# Cannabis in the Treatment of Pediatric Epilepsy

**By Bonni Goldstein, MD**

The author documents the progress of more than 100 patients using CBD-rich cannabis oil to treat seizure disorders.

I have been a medical cannabis physician seeing adult patients in California for the past six years. Occasionally I would be approached by parents who knew of my background and asked me to monitor their children's use of cannabis. (As a doctor who trained in pediatrics and practiced pediatrics and emergency medicine for 12 years, I have considerable experience taking care of children.)

In the summer of 2013 I evaluated a few adolescents for use of cannabis: a teenage boy with cancer; a teenage girl who went through a horrific trauma and was suffering with PTSD, anxiety and depression and had failed all conventional treatment; a teenage boy with Tourette Syndrome; another teenager with epilepsy.

The nature of my practice changed dramatically after Dr. Sanjay Gupta's documentary aired on CNN in August 2013. Parents of children with intractable epilepsy wanted to know about CBD and cannabis as a possible treatment. They learned about my background on the Internet and asked if I'd be willing to treat their children. Many of the parents are connected on a pediatric epilepsy Facebook page, through which most of my current patients found my practice.

Epilepsy is not a rare disorder. In the United States, according to the Centers for Disease Control, some 2.3 million adults and 468,000 children (under 17) have epilepsy. Epilepsy in children is often a genetic or congenital condition. Epilepsy can result at any time in life from head trauma, infections, or tumors.

*About one-third of epilepsy cases are "intractable" —meaning available pharmaceutical drugs do not control the seizures.*

Many patients who get seizure relief from pharmaceutical anticonvulsants suffer intolerable side effects. About one-third of epilepsy cases are "intractable"—meaning available pharmaceutical drugs do not control the seizures.

Between August 2013 and April 2014, I became the medical cannabis consultant to 93 children with intractable epilepsy. Their parents had, in the past, authorized various interventions —surgery, vagus-nerve-stimulator implant, the ketagenic diet. Some had left the country for stem-cell treatment. These are families that are desperately searching.

My first pediatric epilepsy patient was a 14-year-old girl with Lennox-Gastaut Syndrome. Her parents had learned about CBD and signed up to be on the waiting list of Realm of Caring, the Colorado non-profit run by the Stanley Brothers, whose "Charlotte Web" strain was shown to be very effective in the case featured by Dr. Gupta.

**Procedures**

Prior to coming into my office, parents are required to fax over their child's medical records for review. They fill out a questionnaire and sign an informed consent form. We talk about which medications they've tried, what has helped and what has not helped. Is there is a typical pattern to the child's seizures? Do they occur more when the child is awake or asleep? What kinds of seizures does the child have? How are the medications and seizures affecting their child's development? Have they tried cannabis medication yet?

After this evaluation, I decide if the patient qualifies for medical cannabis based on California law and if I think the child may benefit from medical cannabis. If the answers to these two questions are yes, the child is approved and receives a letter of recommendation to use medical cannabis. The parents receive caregiver letters.

I educate the parents about what we know so far about CBD and the endocannabinoid system. It's important that they understand that although clinical trials are lacking, there's a scientific basis for what we're doing.

I explain that I have very high standards for the medication they are going to give their child. They cannot give untested preparations of CBD. In the world of western medicine we have a sense, as consumers, of being protected when we walk into a pharmacy and pick up a medication. We rely on the pharmacist and the companies that make and distribute drugs to produce a clean, consistent product that contains exactly what the label says it does.

Unfortunately, the state of California hasn't done much to regulate who can produce and distribute marijuana as medicine. It is definitely a "buyer-beware" situation. I insist they only use tested preparations, and I explain to them how to read the results of a cannabis lab test report.

For various reasons my edict sometimes gets ignored. I had one family that had obtained medication from a local cannabis dispensary. It had not been tested and I insisted that before giving another dose, they have it evaluated by a cannabis testing facility. The test results showed that the oil contained 9% rubbing alcohol! Not all oils are contaminated but the only way to be sure is to have the oil tested prior to use.

The oil made from Charlotte's Web has a CBD-to-THC ratio of about 25-to-1. The Stanley brothers authorized Ray Mirzabegian of Los Angeles to grow Charlotte's Web plants and produce oil for distribution in California. As of November, 2014, Mirzabegian was providing oil for 81patients. Another 1175 were on his waiting list.

Some of my patients learned online about other California collectives providing CBD-rich oil from a strain called "ACDC," which has a similar CBD:THC ratio to Charlotte's Web and is equally effective. But in my experience, its producers have not been meticulous and patients have reported occasional inconsistencies. One week I had numerous phone calls from parents reporting that their children were acting "high." This is just not acceptable.

Parents ask if they should test every bottle. This is difficult because in addition to paying out of pocket for the oil, the added expense of testing every bottle becomes prohibitive.

**Dosing**

Realm of Caring developed a dosing protocol for children on Charlotte's Web that parents are following. For most epilepsy patients, starting dose is 0.5 milligrams per pound per day, divided into three doses to be given at eight-hour intervals (ideally). Thus a 40-pound child would start at 20 milligrams per day divided into three doses. (In pediatric medicine, everything is based on weight because children can outgrow their dose as they gain weight.)

After starting on CBD oil, the children are observed for one or two weeks. Patients whose seizures are less frequent —for example only three seizures a month— may be observed for a longer period without increasing the dose. Most of the patients I see have daily seizures, which enables parents to tell quite quickly if there is any benefit from the oil. Parents are asked to keep a diary or calendar of seizures and improvements and to check in every one to two weeks

If the child is doing well, after a week or two the dose is titrated up by increments of 0.5 milligrams per pound per day. It appears from the data collected in Colorado that the therapeutic range is 2 – 6 mg per pound per day for many of the children that respond well to CBD treatment.

Some patients do need higher doses to achieve good results. One little boy was still having about 20 seizures a month on three anti-epileptic drugs. With Charlotte's Web oil he became seizure free for six months at a dose of 7.5 milligrams per pound per day, and he has been weaned off almost all of the seizure medications.

In Colorado one patient has gone as high as 8 milligrams per pound per day.

Doctors using GW Pharmaceuticals' Epidiolex reportedly have gone as high as 24 milligrams per kilogram per day in an FDA-approved context.

*continued on next page*

*Bonni Goldstein, MD, sees patients in an office in Lawndale (Los Angeles County) and is the director of the Canna-Centers chain of clinics, with five offices in California. She graduated from the Robert Wood Johnson Medical School in New Jersey and did her internship, residency and Chief Residency at Childrens Hospital Los Angeles. She worked in Critical Care Transport and Pediatric Emergency Medicine for 12 years before becoming a medical cannabis specialist.*

## About Epilepsy

Epilepsy is a condition of recurrent, unprovoked seizures. The seizures may result from a hereditary tendency or a brain injury, but often the cause is unknown. Many use the term "seizure disorder" instead because "epilepsy" seems more serious or stigmatized. However, almost all seizure disorders are epilepsy. A person with epilepsy has had two or more unprovoked seizures, regardless of seizure type.

An estimated 65 million people worldwide are afflicted with epilepsy —some 2.2 million in the U.S. When seizures cannot be eliminated by medication, epilepsy is said to be "refractory" or "intractable" or "treatment-resistant" or "catastrophic." Approximately one-third of all epilepsy cases are refractory.

Many types of epilepsy have been defined in terms of age of onset, seizure types and where they arise in the brain, EEG findings, family history, and neurological history, among other factors.

Seizures are characterized as "generalized" or "partial."

**Generalized seizures** begin with a widespread, excessive electrical discharge involving most or all of the brain.

Absence Seizure: A brief space-out —an episode usually lasting a few seconds, sometimes associated with automatic movements of the hands or mouth, formerly called "petit mal" seizures.

Atypical Absence Seizure: A staring episode that usually lasts longer than 10 seconds and occurs in children who have other types of seizure, lower than average intelligence and difficult to control epilepsy.

Myoclonic Seizure: A brief jerk or series of jerks that may involve a small part of the body such as a finger, hand or foot, or the shoulders or upper arms.

Atonic Seizure: A sudden loss of muscle tone throughout most or all of the body which may cause the head to drop suddenly, objects to fall from the hands, or the person to fall to the ground.

Clonic Seizure: Rhythmic jerking movements of body parts such as the arms or legs.

Tonic Seizure: A stiffening of the body and/or limb, often resulting in a fall if the patient is standing.

Tonic-Clonic Seizure: Whole body stiffening with simultaneous rhythmic jerking of the arms and legs, usually lasting at least one minute and also incuding loss of consciousness. After this type of seizure, the patient typically enters a state of confusion and fatigue lasting 30 minutes or longer. Also known as a "grand mal" seizure.

**Partial seizures** begin with an abnormal electrical discharge restricted to one region of the brain.

Simple partial seizure: An episode of altered sensation, cognitive function, or motor activity during which the patient is fully alert. Patients usually call these seizures "auras" and symptoms vary depending on the brain region involved.

Complex partial seizure: An episode altered behavior, sensation or motor activity during which alertness and responsiveness are also compromised. The motor activity may consist of repetitive automatic movements of the face or limbs, or "automatisms." Often patients are unaware of these seizures.

A partial seizure can develop into a tonic-clonic or "grand mal" seizure.

**Types of Epilepsy**

Temporal Lobe Epilepsy
Frontal Lobe Epilepsy
Parietal Lobe Epilepsy
Occipital Lobe Epilepsy
Primary Generalized Epilepsy
Idiopathic Partial Epilepsy
Symptomatic Generalized Epilepsy
Progressive Myoclonic Epilepsy
Reflex Epilepsy
Febrile Seizures
Benign Rolandic Epilepsy
Juvenile Myoclonic Epilepsy
Infantile Spasms
Lennox-Gastaut Syndrome
Childhood Absence Epilepsy
Benign Occipital Epilepsy
Mitochondrial Disorders
Landau-Kleffner Syndrome
Rasmussen Syndrome
Hypothalamic Hamartoma & Epilepsy

*Source: NYU Langone Medical Center Comprehensive Epilepsy Center*

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**THC free preparation**

Concentrated oil is the formulation easiest for the parent giving a dose. When you're giving close to four milligrams per pound per day to a 50-pound child, you're giving up to 200 milligrams. If the oil only has 15 milligrams per milliliter, you're giving that child a lot of oil. In large quantities, even healthful olive oil or coconut oil can cause diarrhea.

*Many people think that seizure reduction is the goal of treatment, but it's only part of the goal.*

Many people think that seizure reduction is the goal of treatment, but it's only part of the goal. The effects of the conventional anti-epileptic drugs (AEDs) can be debilitating —lethargy, developmental delay, liver damage and more. The ultimate goal for pediatric epilepsy patients is freedom from seizure and the side effects of the AEDs. Interestingly, many parents whose children are having success with CBD oil to treat epilepsy are also reporting that their children have improved sleep, improved appetite, more alertness, and developmental progression. It is these other beneficial effects that make CBD a wonderful option for children suffering with seizures.

**Drug Interactions**

CBD has not been shown to be a pro-convulsant in 21 preclinical and laboratory studies (see below). If a patient using CBD has an increase in seizure activity, it is likely from an interaction with other AEDs that the patient is taking.

Drug interactions are very complex. Each patient is on a different drug regimen and/or special diet. There are many variables: the patient's metabolism, the other medications, the patient's endocannabinoid system, and the profile of the particular cannabis product.

CBD is an inhibitor of the P450 enzyme system, and affects the rate at which other drugs are metabolized. Unfortunately, research is lacking on how CBD interacts with most of the other anti-epilepsy drugs in the liver but there are researchers who have started looking at these very important reactions.

A reassuring fact has been reported by G.W. Pharmaceuticals, the British company that makes Epidiolex and also makes Sativex, which is 50% CBD and has been approved for use in 27 countries to treat pain and spasticity from Multiple Sclerosis. Sativex has been used for 30,000 patient-years by people taking concommitant drugs and there have been no confirmed adverse consequences due to drug-drug interactions.

A journal article from 1977 suggested that CBD potentiated the effects of phenytoin (Dilantin) and phenobarbital, but reduced the anticonvulsant potency of Librium, Clonazepam, Trimethadione, and Ethosuximide.

Laboratory testing has shown that some but not all patients on CBD oil can have decreased Depakote levels and decreased felbamate levels with CBD. It appears that CBD interacts to increase Onfi (clobazam) levels.

**Some parents using THCA**

THCA is the raw, unheated, non-psychoactive phytocannabinoid that converts to THC when heated. THCA has been shown to be a significant anti-inflammatory. There are tested THCA preparations that have become available and have been claimed to have anticonvulsant properties. There are at least five patients in my practice who added THCA to the CBD treatment regimen and had improved seizure reduction.

Treating pediatric epilepsy patients is very complicated. Treatment varies case-by-case, day-by-day and week-by-week. Weaning a child off an anti-epileptic drug involves an act of faith on the part of the parents who have to deal with the withdrawal symptoms. For example, one of my patients achieved an 80% reduction in seizures. When the parents started to wean one of the AEDs that she was on, she had an increase in number of seizures. After about one week, she improved and seizures reduced again. Parents reported that after this difficult week, she was much more alert and responsive. And now the hope is that seizure reduction due to CBD will resume.

**Preliminary Findings**

In June 2014 I reported on what I had learned about cannabis in the treatment of pediatric epilepsy at events put on by the Realm of Caring Foundation and the Epilepsy Foundation of Los Angeles. I reviewed the charts of the 93 patients that I approved to use CBD oil for epilepsy and who had been on the oil for at least three months.

Twelve of the children were on oil from Realm of Caring Foundation (Charlotte's Web oil). Nine of the 12 had reduction in severity and frequency of seizures, and some were in the process of weaning off other medications.

Forty-one children were on AC/DC oil and the success rate was very similar —31 out of 41 reporting reduction in frequency of seizures. One child in this group was seizure free.

Ten children were using other CBD-rich oils, obtained from small collectives. Six experienced seizure reduction.

Twenty-two of the families had not started oil and were waiting for Charlotte's Web to become available.

Eight patients had started taking CBD-rich oil from other sources but had stopped, six for financial reasons.

*Some patients do not show up as seizure-reduction statistics because the frequency of seizures hasn't gone down —but severity and recovery time have gone down.*

On average, the patients had been put on 10 anticonvulsants over the course of their young lives. At present they were on between one and four AEDs. Only one out of the 93 patients was not taking pharmaceuticals at the time I collated my data.

A point worth repeating: some patients do not show up as seizure-reduction statistics because the frequency of seizures hasn't gone down —but severity and recovery time have gone down. Parents may report, "When he has a seizure he's not wiped out for three hours." Each case is so individual.

**Report to the Society of Cannabis Clinicians**

In September 2014 I described my work with pediatric epilepsy patients to colleagues in the Society of Cannabis Clinicians at a meeting in San Francisco. I had by then seen some 200 children with almost every type of Epilepsy diagnosis .

My patients are concurrently being treated by a pediatrician and a neurologist and may be seeing other specialists such as geneticists. Almost all have been categorized as "refractory" or "intractable" cases, meaning anti-epileptic drugs have not eliminated their seizures. Almost all have been on multiple medications with no improvement.

A study published in the New England Journal of Medicine in 2000 showed that the chances of achieving freedom from seizures diminishes sharply with each drug tried. Whereas 47% responded to the first-line drug they were treated with, the response to a second drug —either substituted or added— went down to 13%. The third drug helped only 4% of patients.

The burdens of refractory epilepsy include poor quality of life, the debilitating side-effects of medications, cognitive decline, physical injuries from falling, psychosocial dysfunction, a restricted lifestyle —adults can't drive, which makes living in our society very difficult— and increased mortality: the idea that you're going to drop dead any day now.

SUDEP —Sudden Unexpected Death in Epilepsy— has been explained to my patients by their neurologists. Those who are teenagers and young adults live with this possibility. One patient in her early twenties said to me, "I could have a seizure tonight and not wake up tomorrow."

With cannabis medicine you can offer hope that patients

*The chances of achieving freedom from seizures diminishes sharply with each drug tried.*

who have failed all other options that they may get some control over their seizures and possibly lead a normal life.

The side effects of the anti-epilepsy drugs described by my patients and their families include lethargy and somnolence, loss of focus, learning and memory problems, loss of speech, loss of social skills and motor skills, incontinence, insomnia, anorexia, and failure to thrive. Felbamate can cause aplastic anemia and or liver failure. Vigabatrin can cause permanent loss of vision.

Parents have reported that their child seemed to be tolerating the first one or two drugs, but then they'll add another drug and they stop talking and stop walking, it just shuts them down.

**Endocannabinoids and Epilepsy**

Epilepsy —like any given medical problem— will remain "treatment resistant" if the prescribed medications are not targeting the appropriate metabolic system(s). There is ample evidence that the endocannabinoid system plays an important role in modulating excitatory signals in the brain.

To cite but a few examples, in 2008 Hungarian researchers compared tissue from epileptic patients who had decided to undergo brain surgery to tissue from the brains of people who died naturally. Controlling for age and health status, they found that the level of endocannabinoids in tissue removed from the epileptics was 60% lower than in brain tissue from the cadavers. The strong implication is that a lack of endocannabinoids is associated with loss of neurotransmitter control.

In 2010 Andrea Romigi and colleagues at the University of Rome tested spinal fluid from patients with newly diagnosed temporal-lobe epilepsy and found lower-than-normal endocannabinoid levels. These studies and others suggest that some types of epilepsy are associated with an "endocannabinoid deficiency syndrome." (The concept of an endocannabinoid deficiency syndrome underlying many disorders was introduced by Ethan Russo, MD, himself a pediatric neurologist.)

Because CBD can enhance endocannabinoid tone without inducing psychoactivity, it became a compound of interest to far-sighted medical researchers. In the 1970s and '80s, in addition to animal studies, there were several small, promising studies in Brazil of CBD as a treatment for people with seizure disorders.

A 1978 paper co-authored by Raphael Mechoulam described the treatment of nine patients —four with CBD (200 milligrams/day) and five with placebo. Two of the four CBD patients were seizure-free during the test period and suffered no toxic side effects. None on placebo reported improvement.

In 1980 J.M. Cunha et al treated 16 refractory tonic-clonic seizure patients. Eight received 200-300 milligrams of CBD per day. Of these, three became seizure free, four had seizure reduction, and one was unchanged. In the placebo group, one patient had seizure reduction, seven were unchanged.

"It seemed very promising," said Mechoulam looking back decades later, "but unfortunately, nothing has been done ever since. To the best of my knowledge, nobody has done any work on cannabidiol in the clinic on epilepsy, and I just wonder why?"

At the 2005 meeting of the International Association for Cannnabinoid Medicine, Italian researchers led by A. Pelliccia described an open study ("modulating administration and titration schedules on a case-by-case basis, according to clinical response") in which 18 children with intractable epilepsy were treated with a low dose of CBD in corn oil.

The results were very promising. No patients discontinued due to side effects. Most obtained seizure reduction of 25% or more. And, according to Pelliccia: "in all CBD-

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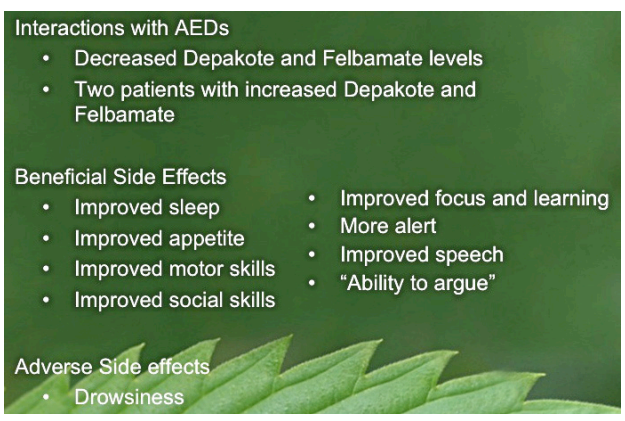
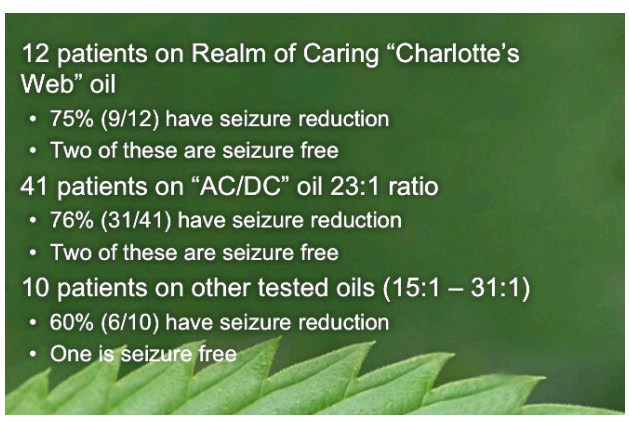



**Slides summarizing Dr. Goldstein's unpublished results were part of her presentation to the Epilepsy Foundation of Los Angeles and the Realm of Caring Foundation in June. Approximately two-thirds of the pediatric epilepsy patients whose cannabis use she has been monitoring have experienced seizure reduction.**

## *Treating Pediatric Epilepsy* *from previous page*

treated children, a clear improvement of consciousness and spasticity (whenever present) was observed.

"However, only nine out of these are currently on treatment, since the parents of the remaining children, although appreciating the improvement of their offspring, not only concerning the fits but also the awareness and the muscular tone, preferred to discontinue due to the economic overcharge induced by the treatment (approximately 300 Euros per month)."

This heartbreaking situation —parents unable to afford a helpful medication— is one I have encountered in my practice. As noted, the issue of affordability should not be ignored by clinicians.

When G.W. Pharmaceuticals got approval from the British government to develop cannabis-based extracts for clinical trials in 1998, the company began funding lab studies to establish the safety of cannabidiol and other so-called "minor" cannabinoids. G.W. provided purified CBD and CBD extracts to many labs, where scientists studied the effects on cell lines and mice, and the mechanism of action.

In 2013 one of the G.W.-supported researchers, Ben Walley of the University of Reading, reviewed the preclinical data (see graphic at top of page) and found no evidence —zero—that CBD acts as a pro-convulsant. To a physician helping patients figure out appropriate dosing levels, this is important information.

G.W.'s interest in CBD and other possibly beneficial cannabinoids inspired U.S. activists to study the contents of marijuana being grown for distribution by dispensaries. O'Shaughnessy's reported in 2010 that about one in 700 varieties being tested by analytic chemistry labs in California and Colorado contained four percent or more CBD. A few plant breeders crossed these "CBD-rich" strains to create increasingly high CBD-to-THC ratios.

By 2013 there were enough epilepsy patients using CBD to inspire a data-collection effort by Stanford University neurologists B.E. Porter and C. Jacobsen that was published in Epilepsy & Behavior in December 2013.

They looked at results from 19 Colorado patients using oil from Charlotte's Web. Thirteen were Dravet's patients, four had Doose syndrome, and one each had Lennox-Gastaut syndrome and idiopathic epilepsy (meaning of uncertain origin). The average number of anti-epileptic drugs tried before CBD was 12.

Sixteen of 19 families reported a reduction in their child's seizure frequency while taking CBD-rich cannabis. Two reported complete seizure freedom. Eight reported a greater than 80% reduction in seizure frequency. (Interestingly, this corresponds to what Walley found in reviewing the animal studies.) Six patients in the Stanford survey experienced a 25-60% reduction.

Beneficial effects included increased alertness, better mood and improved sleep. Adverse effects included drowsiness and fatigue (which may have been brought on in part by AEDs. The authors didn't specify which child was on which pharmaceuticals.)

Also in December 2013, Drs. Margaret Gedde and Edward Maa, at a meeting of the American Epilepsy Society reported very promising results from 11 patients who had used oil from Charlotte's Web for three months. All the children experienced at least 20% seizure reduction. Nine had at least 75% reduction. Eight had at least 98% reduction. And five had 100% reduction. (Gedde notes that the patients in the study "were selected by the provider of the extract.")

**CBD's Anticonvulsant Mechanism of Action**

CBD does not act directly on the CB1 receptor. It works by multiple actions —what has been termed "polypharmacology," exerting various effects within different parts of the brain that might defuse seizures. I explain it in comparison to the AEDs that parents are all familiar with.

CBD blocks NMDA receptors, which are involved in excitation. Felbamate acts similarly.

CBD binds to GABA receptors, enhancing the inhibition of excitation —as do Felbamate, Depakote, Tegratol, Onfi, and Phenobarbital.

CBD stabilizes ion channels —as do Banzel, Lamictal, Dilantin, Keppra, and Trileptal.

CBD modulates calcium release in neurons, blocking the uptake of endocannabinoids in order to normalize endocannabinoid tone.

CBD counters inflammatory reactions that appear to increase neuronal excitability and impair cell survival. This is why the National Football League is reviewing a proposal that CBD be provided to players suffering head injuries. CBD is neuroprotective; it reduces oxidative stress and glutamate toxicity.

**Obtaining Medicine**

The question of where to get their oil and what to use is a family decision. It's hard to find consistent CBD growers in Southern California at this time [September 2014]. There are only a few suppliers of oil that seem to be consistent bottle to bottle. There have been instances of CBD oil products having similar CBD content but having different effects, as they are prepared from different CBD strains.

Having a producer who makes oil from one specific strain increases the likelihood of obtaining consistent medication from month to month. Certain terpenes (essential oils in the cannabis plant) are known to have beneficial medicinal effects. Beta caryophyllene, a terpene that binds to the CB2 receptor, is a potent anti-inflammatory that appears to work synergistically with CBD. Both Charlotte's Web and AC/DC strains contain high amounts of this terpene.

Anybody who is making oil should know that parents get it tested and share the lab results on websites. Some of these parents will get it tested at two or three different labs so they know what is in the oil that they are giving to their child.

Having a reliable supply, one that is available and won't be "out of stock," is also crucial. Patients who start CBD oil treatment may wean their children off other medications. It could be catastrophic if a child is weaned off their anti-epileptic drugs and the CBD oil supplier did not continue to provide the oil that had been working.

**Affordability**

Affordability is a major concern for most families. They are paying anywhere from $150/month for a small child and up to $1800/ month for an adult-sized teenager.

One oil provider in Southern California is trying to be consistent with concentrated oil made from AC/DC plants. Their oil costs nine cents per mg, which is relatively affordable. Other CBD-rich oils used by my patients cost between 17 cents and 33 cents per milligram.

Realm of Caring is subsidized by the Stanley Brothers Social Enterprises so they can make their oil available for five cents a milligram.

I have had five patients who have had to discontinue treatment because they could not afford the oil. These patients have remained on AEDs and are on the waiting list for more affordable oil from Realm of Caring.

Other patients are using lower-than-ideal doses because they're at their limits financially

**CBD use by Diagnosis**

Lennox-Gastaut Syndrome: Of 10 patients with LGS, ages two to 14, the parents all reported > 25% seizure reduction. Parents also reported that their children were more alert, more interactive, happier, and had quicker recovery from seizure. Eight of the 10 were able to wean AEDs, two got off the ketogenic diet. There were no reports of negative side effects.

There were eight Dravet patients, ages four to 20. Four of reported 75-90% seizure reduction. One reports 35% reduction. Three report no change. All parents report improved alertness, behaviors, memory, ability to learn, better speech, improved social and motor skills, improved appetite and sleep. One parent reported "better sense of humor." Half have been able to wean AEDs. There were no reports of negative side effects.

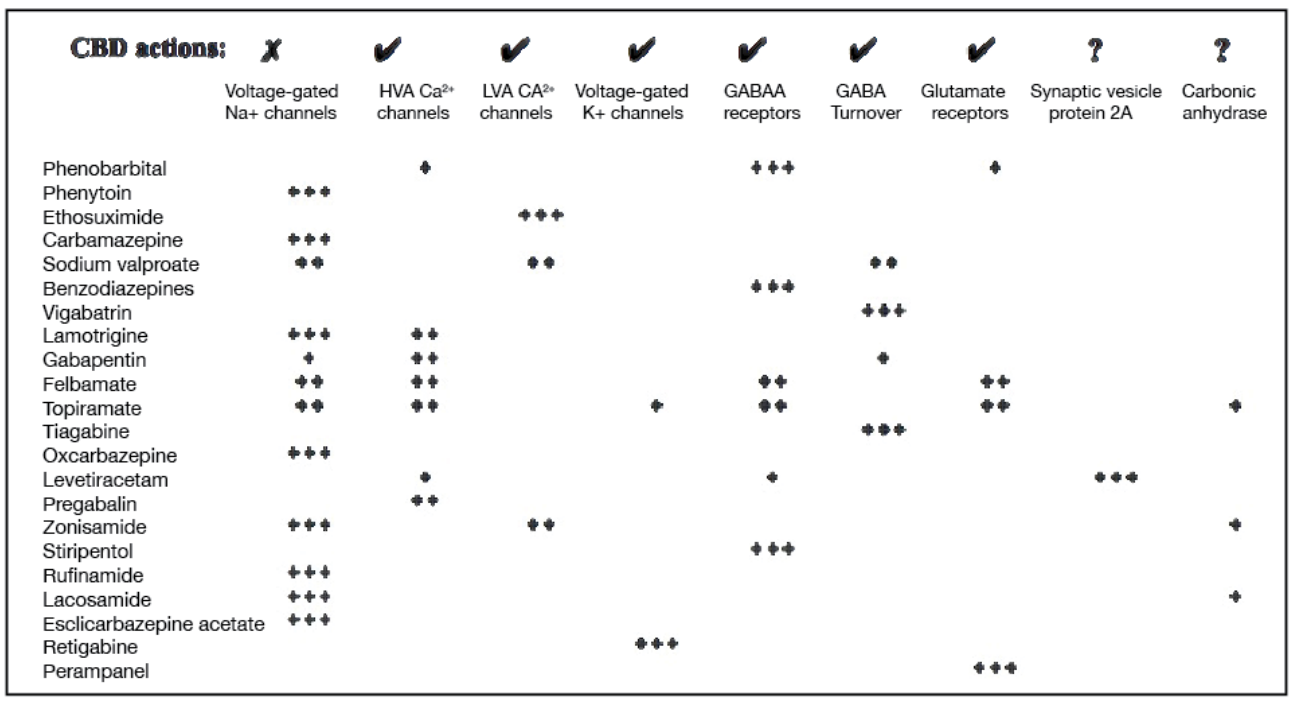
Of nine patients with other genetic syndromes, ages two to 17 years, one was seizure free. Four reported 75-90% reduction in frequency. Three reported 50% reduction. One reported no change. Most reported improved alertness, better sleep and appetite. One parent reported side effect of fatigue. Six of nine weaned at least one AED.

Of four patients with Infantile Spasms (West's Syndrome), ages nine to 18 months, one was seizure free, two had 80-90% reduction, one reported no effect from CBD. All parents reported improved development and better eye contact. All reported no negative side effects. Significant development takes place in the first year of life. Many parents state that development is arrested when their very young child has frequent seizures. With reduction of seizures with CBD, development can continue to move forward.

Tuberous Sclerosis: one patient soon after starting CBD was able to wean off Onfi, reduce trileptal, and had 75% fewer seizures. She improved in that she began trying to vocalize and interact with her caregivers.

| Compound | Species | Studies | Dose | Anticonvulsant | No effect | Proconvulsant |
|---|---|---|---|---|---|---|
| THC | 6 | 31 | 0.25-200 mg/kg | 61% | 29% | 10% [1] |
| CBD | 2 | 21 | 1-400 mg/kg | 81% | 19% | 0% |
| Other plant cannabinoids | 2 | 7 | N/A | 100% | 0% | 0% |
| CB1 agonists | 2 | 55 | N/A | 73% | 18% | 2% |

**Summary of preclinical evidence was presented by University of Reading pharmacologist Ben Walley at the October, 2013, conference on Cannabidiols and Epilepsy at NYU. "Studies" refers to the separate conditions, models, and designs reviewed. In none of the 21 projects involving CBD or CBDV did researchers see a proconvulsant effect.**




**CBD acts in ways similar to various Anti-Epilepsy Drugs listed at left. In this chart developed by AJ Hill and colleagues, + signs indicate the relative strength of the interactions (row at top) that have been observed in the lab. "This is a slide that parents find very useful," according to Goldstein. "Instead of having to take all these different drugs, they can get many of the benefits with one medication."**

**P.S. 3/22/15:** As of December 2014 there was no longer a waiting list for the CBD-rich oil made from the Charlotte's Web strain by the Realm of Caring Foundation. Good quality CBD rich oil from the ACDC strain has also become readily available in Southern California. I have seen an additional 100+ pediatric patients with refractory epilepsy since reviewing my files for this article and will be reporting on their results after three months of treatment and observation. Interestingly, a few patients who have reported excellent results have found, after 9 months or so, an increase of seizures or lethargy that appears to be unrelated to any other cause. Parents in Colorado also noticed this phenomena and found that stopping CBD for a few days, then restarting at a slightly lower dose (10-15% less) completely resolved the issues. It might be that there may be a point at which the endocannabinoid system is "full" and does not need as much cannabinoid medicine. This makes sense as the endocannabinoids are produced "on demand" in response to a trigger. Presumably by taking a break from the CBD oil or decreasing the dose, the endocannabinoid system can reset itself. Research into this phenomenon is greatly needed. —*B.G.*