Medical Cannabis: Lessons Learned by a Family Doctor

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Disclosure: These experiences and views are my own!
Policy

Medical Cannabis legal in 25 states, Schedule 1 by federal law

AAFP Policy Statement

- Recognizes that there is support for the medical use of marijuana
- Does not endorse state laws approving medical use
- Supports federal reclassification and funding of high quality research

Epilepsy Foundation

- “Not unreasonable” to consider compassionate use in drug resistant epilepsy
- Actively advocating for federal rescheduling of cannabis
The Issues

Prohibition has limited research access and funding

Diverse strains with different ratios of > 60 cannabinoids

Societal concerns regarding increased access

   MVAs, opioid OD decreases

Concerns about long term effects

Public pressure, anecdotal cases

The Science
Cannabinoids

Phytocannabinoids bind receptors CB1 and CB2

Found in nervous system, immune system, gonads, organs

Endocannabinoids also bind receptors to produce multiple effects

Anti-inflammatory, anti-oxidants, anti-epileptic, autophagy of malignant cells


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<tr>
<th>CB&lt;sub&gt;1&lt;/sub&gt; receptor activation</th>
<th>CB&lt;sub&gt;1&lt;/sub&gt; and possibly also CB&lt;sub&gt;2&lt;/sub&gt; receptor activation</th>
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<tr>
<td><strong>Decreased</strong></td>
<td>Signs of nausea in rats conditioned to display rejection reactions to a saccharin solution&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>Intestinal hypermotility and inflammation in mouse or rat models of inflammatory bowel disorders&lt;sup&gt;1,3,9&lt;/sup&gt;</td>
<td>Signs of inflammation and possibly also of syndrome progression in the EAE mouse model of multiple sclerosis&lt;sup&gt;a,b&lt;/sup&gt;</td>
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<td>Vomiting induced by cisplatin or other emetic agents in ferrets or shrews&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Clinical signs in mouse models of multiple sclerosis in which demyelination is induced either by injection of Theiler’s murine encephalomyelitis virus or by inoculation with substances that give rise to experimental allergic encephalomyelitis (EAE)&lt;sup&gt;a,b,k,l&lt;/sup&gt;</td>
<td>Glioma, melanoma, skin and colorectal cancer cell growth and angiogenesis&lt;sup&gt;1,3,9&lt;/sup&gt;</td>
<td>Signs of inflammation and leukocyte trafficking in a mouse model of panuveitis&lt;sup&gt;c&lt;/sup&gt;</td>
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<td>Intra-ocular pressure in several mammalian species&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Convulsions in rat and mouse models of epilepsy&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Glioma, melanoma, skin and colorectal cancer cell growth and angiogenesis&lt;sup&gt;1,3,9&lt;/sup&gt;</td>
<td>Mortality or signs of disease progression in a transgenic mouse model of amyotrophic lateral sclerosis&lt;sup&gt;3&lt;/sup&gt;</td>
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<td><strong>Increased</strong></td>
<td>Nociception in a mouse model of visceral pain&lt;sup&gt;9&lt;/sup&gt;</td>
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<td>Atherosclerosis progression in mice&lt;sup&gt;1&lt;/sup&gt;</td>
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<td>Feeding in rats and mice&lt;sup&gt;a,h&lt;/sup&gt;</td>
<td>Survival in rat and mice models of haemorrhagic and cardiogenic shock&lt;sup&gt;8&lt;/sup&gt;</td>
<td>Glioma, melanoma, skin and colorectal cancer cell growth and angiogenesis&lt;sup&gt;1,3,9&lt;/sup&gt;</td>
<td>Increased Apoptosis in murine or human pancreatic tumour, leukaemia and lymphoma cells&lt;sup&gt;9&lt;/sup&gt;</td>
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<sup>a</sup>Pertwee and Thomas (2007).
<sup>b</sup>Parker et al. (2005).
<sup>c</sup>Van Sickle et al. (2003), Darmani and Johnson (2004), Darmani and Crim (2005).
<sup>d</sup>Parker et al. (2003), Limebeer et al. (2006).
<sup>e</sup>Tomida et al. (2004, 2006), Szczesniak et al. (2006).
<sup>f</sup>Wallace et al. (2001, 2003).
<sup>g</sup>Haller et al. (2006).
<sup>h</sup>Järbe and DiPatrizio (2005), Wiley et al. (2005a).
<sup>i</sup>Pertwee (2005b).
<sup>j</sup>Wagner et al. (1997), Mendizábal and Adler-Graschinsky (2007).
<sup>k</sup>Pertwee (2007a).
<sup>l</sup>Maresz et al. (2007).
<sup>m</sup>Pryce and Baker (2007).
<sup>n</sup>Irzi and Coutts (2005).
<sup>o</sup>Kimball et al. (2006), Sanson et al. (2006).
<sup>p</sup>Fox and Bevan (2005), Whiteside et al. (2007).
<sup>q</sup>Guzmán (2003, 2005), McAllister et al. (2005), Blázquez et al. (2006), Aguado et al. (2007), Bifulco et al. (2007).
<sup>r</sup>Xu et al. (2007).
<sup>s</sup>Kim et al. (2006), Shoemaker et al. (2007).
<sup>t</sup>Steffens et al. (2005), Steffens and Mach (2006).
<sup>u</sup>McKallip et al. (2002), Caravedo et al. (2006), Herrera et al. (2006).
Current Research
A Systematic Review and Meta-analysis

Cannabinoids for Medical Use published in JAMA 2015

Analyzed 79 RCTs of cannabinoids for:

- nausea and vomiting due to chemotherapy, appetite stimulation in HIV/AIDS, chronic pain,
- spasticity due to multiple sclerosis or paraplegia, depression, anxiety disorder, sleep
- disorder, psychosis, glaucoma, or Tourette syndrome

6462 patients, studied patient-relevant/disease-specific outcomes

Results

- Moderate-quality evidence: Chronic pain and spasticity
- Low-quality evidence: nausea and vomiting due to chemotherapy, weight gain in HIV infection, sleep disorders, and Tourette syndrome


Increased risk of short term side effects
Use of marijuana for chronic pain, neuropathic pain, and spasticity due to multiple sclerosis is supported by high-quality evidence.

Six trials that included 325 patients examined chronic pain, 6 trials that included 396 patients investigated neuropathic pain, and 12 trials that included 1600 patients focused on multiple sclerosis.

Several of these trials had positive results, suggesting that marijuana or cannabinoids may be efficacious for these indications.
Sativex

27 mg/mL de delta-9-tétrahydrocannabinoïde (de Tetrabiolex® - extrait de Cannabis sativa L.) et 25 mg/mL de cannabidiol (de Nabiolex® - extrait de Cannabis sativa L.)

Vaporisateur buccal

Traitement d'appoint pour le soulagement de la douleur neuropathique en présence de sclérose en plaques chez les adultes

Traitement analgésique d'appoint chez les adultes atteints de cancer

Contre une douleur de fond persistante contre une douleur de fond persistante
CBD in Dravet Syndrome

Phase 3 multicenter, double-blind RCT, 120 2-18 year olds

Orphan drug and Fast Track Designation by FDA

On average, age 10, taking 4 AEDs, 13 convulsive seizures per month

Results

39% reduction in monthly seizures (placebo 13%, p <0.001)

Well tolerated somnolence, diarrhea, decreased appetite, fatigue, pyrexia, vomiting, lethargy, upper respiratory tract infection and convulsion

84% rated side effects mild or moderate

Long-Term Safety

Lack of correlation with lung cancer, anxiety, depression

Increased risk of psychosis, respiratory irritation

Impaired Cognitive Function

Basic motor coordination

Complex executive function tasks

ability to plan, organize, solve problems, make decisions, remember, and control emotions and behavior
599 current studies on Clinicaltrials.gov

What can we do about conditions not well studied?

Clinical Trials
Delaware’s Medical Marijuana Program

- Law passed July 1, 2012
- First State Compassion Center opened July 2015
- Application fee $125, average monthly meds for chronic pain ~$200
- Currently, over 2000 cardholders, certified by > 300 physicians
First State Compassion Center
Adult Qualifying Conditions

Cancer
Positive status for Human Immunodeficiency Virus (HIV Positive)
Acquired Immune Deficiency Syndrome (AIDS)
Decompensated cirrhosis
Amyotrophic Lateral Sclerosis (ALS / Lou Gehrig's Disease)
Agitation of Alzheimer's disease
Post-traumatic Stress Disorder (PTSD) *Note: MUST be a licensed psychiatrist to certify this condition
Intractable epilepsy
Autism with self-injurious or aggressive behavior
Adult Qualifying Conditions

A chronic or debilitating disease or medical condition or its treatment that produces one or more of the following:

- Cachexia or wasting syndrome
- Severe, debilitating pain that has not responded to previously prescribed medication or surgical measure for more than three months, or for which other treatment options produced serious side effects.
- Intractable nausea
- Seizures
- Severe and persistent muscle spasms, including but not limited to those characteristic of Multiple Sclerosis
Pediatric Qualifying Conditions

Intractable epilepsy
A chronic or debilitating disease or medical condition where they have failed treatment involving one or more of the following symptoms
- Cachexia or wasting syndrome
- Intractable nausea
- Severe, painful and persistent muscle spasms

Must be a peds GI, onc, neuro or palliative care
Physician Certification

I have made or confirmed a diagnosis of a debilitating medical condition, as defined in Title 16, Chapter 49A of the Delaware Code (4902A(3)), for the qualifying patient.

I have established a bona fide physician-patient relationship with ____________________________, (patient) beginning ______________________ (date of first patient visit to your office).

This qualifying patient is under my care, either for primary care or the debilitating medical condition listed on this form.

I have conducted an in-person physical examination of the qualifying patient within the last 90 calendar days. I completed an assessment of the qualifying patient’s current medical condition, including presenting symptoms related to the debilitating medical condition I diagnosed or confirmed.

I have completed an assessment of the qualifying patient’s medical history, including medical records from other treating physicians for the qualifying condition. I have established a medical record of the qualifying patient with regards to the medical condition, continued treatment under my care, and will document follow-up to determine efficacy of the medical marijuana treatment.

I have explained the potential risks and benefits of the medical use of marijuana to the qualifying patient.

Physician’s Attestation

I ____________________________, (physician), hereby certify that I am a physician duly licensed to practice medicine. It is my professional opinion that the qualifying patient is likely to receive therapeutic or palliative benefit from the medical use of marijuana to treat or alleviate the patient's qualifying debilitating medical condition or symptoms associated with the debilitating medical condition. Further, it is my professional opinion that the potential benefits of the medical use of marijuana would likely outweigh the health risks for this patient.

I attest that the information provided in this written certification is true and correct.
# Strain Benefits

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<tr>
<th>Benefits of Indica</th>
<th>Benefits of Sativa</th>
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<tr>
<td>1. Relieves body pain</td>
<td>1. Feelings of well-being and at-ease</td>
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<tr>
<td>2. Relaxes muscles</td>
<td>2. Up-lifting and cerebral thoughts</td>
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<tr>
<td>3. Relieves spasms, reduces seizures</td>
<td>3. Stimulates and energizes</td>
</tr>
<tr>
<td>4. Relieves headaches and migraines</td>
<td>4. Increases focus and creativity</td>
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<tr>
<td>5. Relieves anxiety or stress</td>
<td>5. Fights depression</td>
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Menu examples

Hollywood Haze

With a spicy scent accented by hints of citrus and earthy sweetness, this hybrid provides a high-energy, happy and creative buzz. This strain is best suited to help with stress, depression, pain, insomnia and nausea.

818 Headband

818 Headband aka Sour OG is a hybrid with earthy and sweet flavors to compliment its uplifted, euphoric and relaxed effects. Best suited for those suffering from stress, pain, depression, lack of appetite and nausea.

401 Gasband

Gas is a type of sativa-dominant strain that possesses a strong fruity smell with the happy, dreamy and talkative effects it provides. Those suffering from cancer related symptoms such as lack of appetite and nausea might find this strain beneficial.

Pineapple Fields

A hybrid strain that encompasses intense tropical flavors those of pineapple and diesel. Best for stress and pain relief, anti depression, nausea and insomnia.
PA’s Medical Marijuana Program

Law passed April 2016

Regulations for growing and processing currently underway

More than a year before full implementation

Physicians required to do 4 hour DOH course

Can have 25 growers, 50 dispensaries
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<tr>
<td>Cancer</td>
<td>Neuropathies</td>
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<tr>
<td>Positive Status for HIV or AIDS</td>
<td>Huntington’s Disease</td>
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<tr>
<td>Amyotrophic Lateral Sclerosis (ALS)</td>
<td>Crohn’s Disease</td>
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<tr>
<td>Parkinson’s Disease</td>
<td>Post-Traumatic Stress Disorder</td>
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<tr>
<td>Multiple Sclerosis</td>
<td>Intractable Seizures</td>
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<tr>
<td>Damage to the nervous tissue of the spinal cord with objective neurological indication of intra-ictal spasticity</td>
<td>Glaucoma</td>
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<tr>
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<td>Sickle Cell Anemia</td>
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PA Qualifying Conditions

Also terminal illness: “a medical prognosis of life expectancy of approximately one year or less if the illness runs its normal course”

Safe Harbor Letter for minors who require urgent or immediate treatment before the program is active
Approved Forms of Cannabis

Pill

Oil

Topical forms, including gel, creams or ointments;

A form medically appropriate for administration by vaporization or nebulization, excluding dry leaf or plant form

Tincture

Liquid

Unless otherwise provided in regulations adopted by the department under section 1202, medical marijuana cannot be dispensed to a patient in any other form.
Case Examples
Jane

34yo social worker chronically disabled with “double crush” of severe cervical spinal stenosis, carpal tunnel syndrome complicated by MCTD

Unable to type, write, knit

Failed cervical fusion, bilateral carpal tunnel releases

Side effects and incomplete relief of neuropathic pain from NSAIDs, gabapentin, lyrica, amitriptyline, nortriptylne, tramadol, oxycodone, hydrocodone, fentanyl patch

Certified for cannabis, titration down and off opioids

Now working at the Compassion Center, counseling patients

Offers to help my other neuropathic pain patients
Jane

At time of certification, no FH seizures

1 year after certification, sister started workup for "spacing out"

Dx with complex partial seizures

3 episodes after smoking cannabis, witnessed jerking, unawareness

Current eval for seizures, hold cannabis, remember like all AEDs seizures may worsen for some
Cheri

72yo WF with severe peripheral neuropathy, pain uncontrolled with maximally dosed gabapentin, nortriptyline; oxycodone dose increasing

Did not tolerate lyrica, nucynta, morphine, opana, fentanyl, hydrocodone, codeine, NSAIDs

Failed an experimental peripheral neuropathy plastic surgery release
Cheri

Unfamiliar with products, Cheri brings packages to my office

Counseling session with staff at the Compassion Center arranged

Patient overwhelmed, and decides not to use

*May need to arrange extra education for some patients*
Nick

29yo s/p TBI with skull fractures, chronic migraines, vomiting, bipolar d/o

Asks for recertification of his current cannabis card

   Approved by his neuro and psych to do so

Intolerant/lack of effect with topamax, amitriptyline, propranolol, rizatriptan, sumatriptan, NSAIDs, ondansetron, promethazine, compazine

Able to eat, care for self with mother’s and state home health aide’s assistance while using cannabis

   Per mother “it keeps away Atilla the Hun”
Nick

Pt self-discontinues psych meds, and continues cannabis (unknown to caregivers)--gets arrested due to delusions and forfeits cannabis card

Back to vomiting, migraines

Recommended to have marinol, which helps somewhat, but suboptimal results

*If uncomfortable with psych issues, consider psych certification*
Maria

36yo F disabled therapist with lupus, fibromyalgia

Severe pain flares despite plaquenil, benlysta, prednisone, flexeril, tylenol with codeine, PT

Cause her to be unable to wear clothes, leave bed

Unwilling to escalate narcotics, due to experience counseling for addiction

Since starting cannabis, has returned to part-time work

*Alternates T#3 with cannabis due to cost, although she is more functional on cannabis*
Mark

69yo M recently diagnosed with ALS, seen at multidisciplinary clinic

On Riluzole, starting advanced planning

I discussed Compassion Center as another option in the future

Later, received letter of thanks from patient for including this topic in our discussion of palliative care
Walter

86y M with metastatic pancreatic cancer, not a Whipple candidate

Seen in Philly, referred to me by oncologist for cannabis

Enjoying time with grandchildren, good appetite, amused that adult children and grandchildren had to be educated about his therapy
Common Sense Criteria

Condition with clinical trials that show efficacy for cannabis

Failed first- and second-line noncannabinoid therapies (?marinol)

No known substance abuse, psychotic disorder, unstable mood disorder
Common Sense Criteria

Good evidence for chronic pain, neuropathic, MS spasticity

Acceptance for HIV and cancer-caused cachexia, chemo-induced N/V

However, science is weaker

Consider variability of product

Not a panacea

Be aware, discuss openly with patients, conventional options don’t work for everyone
