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February 12, 2014

To the Legislature:

I am a Colorado physician who has helped to treat scores of children who have severe seizure disorders with cannabidiol extract (CBD oil).

These children suffer daily from damaging epileptic seizures that are not stopped by any approved seizure medication. They also suffer from the known side effects and organ damage of the approved medications, many of which are psychoactive and can cause either severe lethargy or aggressive behavior and rage.

A series of studies and clinical observations over centuries have shown the potential of cannabis in treating epilepsy.

In 1988, the Honorable Francis Young, a federal judge, found that there is no lack of accepted safety for use of cannabis under medical supervision. Quoting Judge Young: "The evidence in this record clearly shows that marijuana has been accepted as capable of relieving the distress of great numbers of very ill people, and doing so with safety under medical supervision." (Reference: www.druglibrary.org/schaffer/library/studies/YOUNG/young.html)

Cannabidiol has been reported by the National Institutes of Health to be a neuroprotective antioxidant, and the United States federal government patented CBD for use as a neuroprotectant and antioxidant in 2003. This means that CBD can potentially protect and heal the brains of children and adults who have epilepsy.

When children respond well to cannabidiol, their seizures are significantly reduced, and they are able to reduce or stop other medications. This relieves much of the ongoing damage to their nervous system and other organs. They can start to develop and learn in ways that haven't been possible for years. The children also appear to be helped by the neuroprotective and antioxidant effects of cannabidiol.

It is possible that cannabidiol has long term side effects that we don't know about. Given that humans around the globe have used cannabis for many centuries, any long term adverse effects must be minor, or they already would have been reported in some way.

In contrast, many of the medications currently given to children have severe, known damaging effects that the children suffer from every day.

Randomized controlled human trials are needed to clarify the use of cannabis to treat seizures. Doctors and researchers have called for these studies for decades. However, advanced studies are still prohibited by restrictive laws and by stigma.

Given that cannabis is known through medical experience and scientific study to be far safer and often more effective than medications currently in use, the need for more human studies cannot be used as a valid reason to prohibit access to cannabidiol extract (CBD oil).

Respectfully,

Margaret Gedde, MD, PhD

Good Morning!

Thank you for letting me take the time to share our journey about our son. My name is Sherri Kroening and I have an adorable son Jake who was born on April 26, 1996 who will be 18 this year.

Since Jake was nine months old he has suffered from Epilepsy called Lennox Gastout Syndrome. This type of Epilepsy is a severe form of Epilepsy ranging from Tonic CLonic, Atonic, Myoclonic, and Absence seizures. It causes cognitive impairment, developmental delay that is progressive and huge behavioral problems. LGS considerably takes time and effort by both parents 24 hours a day and 7 days a week. Doctors could never tell us why Jake has developed Epilepsy. Our doctor has told us that Jake is at increase risk of sudden death in Epilepsy due to his uncontrollable seizures and his age.

For 18 years we have watched our son have over 20-30 seizures a day along with weekly Tonic Clonic seizures. Try to imagine what it is like to watch someone you love become so aggressive before a seizure is about to happen that they self abuse themselves from pulling their hair, head banging their head on the floor, bite themselves and bite you, start to throw things at you and come at you full force wanting to hit you until the seizure activity stops in their brain. Try to then imagine the person you love convulsing their whole body in front of you why you time the seizure, and keep them safe, and then pray to God that the seizure ends soon. When the seizure does end this person you love is lying helpless and can't even move their body. For our Jake he then urinates after a Tonic Clonic seizure and we have to try and lift this 18 year old man who can't move his body at all and clean him up and drag him into a safe bed because he can't walk after a seizure. We have never heard our Childs voice, never saw him interact with toys, and is still not trained to use the bathroom due to all the constant seizures in his daily life.

We have tried over 15 FDA approved seizure medications with no success in seizure control for our son. Jake has horrible side effects from the medicine he is currently on and has taken in the past. Side effects like dizziness, headaches, stomachaches, nauseated, anxiety, depression, weakness, **increased seizures from some of the medication along with huge constipation issues and behavioral problems with many** of them. Imagine giving a 18 year old a weekly Enema due to severe constipation from seizure medications. Jake has had the Vagus Nerve Simulator implanted with no success; due to Jake's epilepsy in his brain surgery is not an option for him. So we tried the ketogenic diet a very high fat diet that brings your body into ketosis that helps some individuals with Epilepsy. We tried this diet when Jake was 5, when he was 10, and just recently again when he was 16. We keep trying the diet because there is nothing left to try and the medicines have never helped and only caused him more problems.

As Jake is turning 18 it's a whole new chapter for us. Only three more years left of school and then where do I turn for help??? We already started looking at adult day programs and I'm limited on where I can send him because of his severe medical needs and aggression from seizures. We are physically and emotionally exhausted of the constant care that is needed for our sons Epilepsy. If we his parents can't handle this much longer because of what it is doing to our own health, what does that mean for the state of WI??? It means the state and fed government will be supporting Jake for 24 hour care which is costly due to my research. It's going to cost over $110.000.00 a year just for care and not to mention all of his other needs for living.

Epilepsy has consumed our daily life with heartbreak, helplessness, stress, frustration, tears & anger. For 18 years we have been up every night with seizures and our son is wide awake at 3:00 am every day due to seizure activity. I can't remember the last time we were able to sleep five hours without any uninterrupted sleep. I challenge anyone here today to come live our life for 24 hours and tell me at the end of the day after watching seizures after seizures, aggression from the seizures, cleaning up urine accidents daily, attending to his every want and need constantly, and being worried that it might be his last day on earth due to the risk of sudden death in epilepsy that you wouldn't want a better quality of life for your child.

The results in CO are so inspiring to us on how CBD oil has helped over 300 beautiful children suffering from Epilepsy. I ask every one of you to please give us a chance to help our son with CBD oil to calm his brain and help with his seizures. Give us a chance to hopefully have our son show some cognitive improvement without 20 to 30 seizures a day so we are able to take care of him in his future and that he can be a part of this community. I sincerely thank you for your time today.

Sincerely,

Sherri Kroening
N95 W25867 Riverview Drive
Colgate, WI 53017

Sappenfield, Anne

From: Thorson, Randy
Sent: Wednesday, February 19, 2014 11:54 AM
To: Allen-Hubka, Theresa; Bates, Katherine; Polzin, Cindy M - GOV; Clark, Lauren; Deej Lundgren; Divine, Kathy; Emerson, James; Hanus, Andrew; Karius, Bob; McKinny, Chris; Morouney, Lonna; Ohly, Mitchel; Posca, Dan; Rep.Billings; Rep.Endsley; Rep.Johnson; Rep.Kahl; Rep.Kerkman; Rep.Krug; Rep.Loudenbeck; Rep.Neylon; Rep.Schraa; Rep.Spiros; Rep.Taylor; Rongstad, Tami; Sabrina Gentile; Sappenfield, Anne; Schultz, Rusty; Thorson, Randy; Tierney, Michael; Trost, Craig; Ullsvik, Christian; VerVelde, Brandon; Walsh, Patrick; Zikmund, Alison
Subject: FW: My niece Lydia was born with kleefstra's syndrome

Final piece of submitted testimony for AB 726 (CBD).

Thank you for your attention.

Have a great day/week/month/Spring (upcoming)

Randy

-----Original Message-----
From: Brian Blume [mailto:brianblume@me.com]
Sent: Wednesday, February 12, 2014 1:55 PM
To: Sally Schaeffer; Rep.Krug; Thorson, Randy
Subject: My niece Lydia was born with kleefstra's syndrome

Testimony for Brian Blume:

My niece Lydia was born with kleefstra's syndrome and has endured so much in her short life. She has many battles ahead of her as well.

Lydia has a big health problem right now...seizures. Fortunately, there is a medicine called CBD that will likely help her. Unfortunately, my niece Lydia doesn't have access to this medicine because she is a resident of Wisconsin.

Her seizures are severe enough that brain surgery has been discussed as a "possible" way to end her seizures. I ask who in the room would opt for brain surgery for their child BEFORE exploring EVERY single option available to them?

Currently, CBD is an option that makes sense but it is not legal in Wisconsin. According to the current law in Wisconsin...Lydia should have brain surgery, and have a portion of her brain removed, instead of first having access to a proven (and more importantly) non invasive medicine (CBD) that she needs.

Making progress is hard for my niece. Lydia, along with my sister Sally and my brother in law Tom, fight for every little milestone. Milestones like eating by themselves and walking are givens for most parents...for Lydia these are major victories. The seizures set back Lydia's development and those hard fought milestones start to disappear. That is why time is of the essence in moving this bill forward into law.

I ask that CBD be made available for prescription for Lydia and all others with seizure disorders. I also ask that you not get bogged down in the minutia and move this bill through in fastest way possible because your urgency with bill 726 can save Lydia's life as well as many others.

This is common sense legislation and an opportunity for legislators to provide real and needed help to Wisconsin families dealing with seizures.

Thank you.

Brian Blume
262.378.0142

Sent on the run....

WISCONSIN STATE LEGISLATURE

47TH ASSEMBLY DISTRICT

ROBB KAHL

STATE REPRESENTATIVE

Today I'm here to speak in favor of AB 726, which would allow the use of Cannabidiol in Wisconsin.

Cannabidiol, also known as CBD, is an oil extract derived from specific marijuana plants that contain high levels of CBD and low levels of THC. In fact, the levels of THC in CBD oil extract are so low (less than 1%) that the oil extract has zero psychoactive, hallucinogenic, or addictive properties.

The most important trait of CBD oil extract is its ability to quiet the electrical and chemical activities in the brain that cause seizures, which can be fatal, especially in children. And the health and safety of children is ultimately what this bill is about.

CBD was first brought to my attention by a parent who is doing everything in her power to help her child live a normal life. That parent is Amylynne Volker. Her son Nic has unfortunately spent a large part of his young life in a hospital facing serious medical challenges. Fortunately for Nic, he has overcome many medical challenges in his life but he still faces serious health concerns, seizures being one of them. Amylynne brought her story to me and shared her dilemma: she is running out of options to manage Nic's seizures and CBD could help Nic manage them, but in order to use it Amylynne would have to break the law.

The dilemma Amylynne faces is the same many parents across Wisconsin face. Current treatments for seizures can lose effectiveness over time and have serious side effects. Many parents are going from one treatment to another trying to find a way to manage their child's seizures. Unfortunately, many are running out of options and being forced to contemplate invasive, high risk procedures.

CBD has been shown to dramatically reduce the number and frequency of seizures, and provides parents with a safe option when it comes to managing their child's seizures.

Under current Wisconsin law, parents are prohibited from working with their family physicians to try this treatment option. It is frustrating to many parents, because they know there is this drug out there that can help improve the lives of the children, but they can't get it. Many families are even considering moving out of Wisconsin to a state that allows the use of CBD for the sake of their children's health.

It is just plain wrong to be putting parents in the situation where they have to choose between uprooting their family or watching their children suffer from debilitating seizures. We need to give parents and their family physician the tools they need to manage their children's seizures. We need to approve AB 726 and allow CBD to be used in Wisconsin.

Wisconsin is not alone in looking to legalize CBD. In Georgia, there is a Republican legislator who is currently working on a bill similar to AB 726. Part of Georgia's bill contains a provision that would allow

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CBD to be transported into the state if it is sent to a DEA approved research facility. This would give parents the ability to legally obtain CBD without having to produce it in the state. It was because of that provision in Georgia's bill that I am introducing an amendment to AB 726 that would give the controlled substances board the ability to obtain CBD for parents of children suffering from seizures.

Georiga isn't the only state working on this either. A Republican lawmaker in Florida has introduced a bill to allow CBD and bills are also being drafted in Utah, Kentucky, and Alabama. All of these states see the great benefit CBD would bring to children and Wisconsin should be among them.

This room today is filled with parents who simply want what is best for their children. In this room are parents who have successfully used CBD to manage their children's seizures. In this room are parents who have unfortunately lost children to seizures and want to make sure no other parents have to experience that terrible loss. And in this room are Wisconsin parents who just want to be given the opportunity to help their children the same way parents are able to help their children in other states.

This hearing is the first step in a long journey to give parents and physicians the tools to improve the lives of children. While we have bipartisan support for the bill in the Assembly, there are still several hurdles we need to overcome. However, I hope all recognize that this bill isn't a Democratic or Republican issue and it isn't about politics. This bill is about hope. My hope is that this hearing will help raise awareness of this issue and that folks across the state will contact their legislators and urge them to support this bill.

We have a long road ahead of us, but that journey starts here in this committee. Admittedly this is a baby step. But put yourself in the position of these parents we will hear from today and you will understand that if it were your baby that would benefit from CBD it would be a very important baby step to you. I urge my fellow committee members to support AB 726 and appreciate Chairman Krug for his efforts in working with me as the co-sponsor and for holding this hearing today.

February 12, 2014

My name is Bonni Goldstein, M.D. and I am the Medical Director of Canna-Centers, a medical cannabis specialty practice in California. I received my medical degree from UMDNJ-Robert Wood Johnson Medical School in New Jersey and I completed internship and residency at Childrens Hospital Los Angeles. Additionally I served as Chief Resident at Childrens Hospital Los Angeles. I practiced in the specialty of Pediatric Critical Care Transport and Pediatric Emergency Medicine for 13 years. I have been involved in the specialty of medical cannabis for over six years after witnessing the incredible benefits of this medicine help a loved one. I have evaluated over 3000 patients for the use of medical cannabis in my practice, mostly for chronic pain, cancer, fibromyalgia, rheumatoid arthritis and numerous other serious conditions. I routinely give educational lectures explaining the science of cannabis medicine to patient groups, including cancer support groups, disabled veterans, amputee support groups, and most recently to parents of children with refractory epilepsy. Interestingly, I have the unusual combination of having expertise in both pediatrics and medical cannabis.

Based on my clinical experience and review of the current scientific literature, it is my professional opinion that medical cannabis may have significant benefits for many patients suffering with serious and chronic medical conditions. Over the past year I have evaluated over 70 pediatric patients suffering with difficult-to-treat epilepsy, who have failed pharmacologic treatment, special diets and sometimes neurosurgical intervention. Repeated seizures and toxicity of potent antiepileptic medications can and do cause significant adverse side effects, that for many, are intolerable.[1] Most of these patients suffer with additional significant medical problems, including autism, developmental delay, speech impairment, cerebral palsy and other conditions that lead to a poor quality of life.

Cannabis can be grown and bred to have low levels of delta-9-tetrahydrocannabinol, known as THC, the compound in the plant that is well known to cause a psychoactive or "high" effect, and high levels of cannabidiol, known as CBD, the compound that has no known psychoactive effects. In certain states, cannabis products with ratios of 30 parts CBD to 1 part THC are becoming more available. CBD has been shown in numerous studies to exert an anticonvulsant effect and to have little to no side effects.[2] CBD has also been shown to have anti-inflammatory, anticonvulsant and neuro-protective properties.[3] I believe that it is the combination of these very important medicinal properties that explains the beneficial effects seen in pediatric epilepsy patients.

I have witnessed a number of my pediatric patients experience a reduction of seizure frequency and severity and improved neurodevelopmental function using CBD in a sublingual oil form. In my practice, parents have reported less seizure activity, improved neurocognitive function, better behavior, and little to no side effects with CBD treatment. A few of the patients have been able to decrease doses and numbers of antiepileptic medications. Some parents have reported improvement in speech, behavior, and developmental milestones. I recently received a text from a parent of one of my patients who reports, "just wanted to let you know that A. said "agua" for the first time two days ago, first new word in almost a year! And today with the therapist he tried to say the word "more". He was actually trying to feed himself with a spoon!" This child came to my office just two months ago wearing a helmet because he had so many seizures. He did not speak or acknowledge my presence; in general he acted quite abnormally for his age. The mother tells me that now he is acting normally and "getting into everything" with his healthy twin brother.

These results are similar to results reported by Stanford University researchers in a survey of parents giving CBD to their children with seizures. Eight-four percent of the parents in the survey "reported a reduction in their child's seizure frequency", with other beneficial effects including "increased alertness, better mood, and improved sleep. Side effects included drowsiness and fatigue". Fifty-five percent of the parents were able to wean their children off antiepileptic drugs.[4]

There is no question in my mind that, although more research is needed, CBD improves the quality of life of many patients who have failed currently available treatments. Since cannabis can be grown to limit the psychoactivity and to enhance the CBD levels, there are little to no side effects reported by parents and certainly, this medication is significantly less toxic than many of the currently available antiepileptic drugs.

We have the ability to grow medical cannabis high in CBD. We cannot continue to be afraid of cannabis and deny this treatment to suffering patients and their families. These children deserve better and should have a chance at a better quality of life. When I was in medical school, I had a mentor who taught me that if I treated everyone as if they were my mother, my brother or my best friend, I couldn't and wouldn't go wrong. Knowing what I know about CBD treatment, I would not hesitate to recommend it to a loved one.

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[1] Loring, DW. (2004) Cognitive Side Effects of Anti-Epileptic Drugs in Children. *Neurology* March 23, 2004 vol. 62(6):872-877

[2] Consroe, P., et al. (1982) Effects of cannabidiol on behavioral seizures caused by anticonvulsant drugs or current in mice. *Eur J Pharmacol* 83(3-4); 293-298. Karler, R. and Turkanis, S. A. (1980), Subacute cannabinoid treatment: Anticonvulsant activity and withdrawal excitability in mice. *British Journal of Pharmacology*, 68: 479–484. Izquierdo, I. and Tannhauser, M. (1973), The effect of cannabidiol on maximal electroshock seizures in rats. *Journal of Pharmacy and Pharmacology*, 25: 916–917. Cunha J.M., et al. Chronic administration of Cannabidiol to healthy volunteers and epileptic patients. *Pharmacology* 1980;21:175–185

[3] Castillo, A., et al. (2010) The neuroprotective effect of cannabidiol in an< i> in vitro</i> model of newborn hypoxic–ischemic brain damage in mice is mediated by CB< sub> 2</sub> and adenosine receptors. *Neurobiology of disease* 37(2): 434-440. Molina-Holgado, Francisco, et al. "Endogenous interleukin-1 receptor antagonist mediates anti-inflammatory and neuroprotective actions of cannabinoids in neurons and glia. *The Journal of Neuroscience* 23.16 (2003): 6470-6474. Esposito, G., et al. (2007) Cannabidiol in vivo blunts β ‐ amyloid induced neuroinflammation by suppressing IL ‐ 1β and iNOS expression. *British Journal of Pharmacology* 151(8): 1272-1279. Iuvone, Teresa, et al. (2009) Cannabidiol: a promising drug for neurodegenerative disorders? *CNS Neuroscience & Therapeutics* 15(1): 65-75. Hampson, A. J., et al. (1998) Cannabidiol and (−) Δ9-tetrahydrocannabinol are neuroprotective antioxidants." *Proceedings of the National Academy of Sciences* 95(14): 8268-8273. Scuderi, Caterina, et al. (2009) Cannabidiol in medicine: a review of its therapeutic potential in CNS disorders." *Phytotherapy Research* 23(5): 597-602.

[4] Porter BE, Jacobson C. (2013) Report of a parent survey of cannabidiol-enriched cannabis use in pediatric treatment-resistant epilepsy. *Epilepsy Behav.* Dec;29(3):574-7.

Curriculum Vitae

Bonni Goldstein, M.D.

5539 Bayridge Road
Rancho Palos Verdes, CA 90275
310.890.2399

Education:

1982-1986: Rutgers College, New Brunswick, NJ
B.A. Biology

1986-1990: UMDNJ – Robert Wood Johnson Medical School, Camden, NJ
M.D.

Postdoctoral Training:

1990-1993: Internship and Residency, Childrens Hospital Los Angeles (CHLA)

1993-1994: Chief Resident of Pediatrics, Childrens Hospital Los Angeles (CHLA)
Responsibilities included:

- Management of 80 interns, residents, rotating medical students
- Scheduling all in-patient and out-patient services for 80 interns and residents
- Provided weekly lectures to residents and medical students on current scientific literature pertaining to all aspects of medical care for pediatric patients
- Attended and participated in weekly meetings for Quality Assurance and Utilization Management for CHLA
- Weekly meetings with USC medical students for classroom and clinical instruction
- Weekly in-patient Attending Physician rounds
- Weekly out-patient clinic Attending Physician rounds
- Daily meetings with senior residents to review all new admissions

Professional Experience:

1993-1994: Private Practice in Office of Dr. J. Lauricella and Dr. P Verette, Pasadena, CA

- Delivered quality medical care to children and adolescents in private practice setting

1993-1994: Moonlighting Fellow, Childrens Hospital Los Angeles Community Health Center

- Evaluated and provided treatment to children and adolescents for acute injuries and illness
- Mentored and gave clinical instruction to medical students, interns and residents

1993-1994: Moonlighting Fellow, Childrens Hospital Los Angeles Cardiothoracic Intensive Care Unit

- Provided acute critical care treatment to pre-operative and post-operative infants, children and adolescents with life-threatening cardiac illnesses

1993-1994: Clinical Instructor in Pediatrics, USC School of Medicine, Los Angeles

- Responsible for teaching medical students clinical skills for evaluation and assessment of pediatric disease and illness in low-income community clinics

1994-1996: Critical Care and Emergency Transport Attending Physician, Childrens Hospital Los Angeles

- Provided critical care evaluation services to ill infants, children and adolescents in the Southwest region of US
- Provided physician-accompanied transport via ambulance, helicopter and plane for critically ill patients requiring emergent transport to tertiary care facilities
- Worked effectively as leader of 5-person transport team, which included RN, RT, and EMTs

1996-1999: Urgent Care Physician, Kaiser Permanente, West Los Angeles, CA

- Provided quality medical care to infants, children and adolescents in the Pediatric Urgent Care Department

1994-2003: Emergency Medicine Attending Physician, Pediatric Emergency Department
Los Angeles County-USC Medical Center, Los Angeles, CA

- Provided quality medical care to infants, children and adolescents in the Pediatric Emergency Department of the LAC-USC Medical Center
- Attending Physician overseeing pediatric interns and residents, family practice residents, emergency medicine residents, and USC medical students
- Responsible for evaluating patients referred to LAC-USC from other hospital systems for tertiary care and arranging appropriate medical transport

2000-2003: Medical Author, ExamMaster (Published)

- Created and developed clinically-based vignettes for pre-medical and foreign medical graduate exam preparatory courses

2002-2006: Pediatric Emergency Medicine Physician, Little Company of Mary Hospital, Torrance, CA

- Provided quality medical care to infants, children and adolescents in a private hospital emergency department setting

2006-2008: Owner and Founder, Brainiacs Science Discovery Center, Redondo Beach, CA

- Developed curriculum including life, earth and physical hands-on science experiments for children ages 3 – 12 years
- Provided on-site extracurricular science educational programs
- Provided off-site (public schools, YMCA, Montessori schools) science educational programs

2008-present: Owner and Medical Director, Canna-Centers, Lawndale, CA
Responsibilities include:

- Consulting specialist in use of therapeutic medical cannabis
- Developing policies and procedures for 5 state-wide clinics
- HIPAA Privacy Official for 5 clinics
- Providing HIPAA education to management and ancillary staff
- Managing 6-physician medical group
- Maintaining QA standards and best practices

Memberships:

- International Association of Cannabis as Medicine
- International Cannabinoid Research Society
- Society of Cannabis Clinicians

Licensure: State of California (1991) – no actions or complaints
DEA (1992)
Board Certification (1994, 2001)

Good afternoon! My name is Jennifer Schultz. I am here today from Waukesha County **with my husband, Jeremy, and my 8yo son, Jacob. Jacob was born with a very rare syndrome, called Lenz Microphthalmia Syndrome. One of the many anomalies associated with this syndrome, are recurrent seizures, otherwise known as Epilepsy. He started almost at birth with Infantile Spasms, which he eventually grew out of, and into regular, full-blown seizures. He currently has tonic, as well as myoclonic, seizures. Jacob can go a few days without having a seizure if we're having a "good seizure week", or he can have several seizures per day. As you may imagine, we absolutely loathe seizures in our house.**

Jacob has a common rescue med, called Diastat. It is essentially rectal valium. It's something that we can give him to hopefully help to slow down an active seizure. I say 'hopefully', because it takes about 12 minutes to actually kick in for Jacob. And he cannot go up to the next dosage until he gains nearly 20 pounds. It's a fine line between administering the Diastat and administering it too much, so that he builds up a tolerance to it. And giving it while anywhere but at home is quite tricky, especially the older he gets.

There was a time when we were delivering Jacob's emergency rescue med daily, sometimes twice a day... and even a few times, being at a point that we needed it a third time, so we had to hurriedly pack everything up and head to the hospital so that they could give him a loading dose of a seizure med via IV to hopefully give him a bit of a break from the seizures.

Jeremy and I are willing to try just about anything to give Jacob some relief and get rid of this plague. We have

been playing around with different seizure meds and combinations of different seizure meds for 8 years now and they have yet to completely control Jacob's seizures. He is currently on 5 different seizure meds. We've tried the Ketogenic Diet with no improvement. His case was presented to see if a surgical option called a 'Corpus Callosotomy' would be an option for him and they determined that the benefits did not outweigh the risks at this point. And Jacob's seizures are global, meaning they are not in one focal location, so another type of surgery to go in and remove that part of the brain wouldn't help him right now either. We've also talked about implanting a Vagal Nerve Stimulator to help with seizure control, but again, that wouldn't be a sure-thing with the types of seizures that he is currently having. A derivative of a plant just seems like such a natural, non-invasive way to help him.

Something that has dumbfounded me regarding the controversy surrounding the use of cannabis oil is the argument that there have not been extensive studies done and there is not a ton of research out there. Well... there HAVE been a lot of studies done and there IS a lot of research out there on the meds that we are currently giving our children for their epilepsy and those are scary! The side effects are endless, so now we need to worry about those along with the seizures themselves. So, in effect, the studies and the research don't always put our minds at ease. With the combination of meds that he's currently on, the biggest side effect has been lethargy. This may not seem like a big deal to people, but there are times that he will sleep all day. Obviously therapies and school would be better spent in an AWAKE state, but that isn't always an option for him, because he is just so worn out. Other side effects that are possible

from his current regimen are: aplastic anemia, liver failure, dizziness/drowsiness, numbness, diarrhea, vomiting, vision problems, kidney stones, gastrointestinal problems, respiratory problems, skin rashes, muscle weakness and headaches, to name some of them. Jacob is non-verbal and unable to tell us what he's feeling, so it is extremely difficult to guess at some of the symptoms of these side effects. It's really imperative to stay on top of everything so we don't miss something. Again, a derivative of a plant just seems like such a natural, non-invasive way to help him.

I am so happy to be able to be here with you today to beg you to carry this bill through to the next steps and finally into becoming law. Jacob is not just MY child, but he's really also your child, too. He's a child from Wisconsin that needs your help... he needs you to fight for him and he needs you to care what happens to him. He needs you to give him the chance. I cannot imagine the concrete block that would be lifted from our family's shoulders, if we could help Jacob reduce, or even eliminate, his seizures. With your help, we CAN do this for Jacob... for Lydia... for Nic... for Raegan

and for so many more in our state.

THANK YOU! ☺

EPILEPSY
FOUNDATION®
HEART OF WISCONSIN
Not another moment lost to seizures®

1302 MENDOTA STREET #100
MADISON, WI 53714

February 12, 2014

The Epilepsy Foundation Heart of Wisconsin supports research on the potential antiepileptic effects of CBD or other marijuana-based therapies. While there is experimental evidence that CBD stops seizures in animal models and there are anecdotal reports that it has been effective in patients with epilepsy, there is a lack of scientific data. **The Epilepsy Foundation urges anyone exploring epilepsy treatments, as permitted under their state law, to work with their treating physician to make the best decisions for their own care.**

AB726 will do three important things for families in Wisconsin that struggle with severe epilepsy.

1. Allow physicians to offer compassionate use in cases where all other therapeutic options have been exhausted.
2. Make it easier for Wisconsin families to participate in investigational studies that are being conducted by around the country.
3. Add to the body of knowledge regarding the therapeutic effects of cannabis-related treatments on a variety of CNS disorders.

There are over twenty medications for the treatment of seizures. 30% of people with epilepsy have seizures that do not respond to current medication therapies. Those patients pursue surgical treatments, restrictive diet treatments, nerve and brain stimulation devices and a variety of complementary therapies like bio-feedback and relaxation therapy.

Parents of children with severe childhood epilepsy leave no stone unturned in trying to quiet seizure activity in these young, developing brains. When surgery is not an option parents are eager to pursue promising compounds at the forefront of medical research.

United Way

CBD oil is one such compound and while we think of cannabis as a weed that grows in ditches it is important to remember that most of the approved medications for epilepsy also derive from weeds that grow in important ditches all over the world.

Later this afternoon I'll be attending my second funeral of this year; two women with medically intractable seizures who died from SUDEP, or sudden and unexpected death from epilepsy. One was thirty-seven years old and single; one was a 41 year old mother of two. Sudden unexplained death occurs with elevated frequency among people with epilepsy, especially when the seizures are poorly controlled.

Epilepsy is by no means a benign disorder and if you speak to families who have experienced such a loss you will understand their willingness to leave no stone unturned in seeking relief from the devastating effects of recurring seizures.

AB726 will provide a new sliver of hope for some Wisconsin families who desperately seek to control seizures and help their children achieve their full potential.

Thank you for the opportunity to testify on behalf of this important bill.

Arthur Taggart
Executive Director

From: Brooke Aldrich <brookealdrich22@gmail.com>
Sent: Monday, February 10, 2014 8:12 PM
To: Rep.Krug
Subject: Bill 726
Attachments: Scan 140410001.pdf

Dear Representative Krug,

I wanted to reach out to you via email to voice my concern and hope that you will openly consider passing Bill 726.

I am a nurse working towards my Nurse Practitioner, but more importantly I have watched children like Lydia Schaeffer suffer from seizures in my practice and in the community. I have had the pleasure of knowing Sally and the Schaeffer family for the past 10 years. I have watched Lydia learn to chew, walk, and interact with us. I have always watched her digressed due to side effects of her seizure medications. I have been there to administer emergency seizure medications hoping and praying that the seizure would stop and she would wake up and be the same little girl.

CBD offers relief from these seizures without the side effects of being ‘stoned’. I ask that you consider supporting the bill 726 and legalize CBD for pediatric seizures. In the health care field and for people who have friends or family with seizures we are NOT the vocal minority. We live this on a daily basis. I am very strong in my political beliefs but this is not a political issue it is a humanitarian issue. I struggle sleeping at night knowing that any of us could be in the position of watching someone suffer or become brain dead from a seizure when there is something out there that can help. The current medications used for seizures have risky side effect and often leave the child/person in a daze. CBD offers a treatment that is inexpensive and effect.

Sincerely,

Brooke Aldrich

33604 Karcher Rd.

Burlington, WI 53105

262-210-8361

--

Wednesday, February 12, 2014

Re: Bill 726 – Wisconsin State Committee on Children and Families

Abbie and Jody Testaberg

193 Bobwhite Street, River Falls, WI 54022

abigail.em.inc@hotmail.com 651.323.7831

Thank you for your time today. I am speaking on behalf of my husband, Jody, and myself. We want to be very clear: we do not want to stand in the way of sick children accessing medicine quickly in order to save their lives or increase their quality of life. We have a 17 year old niece, Mary, who was born with Klippel-Feil Syndrome and is currently suffering three-six seizures a month and the rate and severity are increasing. Similar to testaments you have or will hear today, the cause of her seizures is unclear and current interventions are not working. Due to our experiences with Mary, we understand the necessity for access to medicine that can improve seizure activity and support legislation that would do so. Having said this, we have concern over the CBD-only nature of this bill, as evidence is mounting that not all seizure patients respond to CBD-only medicine and access to the whole plant is necessary for many patients to successfully manage their seizures.

Furthermore, it is our hope that this bill would not be so narrow as to only allow patients with seizure disorders access to medical Cannabis. We have two children: Philip, who is three and has Klinefelter's Syndrome and Ari who is eighteen months and has Spina Bifida. Also, Jody's mother has chronic lymphocytic leukemia.

Current medical Cannabis strains, future medical Cannabis strains that have been more finely tuned, and future pharmaceutical drugs derived from medical Cannabis could help health issues my children and mother-in-law currently face and/or will face in the future. We want to reiterate that ways in which medical Cannabis could help them range in the potential of the whole plant, including THC, CBD, CBG or any of the over 60 components of medical Cannabis, as well as various distribution methods.

Beyond how this bill would affect us personally, both positively and negatively, we would like to address broader implications and questions we have.

Creating narrow-scope medical Cannabis legislation has clear short-term intended consequence, but unclear long-term unintended consequences. We fear that CBD only laws allowed only for certain types of patients will lead to the alienation of the many other patients that need whole plant medicine (cancer, MS, ALS and PTSD...just to name a few). Narrow definitions of what part of the plant that can be used, who can use it, and how it can be administered will lead to frustration with medical Cannabis laws and open the door for those people who would not normally support full legalization to do so, because they see no other way for access. These are legitimately sick people, mind you, that would not otherwise support full legalization.

Having stated our concern of the broader implications of this bill, we do have specific questions as well:

As we read the Bill, the amendment to the current law separates CBD from THC and states that CBD oil that does not produce a high can be used by seizure patients under prescription.

If this is an, essentially, accurate reading of the bill, isn't it already legal to purchase CBD oil using industrial hemp that is CBD rich? And, is it possible that current strains of oil that are popular to treat seizure disorders are actually industrial hemp classified anyway, but for some reason kept under the perception of medical Cannabis in order to manipulate cost and access? Please do not be naive to the fact that the medical Cannabis industry has quickly followed suit of the pharmaceutical industry and saving lives is big business. If it is already legal, what is it about the verbage in the amendment that legalizes CBD oil extract from medical Cannabis as compared to industrial hemp? Furthermore, won't medical Cannabis oil extract – in its natural form – always contain some THC? Or, is that why the non-psychoactive effect semantics is used...in order to create an "out" of sorts? If it is not designed as an out, it seems as though the amendment is supporting synthetically derived, or highly processed, CBD oil over medical Cannabis oil in its natural and safer form. Are the health consequences of synthetic and processed oils understood? Additionally, would this bill unintentionally make the purchase of Industrial Hemp CBD-rich oil, which is currently legal, illegal for all those who are not seizure patients and not under a doctor's prescription? What about CBG, CBC, CBN...or the other proven medically viable and non-psychoactive parts of the Cannabis plant? And, lastly, won't it still be illegal to ship medical Cannabis oil extract or buy it and cross state lines with it? If it is still illegal to acquire CBD oil, what additional amendments will be made to grow and process in WI? But again, does the industrial hemp oil potential classification make it a moot point and question whether this bill is necessary in the first place. If importation of CBD oil is allowed, what safeguards will there be to the quality and safety of the medicine?

Our hope is that this committee will work to address these questions and truly understand the consequences of this bill in its current form.

Again, Jody and I truly desire access to medical Cannabis for seizure patients, but hope that you understand how many more patients there are in Wisconsin that would benefit from whole plant medical Cannabis.

Thank you very much for your attention.

From: bla tds.net <bla@tds.net>
Sent: Tuesday, February 11, 2014 6:59 AM
To: Rep.Krug
Subject: Bill 726

Rep. Krug,

I am imploring you to support Bill 726 and legalize the use of CBD for pediatric seizures. I understand there is no being high effect, as this is medical and ideal for the treatment of potentially fatal pediatric seizures. It is unbelievable to me that our government could withhold a potential cure for the debilatating seizures children like Lydia Schaeffer suffer. I can only guess you and your family have not had loved ones who will potentially be cured only to be told "no, it's not legal in the state you reside in".

I ask for your support of Bill 726.

Respectfully,

Julie Aldrich
8754 Hilltop Drive
Burlington, WI. 53104
262-210-6692

Thorson, Randy

From: Host, Monica <MHost@cityofmadison.com>
Sent: Wednesday, February 12, 2014 9:29 AM
To: 'Rep.Krug@legis.wisconsin.gov'; 'Rep.Loudenbeck@legis.wisconsin.gov'; 'Rep.Endsley@legis.wisconsin.gov'; 'Rep.Schraa@legis.wisconsin.gov'; 'Rep.Spiros@legis.wisconsin.gov'; 'Rep.Kerkman@legis.wisconsin.gov'; 'Rep.Neylon@legis.wi.gov'; 'Rep.Taylor@legis.wisconsin.gov'; 'Rep.Billings@legis.wisconsin.gov'; 'Rep.Kahl@legis.wisconsin.gov'; 'Rep.Johnson@legis.wisconsin.gov'
Subject: FW: Assembly Bill 698

Please receive this submission of a written comment regarding Bill 698.

Date: February 12, 2014
To: WI Committee on Children and Families
From: Monica Host, Madison Child Care Coordinator
Re: Assembly Bill 698 Waking Sleeping Infants and Toddlers

I am submitting these comments in opposition to Assembly Bill 698

To promote mental and physical health, brain development and all over growth and development, infants and toddlers under 2 years of age need to sleep when they are tired. The physical and cognitive growth alone that occurs in the first 2 years is monumental. This growth is the foundation for on-going learning, development and self-regulation.

The WI State Group Child Care Center licensing rule which addresses the issue of children's sleeping schedules is DCF 251.09 (2)(b): "Each Infant and each toddler shall be allowed to form and follow his or her own pattern of sleeping and waking."

Teachers and providers are required to follow this rule. This rule protects the child's well-being. It also acknowledges the caregiver's ability to read, understand and meet the child's needs while in care. This is what parents trust their provider to do and pay for.

Having said this, it is imperative that parents and caregivers work together to ensure that the child care experience and life at home are in sync. This requires open-dialogue, listening and the creation of a strong partnership. Providers and parents need to discuss what is happening with the child and work together to adjust schedules, practices and activities to best meet the child's needs. This is where sleep and feeding routines are best addressed.

Please consider these comments and vote against Bill 698.

Thank you.

Monica Host, Child Care Program Coordinator
City of Madison DPCED • Community Development Division
Room 225, Madison Municipal Building
215 Martin Luther King, Jr. Blvd. • P.O. Box 2627
Madison, Wisconsin 53701-2627
Tel 608 267 4995 • ***Fax*** 608 261 9626
Email mhost@cityofmadison.com
Web cityofmadison.com/dpced/communitydevelopment

From:	Host, Monica <MHost@cityofmadison.com>
Sent:	Wednesday, February 12, 2014 8:56 AM
To:	Rep.Krug; Rep.Loudenbeck; Rep.Endsley; Rep.Schraa; Rep.Spiros; Rep.Kerkman; Rep.Neylon; Rep.Taylor; Rep.Billings; Rep.Kahl; Rep.Johnson
Subject:	Assembly Bill 698

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Having said this, it is imperative that parents and caregivers work together to ensure that the child care experience and life at home are in sync. This requires open-dialogue, listening and the creation of a strong partnership. Providers and parents need to discuss what is happening with the child and work together to adjust schedules, practices and activities to best meet the child's needs. This is where sleep and feeding routines are best addressed.

Please consider these comments and vote against Bill 698.

Thank you.

Tod Ohnstad
STATE REPRESENTATIVE

To: Assembly Committee on Children and Families
From: Rep. Tod Ohnstad
Date: February 12, 2014
Subject: Assembly Bill 726, relating to providing that cannabidiol is not a tetrahydrocannabinol and dispensing cannabidiol as a treatment for a seizure disorder

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Chairman Krug and members of the Assembly Committee on Children and Families:

Thank you for holding a hearing on AB 726 this morning. Committee obligations this morning prevent me from sharing my support for the bill with you in person today, but I wanted to provide the two attached items from the *Kenosha News* to you for your information. One is an article about local Kenosha families who would benefit from the passage of AB 726. The other is an editorial from the *Kenosha News* regarding this important bill. I hope you will find them as moving and informative as I did.

Again, thank you for your attention to this very important bill. I would be happy to discuss either item with you if anyone would like to hear more about the impact of AB 726 in Kenosha.

Sincerely,

Tod

Tod Ohnstad
State Representative
65th Assembly District

65th ASSEMBLY DISTRICT
State Capitol: P.O. Box 8953, Madison, WI 53708 • (608) 266-0455 • Toll-free: (888)-534-0065 • Fax: (608) 282-3665
Email: rep.ohnstad@legis.wi.gov • Website: http://ohnstad.assembly.wi.gov

Local families battle for cannabis oil treatments

Medical marijuana sought for children who have seizures

BY JOE WARD
jward@kenoshanews.com

SUBMITTED PHOTO

Raegan Arnold

Rebecca Arnold's daughter Raegan has battled epilepsy since she was 2 years old. Her condition has kept her in hospitals, out of classrooms and on a number of powerful medications that have done little to help.

Last year, Raegan, now 9, saw her condition worsen. Doctors said their last remaining option was a very serious brain surgery that Raegan's parents weren't ready to agree to.

Then, the family, which lives in Pleasant Prairie, learned of experimental treatments with medical marijuana that were showing dramatic improvements in children with seizures. Such treatment is not allowed in Wisconsin, but with the help and leadership of other families in Wisconsin, Arnold and her family are hoping to overturn the ban on medical marijuana and give a better life to children who suffer from seizures.

Coping with medication

In 2006, Arnold noticed her daughter shake. It happened a couple times that day, until Arnold and her husband figured out their daughter was having a seizure.

The Arnolds came home from the hospital with three different medications to help treat Raegan's epilepsy.

But, as parents with seizure-prone children know, medications are not a lasting solution. They often work for a set amount of time before the dosage and combination of drugs needs to be tweaked.

"While you transition from medication to medication, the seizures can get worse," Arnold said. "We've been on this roller coaster ride for a while."

Raegan was on a combination of four different medications before doctors suggested that their best hope would be brain surgery. Doctors were able to pinpoint the location of the seizures within the brain and would be able to remove that portion of the brain so as to stop the seizures, Arnold said.

"That was probably the hardest decision one can make," Arnold said.

A portion of Raegan's right frontal lobe was re-

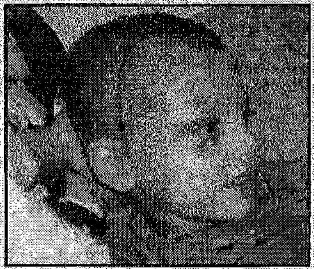
See **RAEGAN,** *Back page*

RAEGAN: Family fights to have marijuana law changed

From **Page A1**

SUBMITTED PHOTOS

The Arnold family, clockwise from upper left: Steve, Mason, Rebecca, Evan and Raegan



Raegan Arnold after brain surgery.

moved. She was seizure-free for eight months, until the problem surfaced again.

Other treatment

In June of last year, Raegan suffered 50 seizures a day. Medicine was again prescribed, but Raegan's family knew that would only be a temporary fix, and a costly one at that.

"She had a lot of frustration, a lot of impulsivity and balance issues," Arnold said. "We knew this cocktail of medications wouldn't last."

Once again, doctors suggested brain surgery. Only this one would be much more serious: it would require doctors to split completely the right and left lobe of the brain.

That option did not seem to be as sure a bet as the first brain surgery. Then, the Arnold family found about another, albeit illegal, alternative treatment. One that was gaining national recognition thanks to a CNN documentary.

To learn more about medical marijuana, Arnold reached out to Sally Schaeffer.

Another battle

Schaeffer's daughter Lydia was diagnosed with a rare chromosome disorder when she was 5 months old. Now Lydia is 6 and still battling her disorder.

Like Raegan, Lydia's seizures had been kept at bay with a litany of drugs. But, also like Raegan, those drugs caused Lydia to regress almost as much as her disorder.

"She was self-mutilating, biting furniture, biting me," Schaeffer said. "It was like my daughter disappeared."

Lydia's doctors also recommended brain surgery. Around that time, Schaeffer also heard about the CNN documentary, where Dr. Sanjay Gupta extolled the breakthroughs in medical marijuana.

Gupta told the story of a little girl who, like Lydia and Raegan, suffered from debilitating seizures. But when the girl was prescribed a form of cannabis oil that does not produce a psychotrophic high, her symptoms disappeared.

That got Schaeffer thinking about how to get her daughter a similar kind of treatment.

"I had very much dismissed (medical marijuana) because I thought I had options for my daughter," she said. "But after that surgery meeting, I felt that our options were diminishing."

Fighting to change the law

Both families ruled out moving to Colorado. They decided to stay put in Wisconsin and fight to get their daughters the same rights as those in Colorado.

Schaeffer, of Burlington, led a legislative effort to get Wisconsin politicians to allow for the use of cannabis oil for young patients.

She found out that a bill to allow for medical marijuana already had been authored, but had stalled in the Legislature. A bill that would specifically allow for the use of cannabis oil in patients suffering from seizures also was authored.

That bill will be the subject of a hearing, the first step in its path toward ratification, on Wednesday. Schaeffer is fundraising to get both the doctor and the family who were profiled in Gupta's documentary to come testify at the hearing. Both parties have agreed to be there Wednesday.

Schaeffer will testify at the hearing, too. So will Arnold.

After seeing the side effects of the seizure medicines on their children, both women said they are positive that cannabis oil would not be more harmful than the combination of prescription drugs that were only temporary solutions.

"I want to be able to try it," Arnold said. "I couldn't fathom putting her through another brain surgery. Right now, she has no other option. Time is of the essence."

Medical marijuana bill deserves a chance

Local families to testify at hearing in Madison

OUR VIEW

A pair of local families are taking their case for the legalization of medical marijuana to Madison next week.

Both families have children who suffer from seizures, a condition that is sometimes treated with cannabis oil extract, but that treatment is not legal in Wisconsin.

Efforts to legalize medical marijuana, which this newspaper has supported, have gone nowhere in Wisconsin, despite a clear trend among states to accept it. At least 20 states allow some uses of medical marijuana, including Illinois, which just began a four-year pilot program.

On Wednesday the Assembly's Committee on Children and Families will hold a public hearing on Assembly Bill 726, a bill that narrowly targets cannabis oil extract as a legal treatment for seizure disorder if prescribed by a medical practitioner. State Rep. Tod Ohnstad, D-Kenosha, and state Sens. Bob Wirch, D-Somers, and John Lehmann, D-Racine, are among the sponsors of the bill, which has sponsors from both parties.

Rebecca Arnold of Pleasant Prairie, whose 9-year-old daughter Raegan has epilepsy, and Sally Schaefer of Burlington, whose 6-year-old daughter has seizures, both plan to testify at the hearing Wednesday. Their stories, featured in the Kenosha News on Friday, ought to have some impact. The families have tried other medicines with no long-term relief. It seems cruel to deny them an opportunity for relief just because the medicine is derived from marijuana.

In the Arnold family's case, a medicinal treatment that works could make a serious brain surgery unnecessary. That is a very high potential reward for a legislative step that has very little risk.

Marijuana, even though it is illegal, is quite popular as a recreational drug. That won't change if the Legislature passes or rejects the bill to make cannabis oil extract legal as a treatment for seizures.

What might change is some families may find relief from having to constantly try new medicines, some of which have side effects, to control a child's seizures.

We think the Legislature should be open to more legitimate uses of marijuana, but at the very least, this narrowly written piece of legislation ought to move forward.

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died of [illegible] ia)
1/24/14- [illegible]
Cannabis [illegible] ALL

Cannabis Extract Treatment for Terminal Acute Lymphoblastic Leukemia with a Philadelphia Chromosome Mutation

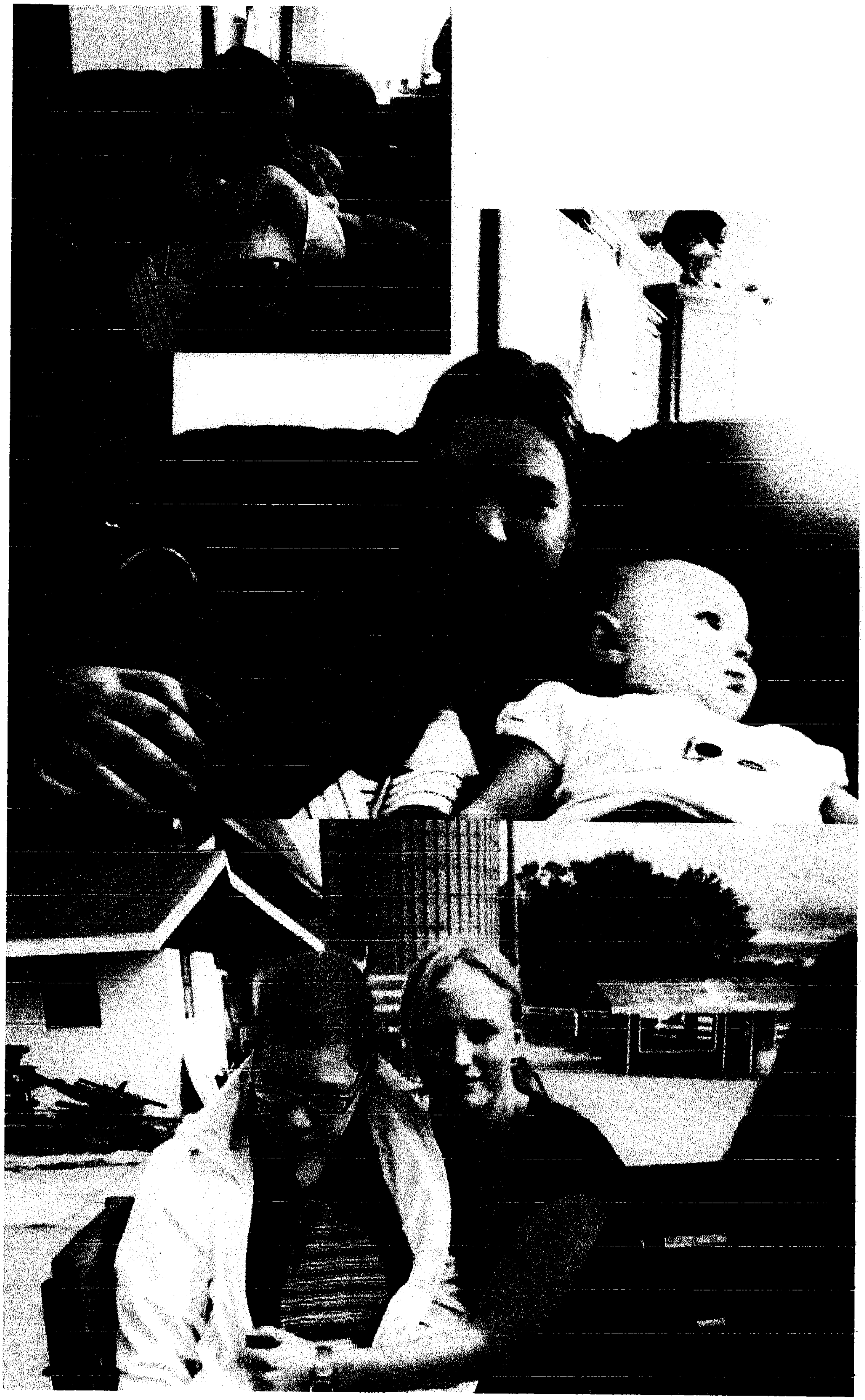
Yadvinder Singh[a] Chamandeep Bali[b] [illegible]

[a]Brampton, Ont. and [b]Ajax, Ont., Canada

Key Words
Acute lymphoblastic leukemia · Philadelphia chromosome · Cannabinoids ·

Abstract

Acute lymphoblastic leukemia (ALL) is a cancer of the white blood cells and is typically well treated with combination chemotherapy, with a remission state after 5 years of 94% in children and 30–40% in adults. To establish how aggressive the disease is, further chromosome testing is required to determine whether the cancer is myeloblastic and involves neutrophils, eosinophils or basophils, or lymphoblastic involving B or T lymphocytes. This case study is on a 14-year-old patient diagnosed with a very aggressive form of ALL (positive for the Philadelphia chromosome mutation). A standard bone marrow transplant, aggressive chemotherapy and radiation therapy were revoked, with treatment being deemed a failure after 34 months. Without any other solutions provided by conventional approaches aside from palliation, the family administered cannabinoid extracts orally to the patient. Cannabinoid resin extract is used as an effective treatment for ALL with a positive Philadelphia chromosome mutation and indications of dose-dependent disease control. The clinical observation in this study revealed a rapid dose-dependent correlation.



Cannabis and Cannabinoids:

Relatively Safety Compared To Conventional Therapeutics

Paul Armentano
Deputy Director
NORML, NORML Foundation
April 23, 2011
40th Annual National NORML Conference
Denver, CO

Common Safety-Specific Criticisms of Cannabis as a Medicine

- Medical cannabis is far too dangerous to recommend as a medicine
- Medical cannabis poses far too many unwanted side effects
- Medical cannabis has not yet been subjected to adequate study
- Not enough clinical trials exist evaluating medical cannabis
- No medicine is smoked
- Cannabis isn’t FDA approved

Cannabis Is Too Dangerous

- “Marijuana, in its natural form, **is one of the safest therapeutically active substances known to man**. By any measure of rational analysis marijuana can be safely used within a supervised routine of medical care.”
  (DEA Chief Administrative Law Judge Francis Young, 1988)
- “[E]xcept for the harms associated with smoking, the adverse effects of marijuana use are **within the range of effects tolerated for other medications**.”
  (U.S. National Academy of Sciences, Institute of Medicine, 1999)
- Cannabiniods have **no practical LD50 rating** in humans
- Cannabinoids possess a remarkable ‘safety ratio’
- Cannabinoids are not ‘intoxicants,’ but behave like **supplements**

Cannabis Poses 'Unwanted Side Effects'

- Virtually all conventional therapeutic substances possess side effects
  - **Typically these side effects are potentially toxic or fatal**
    - Opioids – addiction, overdose death, suicidal thoughts, arrhythmia
    - Acetaminophen – liver damage
    - NSAIDS – kidney failure, ulcers, erectile dysfunction, heart attack, stroke
    - benzodiazepenes, -- amnesia, memory impairment, motor coordination
    - SSRI – seizures, heart disease, liver damage, suicidal thoughts, tremor
- Many conventional medication are 'impairing'
  - Opioids, benzodiazepenes, common cold medicines
- Many conventional medications alter mood
- **What is wrong with elevating the patient's mood anyway?**

Scientists Haven't Adequately Studied Cannabis

- "Research … of cannabinoids and endocannbinoids has reached enormous proportions, **with approximately 15,000 articles on cannabis sativa and cannabinoids** and over 2,000 articles of endocannabinoids."
  (Hanus, 2008, *Medicinal Research Reviews*)

- There were over **2,700 published papers** on cannabis in 2009.
  (Author's search on pubmed using keyword terms 'marijuana and '2009')

- There were over **2,000 published papers** on cannabis in 2010.
  (Author's search on pubmed using keyword terms 'marijuana and '2009')

- There have been over 850 papers on cannabis published this year
  (Author's search on pubmed using keyword terms 'marijuana and '2011')

Scientists Haven't Conducted Enough Clinical Trials of Cannabis

- Lynch and Campbell, 2011: "Cannabinoids for treatment of chronic non-cancer pain: a systemic review of randomized trials"
  - "**Overall quality of trials was excellent.** Fifteen of the eighteen trials that met inclusion criteria demonstrated a significant analgesic effect of cannabinoid as compared to placebo, several reported significant improvements in sleep. There were no serious adverse effects."
- University of California, 2010
  - "This research used the **gold standard design** for assessment of therapeutic effects. ... As a result of this program of systemic research, we now have reasonable evidence that cannabis is a promising treatment in selected pain syndromes ... and possibly for painful muscle spasticity due to multiple sclerosis.
- Grotenhermen, 2010: "Review on clinical studies with cannabis and cannabinoids 2005-2009"
  - "In total, **37 controlled studies** evaluating the therapeutic effects of cannabis or cannabinoids were identified. ... Based on the clinical results, cannabinoids present an interesting therapeutic potential mainly as analgesics, appetite stimulants, as well as in the treatment of multiple sclerosis."
- Amar, 2006: "Cannabinoids in medicine: a review of their therapeutic potential"
  - "**Seventy-two controlled studies** evaluating the therapeutic effects of cannabinoids were identified. Cannabinoids present an interesting therapeutic potential as antiemetics, appetite stimulants in debilitating diseases (cancer and AIDS), analgesics, and in the treatment of multiple sclerosis, spinal cord injuries, Tourette's syndrome, epilepsy and glaucoma."

No Medicine Is Smoked

- But many conventional medications are inhaled
  - steroids (e.g., beclomethasone/Qvar, budnesonide/Pulmicort), nitrous oxide, general anesthesia, etc.
- Why inhalation?
  - rapid onset
  - Patients can readily self-regulate the dose
  - Low risk of overdose
- Smoking versus vaporization
  - "**Vaporization of marijuana does not result in exposure to combustion gases and [was] preferred by most subjects compared to marijuana cigarettes. … [It] is an effective and apparently safe vehicle for THC delivery**, and warrants further investigation in clinical trials of cannabis for medical purposes."

    (Abrams et al., 2007, *Clinical Pharmacology & Therapeutics*)

But Cannabis Isn't FDA Approved

- The FDA only evaluates patented products from private companies
- FDA trials are short-term in duration
- FDA trials typically include only a small group of homogenous subjects (few women, minorities, young people, older adults)
- FDA trials typically look at single symptoms
- FDA trials exclude subjects with certain, pre-existing conditions
- Cannabis has established safety and efficacy in the global laboratory over a period of thousands of years; **it has surpassed standards that are far higher than those set by the FDA or any other federal regulatory agency**

Why No Parent Should Support CBD-only Legislation

[illegible]

PHOTO: Renee Petro

In recent weeks, there has been an explosion of newly proposed legislation on CBD-rich cannabis extracts, the type of medical marijuana featured as a treatment for epilepsy in Sanjay Gupta's "Weed" special in the summer of 2013. Parents fighting for the lives of their epileptic children are desperate for treatment that works, and the power with which these parents can fight should not be underestimated. One would imagine their strong voices would be a huge boon to the reform movement, but instead what has happened is the creation of a great divide: CBD-only vs. whole plant medical marijuana. And in the pediatric cannabis advocacy community, the debate has gotten really ugly.

While advocates for broader medical marijuana legislation often cite a "no child left behind" policy – meaning that children with cancer, autism, and other conditions would respond better to medicine with higher levels of THC – there is another part of the debate that has been largely missing from the media coverage:

According to parents who have been effectively treating their children's epilepsy with cannabis for years, CBD-rich extracts alone are unlikely to provide adequate seizure control without THC supplementation.

Renee Petro and son Branden

"Initially, when I leaned about CBD I would hear high CBD, low THC is the way to treat seizures," says Renee Petro, a Florida advocate whose son Branden suffers from FIRES, a form of intractable pediatric epilepsy. "I lobbied for CBD-only legislation because I thought it would save Branden's life. But as I learned more, I realized that was wrong."

While Petro acknowledges the importance of broader legislation to help kids with conditions like cancer – "we don't want to help just ourselves, we want to help everybody," she says – as Petro learned more about cannabis, she also realized that Branden would likely need more THC than the law would allow in order to control both his seizures and the other symptoms of his disease.

One of the people who helped Petro learn about medical cannabis was Rebecca Hamilton-Brown, whose son Cooper has Dravet Syndrome, the same form of pediatric epilepsy as Charlotte, the namesake of the CBD-rich Charlotte's Web strain. Hamiton-Brown has been treating Cooper with medical cannabis for two years, so she has had more experience with this treatment than most of the parents in the online Pediatric Cannabis Therapy (PCT) group she founded with a handful of other parents in early 2012. The group has now grown to more than 3,000 members, and is a virtual hotbed in the debate over CBD vs. THC.

When she first learned about medical cannabis treatment for epilepsy, says Hamilton-Brown, "I drank the kool-aid. It was all about CBD, it was going to be a cure, and I preached it to anyone who would listen." She located a strain in her home state of Michigan with the highest CBD:THC ratio she could find.

"In February 2012 there were only a handful of us doing it," recalls Hamilton-Brown. "I started PCT because we had no idea what we were doing and we needed other parents to talk to, to ask *what are you using? What's working*? and hammer our way through it."

Rebecca Hamilton-Brown's son Cooper

What Hamilton-Brown found was that no two children seemed to have the same exact response to treatment, nor did even the same child at different times. "This is not a therapy that's like going to a pharmacy for a pill," she explains. "It's something you have to tinker with and as your child is on it longer, you need to adjust it, not just in dosage but in terms of THC content. There are a lot of factors that create a need to change the regiment. If you want the best seizure control, there's not necessarily a dose you can always just stick with. You need to be open-minded."

Currently, Hamilton-Brown is treating her son with both a 25:1 and a 2:1 strain. "We give (higher THC oil) to him as needed," she explains. "Anything that causes stress or excitement is a (seizure) trigger for him, and THC takes the edge off and helps him not to have a seizure." Hamilton-Brown says factors like puberty, medication changes, minor illnesses, and any type of excitement in her home can cause stress which leads to increased seizure activity; she supplements Cooper with higher THC during stressful times.

But regardless of ample evidence that adding THC can help control seizures, many parents are reluctant to consider anything but CBD-rich strains for their child. "People in Colorado are doing the same thing (adding THC), but they are reluctant to talk about it," says Hamilton-Brown, who believes that many parents are fearful of making their children "high."

This is no wonder, considering that one of the powerful political arguments for CBD-only legislation is that such strains are not psychotropic, and parents who have watched their children suffer through highly psychotropic pharmaceutical treatments are clinging to the hope that seizure control can be achieved without any psychoactivity. It's a belief system that Hamilton-Brown says is highly unrealistic.

Dana Ulrich with daughter Lorelei

"They hear CBD and think that's all they need, and it's not," she says. "Their lack of experience and lack of knowledge is being used to shape legislation that will affect a lot of people."

lb. ladybud.com http://www.ladybud.com/2014/02/04/project-cbd-responds-to-sams-cbdisinformation/

Project CBD Responds To SAM's CBDisinformation

Ladybud Admin

By Martin Lee

The misnamed Smart Approaches to Marijuana (SAM) recently produced a "fact sheet" entitled, ***Everything You Need to Know About CBD***, that seeks to justify the continued prohibition of cannabis by misinforming the public about cannabidiol and THC.

Cannabidiol (CBD), a "nonpsychoactive" component of marijuana, is a hot ticket right now among medical scientists and heath professionals. A growing number of physicians are recommending CBD-rich cannabis oil extracts for patients in states where medical marijuana is legal. CBD has been shown to shrink malignant tumors, improve insulin sensitivity, quell anxiety, and ease chronic pain – without making people feel high. Extensive preclinical (and some clinical) research validates the experience of many patients, including children with catastrophic seizure disorders, who successfully medicate with CBD-rich products.

Kevin Sabet, cofounder and director of SAM, stated in a letter to the *Boston Globe*: "Medical marijuana is a big fat headache that serves no one but people who want to get high." But the clamor for non-psychoactive CBD-rich cannabis proves Sabet is wrong. Medical marijuana is not – *and never was* – just a front for stoners.

An anti-marijuana ideologue who served as an advisor to the drug czar's office under Obama and George W. Bush, Sabet takes pride in *Rolling Stone's* description of him as "Legalization Enemy #1." *Salon* called him "the quarterback of the new anti-drug movement." If Sabet is the quarterback, then what's the game plan?

Not long after Project CBD was formed in 2010, we predicted that recalcitrant drug warriors would attempt to coopt the news about CBD to advance a prohibitionist agenda. As we note on www.projectcbd.org: "Marijuana prohibitionists will try to exploit the news about CBD to further stigmatize high-THC cannabis, casting The High Causer, THC, as the bad cannabinoid, whereas CBD is pegged as the good cannabinoid. Project CBD categorically rejects this dichotomy in defense of whole plant cannabis therapeutics."

SAM's CBD polemic essentially boils down to this:

- Specific components of the marijuana plant, including CBD, have medical value, but the marijuana plant itself does not have medical value.
- THC, marijuana's psychoactive component, is a horrible, dangerous substance, and children should not be exposed to it under any circumstances.
- Marijuana-derived products are against federal law and are not adequately tested for safety and efficacy, unlike FDA-approved corporate pharmaceuticals.
- State governments should not legalize marijuana to facilitate access to CBD. Those who need CBD should wait patiently until the federal government decides what CBD-rich medicines we are allowed to consume.

SAM's latest missive asserts: "We should find a way to get CBD to patients who need it, but we owe those who suffer a product with safety assurances. Many products on the current 'medical' marijuana market have no such assurances, are never tested in FDA-registered labs, and have no guarantees of quality and content or information on dosing or side effects."

True enough. CBD-rich products should be made from organically grown cannabis, lab-tested for potency, mold and pesticides, and labeled for content and dosage. Certain CBD-products meet these criteria; others do not. Measurable doses of high quality, CBD-rich oil extracts, initially introduced in California, are currently available in some medical marijuana states. But cannabis products, including CBD-rich varieties, can't be tested by "FDA-registered labs" because of the prohibitionist policies that SAM supports. Marijuana's illicit status makes it impossible for analytical labs to handle such products with the FDA's blessing.

In the world according to SAM, a product can't be a medicine unless the FDA approves it as safe and effective. The FDA, however, is not in the business of approving plants as medicines. And the FDA approval process ensures neither safety nor efficacy. There are numerous examples of the FDA approving lethal Big Pharma meds that cure no better than a placebo. Pharmaceutical companies routinely hide clinical trial data about adverse side effects, falsify studies to win approval, and then rely on bribery, fraud, and deception to market dangerous drugs to unsuspecting patients, including children – all with a wink and a nod from the FDA, which treats corporate criminals like royalty. Big Pharma pays the FDA to fast-track cursory reviews, and the FDA enables widespread corruption within the pharmaceutical industry by routinely accepting drug company claims at face value while ignoring pertinent safety data. FDA scientists and whistleblowers risk retaliation by FDA management when they challenge Big Pharma prerogatives.

SAM is silent about FDA and Big Pharma malfeasance, while perpetually demonizing marijuana and THC. SAM warns that products infused with CBD, the good cannabinoid, are tainted with varying amounts of THC, The Horrible Cannabinoid. SAM alludes to unnamed physicians who "report instances of THC toxicity in children taking 'high CBD' preparations" and parents who "are horrified that their children become 'high.'"

SAM contends that the best course of action "would be to remove THC entirely from a CBD product." Pure CBD is the only legitimate option, according to the non-medical experts at SAM, which claims there is "no reliable scientific evidence that THC is necessary to synergize the effects of CBD."

Actually, there is solid scientific evidence that **CBD and THC potentiate each other's therapeutic effects**. The California Pacific Medical Center (CPMC) in San Francisco studied **the effects of CBD and THC on breast cancer** cells and found that both compounds have significant antitumoral properties, but the combination of CBD and THC had a more potent antitumoral effect on human cell lines than either compound when tested alone.

In another experiment, CPMC scientists found that CBD enhances the inhibitory effect of THC on human glioblastoma cells, a deadly form of brain cancer. "THC's anti-cancer benefits were derived largely from activating cannabinoid receptors, something CBD is not known to do," explained Dr. Jahan Marcu, lead author of the **glioblastoma study**. "CBD works through other molecular pathways. It enhances the benefits of THC while reducing side effects."

The painkilling properties of THC were initially documented in the ***Journal of Clinical Pharmacology and Therapeutics*** in 1975. Subsequent clinical studies in Europe demonstrated that whole plant THC combined with whole plant CBD work better than THC alone for treating chronic pain.

U.S. government-sponsored research at the National Institute of Mental Health determined that**THC and CBD both protect brain cells** from the effects of stroke and acute head injuries. Drawing upon this research, the U.S. Department of Health and Human Services secured a patent, titled "**Cannabinoids as Antioxidants and Neuroprotectants**," in 2003. The patent asserted that THC and CBD "are found to have particular application as neuroprotectants, for example in limiting neurological damage following ischemic insults, such as stroke and trauma, or in the treatment of neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease and HIV dementia."

Other scientific findings that SAM prefers to ignore:

- Harvard University researchers found that **THC cuts tumor growth in common lung cancer** in half and "significantly reduces the ability of the cancer to spread" – which helps to explain why smoking marijuana doesn't cause lung cancer.
- Investigators at the Scripps Research Institute in La Jolla, California, showed that **THC inhibits an enzyme** responsible for the accumulation of amyloid plaque that disrupts communication between brain cells, the hallmark of Alzheimer's-related dementia.
- A 2010 study in the *Journal of Clinical Psychopharmacology* reported that oral **THC improved symptoms of ADHD** and Tourette's syndrome in a teenager.

The notion that high THC marijuana could be anything but terrible for children is anathema to SAM, which maintains that "chronic use of THC can impair IQ in adolescents." This oft-repeated canard is based on a **single study (later repudiated in the same journal)** that failed to establish a causal link between juvenile marijuana smoking and lower IQ. Scientists have identified many factors that contribute to impaired IQ – and cannabis isn't one of them. **A junk food diet lowers IQ** and damages memory. **Children who regularly skip breakfast** – poor kids – have lower IQs than other children.

SAM's chronic fear-mongering about THC and brain damage is at odds with a 2012 study published in the journal ***Alcoholism: Clinical & Experimental Research***, which found that a teenager who consumes alcohol is likely to have reduced brain tissue health, but teen marijuana use shows no effect on brain tissue.

Single-molecule THC is classified as a Schedule III drug, a category reserved for medically valuable substances with low abuse potential that are unlikely to lead to physical dependence. Whole plant marijuana, meanwhile, continues to be classified as a dangerous Schedule I drug with no medical utility.

SAM tries to reconcile Uncle Sam's illogical, incoherent, and unscientific marijuana policy by emphasizing the supposed superiority of single-molecule medicine over "crude" whole plant remedies. SAM's single-molecule fetish reflects a cultural and political bias that privileges corporate
harmaceuticals. Single-molecule medicine is the predominant corporate way, the Big Pharma way, but it's not the only way, and it's not
ecessarily the best way to benefit from cannabis therapeutics.

arijuana contains several hundred compounds, including various flavonoids, aromatic terpenes, and dozens of minor cannabinoids in addition
THC and CBD. Each of these compounds has specific healing attributes, but when combined they create what scientists refer to as a
nergistic "entourage effect," so that the therapeutic impact of the whole plant is greater than the sum of its single-molecule parts.

AM says it's working on "a long-term solution to expand and accelerate the current research so that every patient who might benefit from CBD
n obtain it." But SAM's belated promise to help bring CBD to the masses rings hollow given its ongoing support for cannabis prohibition, a
honest, venal, and destructive policy that has thwarted clinical research and impeded medical progress for decades to everyone's detriment.
r this SAM owes America an apology.

ce the passage of Proposition 215, California's landmark 1996 ballot measure that legalized marijuana for therapeutic use, a unique
oratory experiment in democracy has unfolded in the Golden State and elsewhere with positive results. Thanks to the rediscovery of CBD-
cannabis strains by outlaw plant breeders and growers in Northern California five years ago, cannabis clinicians and medical marijuana
ents can avail themselves of additional therapeutic options today.

cessful CBD-rich treatment regimens have extended the lives of advanced cancer patients and others suffering from a wide range of
ases. Most remarkable of all is the dramatic improvement in numerous cases of pediatric epilepsy attributable to CBD-rich oil extracts,
h stop seizures when nothing else is effective.

But CBD-rich remedies with little THC don't always work. Parents of epileptic children have found that adding some THC helps with seizure control in many instances. For some epileptics, THC-dominant strains are more effective than CBD-rich products.

Physicians and patients are finding that different ratios of CBD and THC are optimal for different conditions and individuals. A CBD-rich strain or product with little THC is not necessarily a superior treatment option compared to a balanced CBD-rich remedy with an equal amount of CBD and THC. A CBD-rich extract or strain with little THC might be optimal for treating anxiety and many seizure disorders, whereas pain syndromes, cancers, and neurodegenerative conditions could benefit from an appropriate amount of THC. One size doesn't fit all with respect to cannabis therapeutics, and neither does one compound or one product or one strain.

*Martin A. Lee is the director of **Project CBD**, a medical science information service, and author of **Smoke Signals: A Social History of Marijuana – Medical, Recreational, and Scientific.***

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- http://www.sciencedirect.com/science/article/pii/S0378874106000821

Review

Cannabinoids in medicine: A review of their therapeutic potential

- Mohamed Ben Amar ✉

Abstract

In order to assess the current knowledge on the therapeutic potential of cannabinoids, a meta-analysis was performed through Medline and PubMed up to July 1, 2005. The key words used were cannabis, marijuana, marihuana, hashish, hashich, haschich, cannabinoids, tetrahydrocannabinol, THC, dronabinol, nabilone, levonantradol, randomised, randomized, double-blind, simple blind, placebo-controlled, and human. The research also included the reports and reviews published in English, French and Spanish. For the final selection, only properly controlled clinical trials were retained, thus open-label studies were excluded.

Seventy-two controlled studies evaluating the therapeutic effects of cannabinoids were identified. For each clinical trial, the country where the project was held, the number of patients assessed, the type of study and comparisons done, the products and the dosages used, their efficacy and their adverse effects are described. Cannabinoids present an interesting therapeutic potential as antiemetics, appetite stimulants in debilitating diseases (cancer and AIDS), analgesics, and in the treatment of multiple sclerosis, spinal cord injuries, Tourette's syndrome, epilepsy and glaucoma.

Keywords

- Cannabinoids;
- Cannabis;
- Therapeutic potential;
- Controlled clinical trials;
- Efficacy;
- Safety

- http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2125.2011.03970.x/abstract

Cannabinoids for treatment of chronic non-cancer pain; a systematic review of randomized trials

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Keywords:

- cannabinoids;
- chronic non-cancer pain;
- neuropathic pain;
- systematic review

Effective therapeutic options for patients living with chronic pain are limited. The pain relieving effect of cannabinoids remains unclear. A systematic review of randomized controlled trials (RCTs) examining cannabinoids in the treatment of chronic non-cancer pain was conducted according to the PRISMA statement update on the QUORUM guidelines for reporting systematic reviews that evaluate health care interventions. Cannabinoids studied included smoked cannabis, oromucosal extracts of cannabis based medicine, nabilone, dronabinol and a novel THC analogue. Chronic non-cancer pain conditions included neuropathic pain, fibromyalgia, rheumatoid arthritis, and mixed chronic pain. Overall the quality of trials was excellent. Fifteen of the eighteen trials that met the inclusion criteria demonstrated a significant analgesic effect of cannabinoid as compared with placebo and several reported significant improvements in sleep. There were no serious adverse effects. Adverse effects most commonly reported were generally well tolerated, mild to moderate in severity and led to withdrawal from the studies in only a few cases. Overall there is evidence that cannabinoids are safe and modestly effective in neuropathic pain with preliminary evidence of efficacy in fibromyalgia and rheumatoid arthritis. The context of the need for additional treatments for chronic pain is reviewed. Further large studies of longer duration examining specific cannabinoids in homogeneous populations are required.

- http://www.ncbi.nlm.nih.gov/pubmed/15313899

- Cancer Res. 2004 Aug 15;64(16):5617-23.
- **Cannabinoids inhibit the vascular endothelial growth factor pathway in gliomas.**
- Blázquez C, González-Feria L, Alvarez L, Haro A, Casanova ML, Guzmán M.
- **Author information**
- **Abstract**
- Cannabinoids inhibit tumor angiogenesis in mice, but the mechanism of their antiangiogenic action is still unknown. Because the vascular endothelial growth factor (VEGF) pathway plays a critical role in tumor angiogenesis, here we studied whether cannabinoids affect it. As a first approach, cDNA array analysis showed that cannabinoid administration to mice bearing s.c. gliomas lowered the expression of various VEGF pathway-related genes. The use of other methods (ELISA, Western blotting, and confocal microscopy) provided additional evidence that cannabinoids depressed the VEGF pathway by decreasing the production of VEGF and the activation of VEGF receptor (VEGFR)-2, the most prominent VEGF receptor, in cultured glioma cells and in mouse gliomas. Cannabinoid-induced inhibition of VEGF production and VEGFR-2 activation was abrogated both in vitro and in vivo by pharmacological blockade of ceramide biosynthesis. These changes in the VEGF pathway were paralleled by changes in tumor size. Moreover, intratumoral administration of the cannabinoid Delta9-tetrahydrocannabinol to two patients with glioblastoma multiforme (grade IV astrocytoma) decreased VEGF levels and VEGFR-2 activation in the tumors. Because blockade of the VEGF pathway constitutes one of the most promising antitumoral approaches currently available, the present findings provide a novel pharmacological target for cannabinoid-based therapies.

- http://www.aacrmeetingabstracts.org/cgi/content/abstract/2006/1/1084

[Proc Amer Assoc Cancer Res, Volume 47, 2006]

Experimental and Molecular Therapeutics 35: Identification and Characterization of Novel Cellular Targets

Abstract #4615

Cannabinoid receptors as a target for therapy of ovarian cancer

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Ovarian cancer represents one of the leading cause of cancer-related deaths for women and is the most common gynecologic malignancy. In spite of relative low morbidity, ovarian cancer has a high fatality ratio, with overall 5-year survival of less than 30%. At present, there are inadequate treatment options for the management of advanced ovarian cancer, and therefore development of novel approaches for treatment of this disease are needed. Cannabinoids,the active components of *Cannabis sativa linnaeous* and their derivatives have received considerable attention in recent years due to their diverse pharmacological activities such as cell growth inhibition and tumor regression. To date, two different cannabinoid receptors have been characterized and cloned from mammalian tissues: the "central" CB_1 receptor and the "peripheral" CB_2 receptor. We found that compared to normal Chinese hamster ovarian (CHO) cells, the expression levels of both cannabinoidreceptors CB_1 and CB_2 were significantly higher in human ovarian cancer cells OVCAR-3 and SKOV-3. We then determined expression levels of the cannabinoid receptors in different grades of human ovarian cancer specimens and employing western blot analysis found that both CB_1 and CB_2 receptors were expressed. To evaluatethe cell growth response of WIN-55,212-2 (a mixed CB_1/CB_2 agonist) on CHO, OVCAR-3 and SKOV-3 cells, we employed MTT assay. Of interest, our results demonstrated that treatment of CHO cells with WIN-55,212-2 (5-20 μM; 48 h), did not affect cell viability. In sharp contrast, treatment of OVCAR-3 and SKOV-3 cells with WIN-55,212-2 under similar conditions significantly decreased the viability of cells. The decrease in cell viability in OVCAR-3 and SKOV-3 cells suggests the involvement of either or both CB_1 and CB_2 receptors in the antiproliferative

action of cannabinoids. To evaluate the possible implication of CB_1 and CB_2 receptors in WIN-55,212-2-mediated decrease in cell viability, the effect of selective receptor antagonists was studied. Blocking of both receptors by their antagonists SR141716 (CB_1) and SR144528 (CB_2) significantly prevented this growth inhibitory effect. Further, WIN-55,212-2 treatment of both OVCAR-3 and SKOV-3 cells resulted in G_1 arrest in cell cycle progression, which was associated with a marked decrease in the protein expression of cyclin D1, D2, and E and their activating partner cdk2, 4 and 6. In addition WIN-55,212-2 treatment of both OVCAR-3 and SKOV-3 cells was found to result in induction of apoptosis as determined by PARP cleavage and flow cytometry. We also found that treatment of both OVCAR-3 and SKOV-3 cells with WIN-55,212-2 resulted in down-regulation of the expression of PCNA and VEGF.These results support a new therapeutic approach for the treatment of ovarian cancer. It is also conceivable that with available cannabinoids as lead compounds, non-habit forming agents that have higher biological effects could be developed.