restlessness
- Craving for cannabis



Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

The New York Times

- March 27th, 2017
- Los Angeles drug rehabilitation clinic named High Sobriety
- Uses marijuana as a treatment for heroin addiction
- Rather than being a gateway into drugs, could it be a gateway out

○ <https://www.nytimes.com>

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Implications in Pregnancy

- THC crosses the placenta rapidly, but its major metabolite does not
- Marijuana can remain in the body for up to 30 days = prolonging fetal exposure
- smoking marijuana = 5 x the amount of carbon monoxide as cigarette smoking (perhaps altering fetal oxygenation)
- Marijuana alters brain neurotransmitters and brain biochemistry
- There may be subtle abnormalities in infant neurobehavior related to prenatal marijuana exposure
- No significant effects on fetal growth, congenital anomalies, or withdrawal
- Long-term studies = affects on behavior, cognition, and achievement but not on language or growth (Behnke et al, 2013)
- Mixed reports on low birth weights, seems to correlate with tobacco use
- May increase risk for NICU admission (Warshak et al, 2015)

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Social Implications of Long Term use and Increased Accessibility of the drug

- Regular use of cannabis, or using cannabis from earlier ages, increases risk of:
 - Lower levels of educational attainment
 - Welfare dependence and unemployment
 - Using other, more dangerous illicit drugs
 - Psychotic symptomatology
- Of note, a substantial proportion of regular adult users do not experience harmful consequences as a result of cannabis use (Fergusson et al, 2015)
- Repeated exposure to cannabis during adolescence may have detrimental effects on brain
 - Resting functional connectivity
 - Intelligence
 - Cognitive function
- A Longitudinal Study (Camchong, 2016)

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Social Implications of Long Term use and Increased Accessibility of the drug

- Medical marijuana use could impact driver safety
 - reflecting marijuana's disruptive effects on motor coordination and time perception (Volkow, 2015)
- Marijuana use by adolescents is more prevalent in states that passed a medical marijuana law (Hasin et al, 2015)
- The epidemiological literature in the past 20 years shows that cannabis use increases the risk of accidents and can produce dependence
- There are consistent associations between regular cannabis use and poor psychosocial outcomes and mental health in adulthood (Hill, 2015)

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Legal Marijuana Ends at Airport Security, Even if It's Rarely Stopped

By JULIE WEED APRIL 10, 2017



The singer Melissa Etheridge in Nashville before a performance last month. She uses medical marijuana for pain relief from breast cancer treatment and has kept it in checked luggage with a doctor's recommendation attached. *© iStockphoto.com for The New York Times*

People in 29 states can legally use medical marijuana for a variety of problems, including the relief of pain, anxiety or stress. But what if they want to travel with it?

Traveling with Marijuana can be a challenge – even if it was legally prescribed

<http://www.nytimes.com/>

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Everyone is Watching Colorado

Colorado has had 14 years of medical-marijuana legalization and now recreational legalization

Early identification of trends

- Created surveillance systems to monitor the numbers of ED visits and hospitalizations related to marijuana use
- Data on calls to poison-control centers
- Proposed regulations would ensure that products are easily separable into single servings containing no more than 10 mg of THC
- Public health officials also launched a public awareness campaign about safe storage of marijuana products and child-resistant packaging in January 2015. (Ghosh, et al 2015)
- October 2016 - 60 Minutes on CBS – Highlights Problems After Marijuana Legalization in Colorado
 - Interview a Dr. LaPook who supports a ban of marijuana in his county
 - Positive THC in newborns and teens

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

Patient Education

- Considerations: Driving or operating machinery
- Being aware of the metabolism and how marijuana completes from the same pathways as many medications. This may affect medications requiring balance: eg: warfarin, digoxin and levothyroxine
- Educate on signs of addiction
 - Needing the drug
 - Lack of control over the amount being used
 - Spending increased amount of time using or attaining the drug
 - Negatively affects relationships or work
 - Neglecting appearance or responsibilities
- Be aware of potential side effects – especially cardiac
- Safe storage: Keep cannabis away from children in a child proof locked area
- Mixing with tobacco or smoking: consider second hand smoke

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

http://medicalmarijuana.procon.org/view.resource.php?resourceID=000881

| State | Year Passed | How Passed | Possession Limit |
|--|-------------|--|--|
| Marijuana State Laws - Summary Chart from ProCon.org | | | |
| Alaska | 1998 | Ballot Measure 6 (58%) | 1 oz usable; 6 plants (3 mature, 3 immature) |
| Arizona | 2010 | Proposition 203 (50.13%) | 2.5 oz usable; 12 plants |
| Arkansas | 2016 | Ballot Measure Issue 4 (53.2%) | 3 oz usable per 14-day period |
| California | 1996 | Proposition 215 (56%) | 8 oz usable; 6 mature or 12 immature plants |
| Colorado | 2000 | Ballot Amendment 20 (54%) | 2 oz usable; 6 plants (3 mature, 3 immature) |
| Connecticut | 2012 | House Bill 5389 (66-31 H, 21-13 S) | 2.5 oz usable |
| Delaware | 2011 | Senate Bill 17 (27-14 H, 17-4 S) | 6 oz usable |
| Florida | 2016 | Ballot Amendment 2 (71.3%) | Amount to be determined |
| Hawaii | 2000 | Senate Bill 682 (20-18 H, 13-12 S) | 4 oz usable; 7 plants |
| Illinois | 2013 | House Bill 1 (81-57 H, 38-21 S) | 2.5 ounces of usable cannabis during a period of 14 days |
| Maine | 1999 | Ballot Question 2 (81%) | 2.5 oz usable; 6 plants |
| Maryland | 2014 | House Bill 881 (125-11 H, 44-2 S) | 30-day supply amount to be determined |
| Massachusetts | 2012 | Ballot Question 3 (83%) | 60-day supply for personal medical use (10 oz) |
| Michigan | 2008 | Proposal 1 (63%) | 2.5 oz usable; 12 plants |
| Minnesota | 2014 | Senate Bill 2470 (46-16 S, 89-40 H) | 30-day supply of non-smokable marijuana |
| Montana | 2004 | Initiative 148 (62%) | 1 oz usable; 4 plants (mature); 12 seedlings |
| Nevada | 2000 | Ballot Question 6 (65%) | 2.5 oz usable; 12 plants |
| New Hampshire | 2013 | House Bill 573 (284-66 H, 18-4 S) | Two ounces of usable cannabis during a 10-day period |
| New Jersey | 2010 | Senate Bill 119 (48-14 H, 25-13 S) | 2 oz usable |
| New Mexico | 2007 | Senate Bill 523 (26-31 H, 22-3 S) | 6 oz usable; 16 plants (4 mature, 12 immature) |
| New York | 2016 | Assembly Bill 6527 (117-13 A, 49-10 S) | 30-day supply non-smokable marijuana |
| North Dakota | 2016 | Ballot Measure 5 (63.7%) | 3 oz per 14-day period |
| Ohio | 2016 | House Bill 523 (71-26 H, 18-15 S) | Maximum of a 90-day supply amount to be determined |
| Oregon | 1998 | Ballot Measure 47 (58%) | 24 oz usable; 24 plants (8 mature, 18 immature) |
| Pennsylvania | 2016 | Senate Bill 3 (149-46 H, 42-7 S) | 30-day supply |
| Rhode Island | 2006 | Senate Bill 0710 (52-10 H, 33-1 S) | 2.5 oz usable; 12 plants |
| Vermont | 2004 | Senate Bill 76 (22-7) (88-64 S, 92-99) | 2 oz usable; 9 plants (2 mature, 7 immature) |
| Washington | 1998 | Initiative 692 (59%) | 8 oz usable; 6 plants |
| Washington, DC | 2010 | Amendment Act 818-622 (13-0 vote) | 2 oz dried limits on other forms to be determined |
| Marijuana State Laws - Summary Chart from ProCon.org | | | |

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

In Conclusion

- Marijuana is a continued battle in legislation, political arenas and the court of public opinion
- Effects may be felt throughout Healthcare
- Continue to put the patient first
- Focus on evidence based practice
- You don't have to take a stance, you simply have to care for your patient
- Questions?



- Contact: Andreaefre@yahoo.com
- Please contact me for the extensive reference list for further reading

Dr. Andrea Efre, Healthcare Education Consultants, HEC.LLC. Medical Marijuana ©

