High times for medicinal marijuana

8 June 2008

On Oct. 19, 2009, the U.S. Justice Department announced that federal prosecutors would not pursue medical-marijuana users and distributors who comply with state laws, formalizing a policy change from the Bush Administration to the Obama Administration.

Currently, 23 states and the District of Columbia allow doctors to prescribe medical marijuana to patients suffering from ailments ranging from AIDS to glaucoma, and in Maryland a prescription can soften punishment if a user faces prosecution. But until now those laws didn't provide any protection from federal authorities.

Legalized Medical Marijuana

Medical marijuana is not new, and the medical community has been writing about it for a long time.

As early as 2737 B.C., Emperor Shen Neng of China was prescribing marijuana tea for the treatment of gout, rheumatism, malaria and, oddly enough, poor memory. The drug's popularity as a medicine spread throughout Asia, the Middle East and down the eastern coast of Africa, and certain Hindu sects in India used marijuana for stress relief. Ancient physicians prescribed marijuana for everything from pain relief to earache to childbirth. Doctors also warned against overuse of marijuana, believing that too much consumption caused impotence, blindness and "seeing devils."

Pharmaceutical companies in the U.S. including Bristol-Myers Squib and Eli Lilly used cannabis in medicines – widely sold in U.S. pharmacies – to treat insomnia, for example, or migraines and rheumatism. Between 1840 and 1900, U.S. scientific journals published hundreds of articles touting the therapeutic benefits of cannabis.

Marijuana has been used as medicine since ancient times, as described in Chinese, Indian and Roman texts, but U.S. drug laws in the latter part of the 20th century made no room for it. In the 1970s, many states passed symbolic laws calling for studies of marijuana's efficacy as medicine, although virtually no studies ever took place because of the federal prohibition.

In 1988, the Drug Enforcement Administration's administrative law judge, Francis Young, concluded that "marijuana, in its natural form, is one of the safest therapeutically active substances known to man."

“If marijuana were a new discovery, without cultural and political baggage, "it would be hailed as a wonder drug," wrote Dr. Lester Grinspoon, a Harvard psychiatrist, in 2007.

Since California became the first state to legalize medical marijuana in 1996 with Proposition 215 -- the Compassionate Use Act -- nineteen states and the District of Columbia have followed.

By approving the use of marijuana as a medicine — with varying kinds of restrictions — these jurisdictions are bypassing the federal government's elaborate processes for approving medicines.

If you want to understand why it's happening, you should spend some time with Ellen Lenox Smith of suburban Rhode Island: a lively, petite, 60-year-old grandmother, former schoolteacher and one-time master swimmer.

When you meet Smith, you don't suspect anything's seriously wrong with her health. But in fact, she has two incurable diseases: One, called sarcoidosis, is ravaging her lungs. The other makes her tendons and ligaments loose and fragile.

"My knee tore, and two weeks later the other knee tore," Smith says. "And the same thing with my shoulder. It was one shoulder and then the other shoulder. So I was tearing like tissue paper, and no one knew why."

After years of misdiagnosis and surgical repairs, Smith learned she has a rare genetic disease of connective tissue called Ehlers-Danlos syndrome.

"My condition causes pain throughout the entire body," Smith says. Most people with Ehlors-Danlos "live on morphine and OxyContin," she says, but she has bad reactions to these and nearly all other painkillers. "I can't tolerate them."

Feeling desperate with pain and suffering sleepless nights, Smith consulted pain specialist Dr. Pradeep Chopra. This was just after Rhode Island became the 11th state to legalize medical marijuana. Chopra had never recommended marijuana to a patient, and he never imagined he would.

But in Smith's case, he says, "she had absolutely no other option. So very, very hesitantly, I said, 'Listen, why don't you try medicinal marijuana?' "

Because of her lung condition, she couldn't smoke it, so she soaked it in oil and stirred the oil into applesauce.

“I took this oil, went to bed, and the next thing I know, it was morning," Smith says. "I had literally slept through the entire night for the first time in months."

She's used marijuana ever since.

Some researchers believe patients who use marijuana medically do have psychoactive effects, but they have the effect of shifting patients' attention away from their pain, perhaps in addition to a direct pain-relieving effect. JoAnne Leppanen of the Rhode Island Patient Advocacy Coalition says: "What pain patients tell me is, 'Cannabis does not get rid of my pain. It's still there. But I don't care so much.' So it's affecting their mental attitude."

For Smith, relief is far from total, but she can deal with her pain now, especially since she sleeps well. Smith says marijuana has saved her life.

"My husband says it, too," she says. "I don't think I'd be here. I think I probably would have passed away if I didn't have this drug. There was nothing — nothing left to help me."

Chopra believes marijuana should be available to patients with no other good options. It's the patients who are driving this movement, he says.

"The people have spoken," Chopra says. "It's basically the people who have come up and said, 'It does help us, look at us, we're doing well.' They're telling the establishment, 'You're wrong,' and the establishment has listened to them."

The science of marijuana

The science of marijuana--especially its potential medical uses--is malleable because it's so young and so contradictory.

It's fairly settled science that pot has analgesic and anti-nausea properties, which is why it can be so soothing for people undergoing chemotherapy or suffering from pain. But does that mean it's harmless?

Scientists agree on one thing: the active ingredient in marijuana, THC, has some healing powers. In 1985, the U.S. Food and Drug Administration (FDA) approved dronabinol, an oral form of synthetic THC, to treat chemotherapy-induced nausea. Dronabinol, marketed as Marinol, is a pill. A few years later, the pill also won FDA approval to stimulate the appetite of people wasting away from AIDS or cancer.

The debate, medically speaking, is about smoking a plant or swallowing a pill.

Government scientists agree research shows smoking marijuana gets THC into the bloodstream faster than a pill. But the FDA argues that marijuana must go through the same hurdles as any medicine to be proven safe and effective, and that it's impossible to ensure the dose and potency of something that grows wild. The FDA has never approved any medicine to be smoked.

Smoking joints does not seem to pose as many pulmonary risks as smoking cigarettes, in part because people simply smoke fewer of them. One large study in 2006 found no increased risk of lung cancer. But a French study in 2009 found an "independent role of cannabis in the

development of lung cancers." A 2009 study in the U.K. concluded that acetaldehyde, which is present in both marijuana and tobacco smoke, can cause DNA damage "with the possibility to initiate cancer development."

Another U.K. study showed that the anti-inflammatory properties of cannabis may have an anti-cancer effect. And a 2009 study in Spain found that tetrahydrocannabinol (THC), the main intoxicating component of pot, can lead human brain-cancer cells to self-destruct—though the study involved introducing the cells into mice and treating them with THC.

A recent British study looked at how users are affected by different ratios of THC and cannabidinol (CBD), pot's other principal intoxicant. It's THC that's behind a pot high's otherworldly edge—and also behind the paranoia and hallucinations it can cause. It's CBD that gives the drug its sedating power. The lower the concentration of CBD relative to THC, the worse the subjects in the British study performed on word-recall tests; the higher the concentration, the better they did. Graded on the generous curve required when all the subjects were wasted, the people with the mellower buzz were generally smarter. While there is some conflicting data, most studies do not find lasting effects on cognition.

No one has ever died of THC poisoning, mostly because a 160-lb. person would have to smoke roughly 900 joints in a sitting to reach a lethal dose. But that doesn't mean pot can't contribute to serious health problems.

A paper published in 2001 in the journal Angiology found 10 odd cases in France of heavy herb smokers who developed ischemia (an insufficient blood supply) in their limbs, leading in four cases to amputations. It's not clear that marijuana caused the decreased blood flow, but the vascular problems did worsen during periods of heavy use. Another 2001 paper, in Circulation, found a nearly fivefold increase in the risk for heart attack in the first hour after smoking marijuana--though statistically that means smoking pot is about as dangerous for a fit person as exercise.

Marijuana may directly affect the immune system, since one of the body's two known receptors for cannabinoids is located in immune cells. But the nature of the effect is unclear. A recent study showed that THC inhibits production of immune-stimulating substances.

Although pot's rep for diminishing short-term memory is deserved, it surprisingly may have therapeutic value in treating Alzheimer's disease. A 2008 study in rats showed that the anti-inflammatory effect of a THC-like compound might slow the progression of the degenerative illness. The compound may also promote the growth of new cells in aging brains.

And what about addiction? Can you get hooked on pot? The answer is yes—depending on how addiction is defined. There are substance addictions and process addictions—heroin vs. sex or

gambling, say—and they all target similar reward pathways in the brain. Heroin, alcohol and other substances, however, trigger violent withdrawal symptoms if the chemical is cut off, and that clearly doesn't happen with pot—to say nothing of sex and gambling.

Nearly everyone now goes by the broader definition of addiction in the Diagnostic and Statistical Manual—psychology's field guide to mental illness. The DSM describes addiction as compulsive use of a substance or repetition of a behavior despite repeated negative consequences.

The Institute of Medicine, the health arm of the National Academy of Sciences, said in a 1999 study that 32% of tobacco users become dependent, as do 23% of heroin users, 17% of cocaine users, and 15% of alcohol drinkers. But only 9% of marijuana users develop a dependence.

"Although few marijuana users develop dependence, some do," according to the study. "But they appear to be less likely to do so than users of other drugs (including alcohol and nicotine), and marijuana dependence appears to be less severe than dependence on other drugs."

Marijuana unquestionably causes cognitive impairment; nobody would smoke it for fun otherwise. Loss of memory and a decline in decision-making ability are the most pronounced effects, data confirmed anecdotally. How long the impairment lasts—whether a month or a lifetime—and to what degree are open questions. Use of marijuana has been linked clinically to the onset of depression, anxiety and schizophrenia; the link is especially strong in younger users and stronger still in young men with a predisposition to mental illness.

At least three recent studies have demonstrated that heavy pot smokers who quit can experience such withdrawal symptoms as anxiety, difficulty sleeping and stomach pain.

"There is clear evidence that in some people marijuana use can lead to withdrawal symptoms, including insomnia, anxiety and nausea," Dr. Sanjay Gupta, a neurosurgeon and CNN's chief medical correspondent, said in 2013.

On the other hand, the risk of becoming dependent on marijuana is comparatively low. Just 10% of those who have used the drug develop dependence. By comparison, 15% of drinkers become dependent on alcohol, 25% of heroin users get hooked, and a third of tobacco smokers become slaves to cigarettes.

According to Dr. Gupta, the issue is on the age of the user and its impact on the developing brain. "Young, developing brains are likely more susceptible to harm from marijuana than adult brains. Some recent studies suggest that regular use in teenage years leads to a permanent decrease in IQ. Other research hints at a possible heightened risk of developing psychosis.

"Much in the same way I wouldn't let my own children drink alcohol, I wouldn't permit marijuana until they are adults. If they are adamant about trying marijuana, I will urge them to wait until they're in their mid-20s when their brains are fully developed," Dr. Gupta said in 2013.

Controversy

But some think legalization is dangerous.

"Approving medical use of marijuana by political referendum is a slippery slope," says Joseph Califano, director of the National Center on Addiction and Substance Abuse at Columbia University and former US Secretary of Health, Education, and Welfare. "What's the next substance we'll approve by political referendum?"

"We have the best system in the world for clearing drugs in the Food and Drug Administration, and that's the system we should follow," he says.

The FDA specifically opposes smoking marijuana for medical purposes. But spokeswoman Karen Riley said that the FDA "is willing to consider proposals by investigators to conduct clinical trials using marijuana."

Scientists say doing research with marijuana requires patience, largely because the federal government still classes marijuana as a Schedule I controlled substance with no legitimate medical use. That status requires researchers to get a license from the Drug Enforcement Administration, part of the Justice Department. The DEA relies on the National Institute on Drug Abuse (NIDA) for advice on research proposals.

Dr. Glen Hanson, a former acting director of NIDA, who does drug research at the University of Utah and heads the Utah Addiction Center, is familiar with the scientific evidence on marijuana. Running through a list of things some people claim marijuana's good for, Hanson says there is legitimate support for many conditions.

Pain, for instance. "Yes, there's some significant evidence that it's useful in some types of pain," Hanson says. In patients with postoperative pain, THC is more effective than a placebo, and some reports suggest smoking pot may reduce the need for highly addictive opioids.

Multiple sclerosis? "That's more controversial," he replies. "There are clearly some individuals with multiple sclerosis who say that it helps them."

Glaucoma: "There is some [evidence], but again, controversial." Marijuana does reduce pressure on the eyeball, about 25%, but the drug isn't always practical as a glaucoma treatment. Many who have the disease are elderly and can't tolerate pot's tendency to raise heart rates.

Seizures: "Again, some evidence that it may be useful in dealing with some seizures."

Marijuana can also help people with spasticity (extreme muscle tension) and tremor due to multiple sclerosis and trauma. But the drug hasn't been rigorously compared with the standard antispastic treatments.

The list goes on. Forget migraines and insomnia, back pain and lack of appetite: pot is routinely sold as a cure for irritable-bowel syndrome, Tourette's, muscular dystrophy, herpes, diabetes, gonorrhea, bulimia, eczema and—oddly enough—both obesity and weight loss.

Hanson says there's evidence for some other claims, but not for others.

Already Canada and the U.K. have approved the use of Sativex, a cannabis-based spray for the nose and mouth that was developed by GW Pharmaceuticals, and it's in late-stage testing in the U.S. Sativex has been effective for pain from MS spasms and cancer treatment without causing the marijuana high.

One controversial ailment is PTSD. The Department of Veterans Affairs finds itself in a difficult position because some vets want to use marijuana to treat symptoms of post-traumatic stress disorder. Pot possession remains illegal under federal law. The VA says that as a federal agency its doctors can't recommend using it.

The problem is especially acute in New Mexico, where one-fourth of the state's more than 1,600 medical marijuana patients are PTSD sufferers.

Paul Culkin traces his PTSD back to 2004 when he was in Kosovo and part of an Army bomb squad. A car crashed into a business. The manager was inside trying to put out a fire. Culkin went in once to try to get him to leave, but he wouldn't go. The car bomb exploded. He recovered from the physical wounds, but years later the trauma of that moment can come back without warning.

He says the treatment he's received from the VA — mostly counseling and antidepressant medication — has helped. But, he says, marijuana also works well to relieve his anxiety.

To be legal in New Mexico, he had to go outside the VA system and pay for another doctor and a psychiatrist to recommend him for the state's medical marijuana program.

Culkin says he doesn't usually smoke the marijuana, instead choosing to dissolve an extract in hot chocolate or tea so he can control the dose better.

His wife, Victoria, says the marijuana has made a big difference.

"He's a different person. He's a better person. He's more open. He's more communicative," she says. "At one point, we almost got a divorce, and I can honestly say that I think medical cannabis saved our marriage and our family."

"There is no solid evidence that cannabinoids — that marijuana — is, in itself, an effective treatment for post-traumatic stress disorder," says Dr. David Spiegel, director of the Stanford Center on Stress and Health. "Before anyone can claim that, there needs to be some more solid research on that topic."

The thing scientists are really excited about, Hanson says, is the discovery that many organs in the human body and brain have receptors for the chemicals in cannabis, which was first made in 1988.

At the same time, Dr. Pradeep Chopra believes marijuana should be available to patients with no other good options. It's the patients who are driving this movement, he says.

"The people have spoken," Chopra says. "It's basically the people who have come up and said, 'It does help us, look at us, we're doing well.' They're telling the establishment, 'You're wrong,' and the establishment has listened to them."

Dr. Sanjay Gupta, a neurosurgeon and CNN's chief medical correspondent, had consistently been opposed to medical marijuana up until August 2013. Gupta, who recently traveled around the world to interview medical leaders, experts, growers and patients for a documentary on the subject, said that what he found was "stunning."

"Long before I began this project, I had steadily reviewed the scientific literature on medical marijuana from the United States and thought it was fairly unimpressive. Reading these papers five years ago, it was hard to make a case for medicinal marijuana. I even wrote about this in a TIME magazine article, back in 2009, titled "Why I would Vote No on Pot."

"I mistakenly believed the Drug Enforcement Agency listed marijuana as a schedule 1 substance because of sound scientific proof. Surely, they must have quality reasoning as to why marijuana is in the category of the most dangerous drugs that have "no accepted medicinal use and a high potential for abuse," Dr. Gupta said in 2013.

"I now know that when it comes to marijuana neither of those things are true. It doesn't have a high potential for abuse, and there are very legitimate medical applications. In fact, sometimes marijuana is the only thing that works. Take the case of Charlotte Figi, who I met in Colorado. She started having seizures soon after birth. By age 3, she was having 300 seizures a week, despite being on seven different medications."

Charlotte suffers from a debilitating genetic disease – Dravet syndrome - that left her unable to walk, talk or eat.

"Medical marijuana has calmed her brain, limiting her seizures to 2 or 3 per month. I have seen more patients like Charlotte first hand, spent time with them and come to the realization that it is irresponsible not to provide the best care we can as a medical community, care that could involve marijuana."

Paige Figi, Charlotte's mom, is now an advocate for medical marijuana, especially for children who suffer from medical conditions like Charlotte does. Figi says an oil extracted from a particular strain of marijuana has helped save her daughter's life. The specific strain of marijuana used to treat Charlotte, named Charlotte's Web, is from a variety of marijuana with

very little THC, the primary component that produces the high. Instead, the strain has very high amounts of another compound — cannabidiol, or CBD.

After trying every drug and therapy she and her husband could think of, they started Charlotte on a marijuana extract that contained high amounts of CBD. She now takes just a few milligrams of the oil each day in her food.

The results have been dramatic, Figi says. "She's 99 percent — almost 100 percent — seizure-free," she adds. "She has about one or two seizures a month now, [down] from 1,200."

But the marijuana extract isn't a cure. Charlotte and others with Dravet have a genetic disease they'll have forever. Figi says her daughter will never be able to live independently.

But Charlotte used to have to rely on a feeding tube, Figi says, and now can eat and drink on her own. She has a vastly improved quality of life.

For families like hers, Figi says Charlotte's Web and similar strains of marijuana represent a lifeline.

"It's brand-new, and it's very, very exciting for these parents who have nothing left," Figi says.

There's now a waiting list for Charlotte's Web, and the grower in Colorado is working to ramp up production.

About 100,000 U.S. children have intractable epilepsy—a treatment-resistant category of the disease characterized by uncontrolled seizures—and for some of their parents, medical marijuana has gained a reputation as a wonder drug. Fueled by success stories on Facebook and family blogs, these parents are acquiring marijuana through quasi-legal and illegal means.

Families from Florida and other states have even been moving to Colorado to get their kids started on the therapy.

Families like Cory Browning's, who bought a house in Breckenridge, Colorado.

Browning is a lawyer in north Florida whose daughter has Dravet syndrome and who has suffered from as many as 200 seizures a day.

In California, Ray Mirzabegian’s daughter Emily had her first seizure when she was five months old. By the time she was four, she was having hundreds of seizures a day. “Our lives were 60 percent in the hospital for years,” says Mirzabegian. Each seizure a child has can cause damage to the developing brain.

Over the years, Emily has been prescribed 12 separate medications—none seemed to help and most caused side effects, including depression, vision loss, insomnia and lethargy that left her “sitting on the couch in a vegetative state,” says Mirzabegian. The family tried a ketogenic diet,

which consists largely of fat, as well as acupuncture and Chinese medicine. They sent Emily's medical records to doctors in France and Iran, and even flew to the Dominican Republic where a doctor injected Emily with a pink liquid he claimed was filled with stem cells that would cure her epilepsy. The cost: $30,000 in traveler's checks. "We were so desperate we even went back for a second round," says Mirzabegian.

Meanwhile, the family met with eight neurologists, eventually finding Raman Sankar, chief of pediatric neurology at the University of California, Los Angeles, who diagnosed Emily with Dravet Syndrome, a type of epilepsy that, with related causes, kills up to one-fifth of sufferers before age 20.

Mirzabegian decided to give Charlotte's Web a shot, and he says the results were astounding. Nearly two years after she began a three-times-a-day treatment plan, Emily is down to four seizures per month and is off nearly all the prescription drugs.

He was so impressed with the results he decided to go into business with the Stanleys, who run the farm where Charlotte's Web was first discovered and produced. Mirzabegian became their first licensee outside of Colorado with his business in California. Mirzabegian now has his own facility, and the oil he gives Emily is from the plants he grows himself; he sells the rest to parents who visit his office. Demand for Mirzabegian's product is fierce, with a waiting list of 1,000 families; the Stanleys in Colorado have a waiting list of 12,000 families.

Among the patients who came to Mirzabegian's office on the days was the mother of a severely developmentally delayed 5-year-old boy who weighs 20 pounds. She paid $65 for a month's supply of Charlotte's Web. There was also a single mother who lives in fear that her son's doctor, who opposes the use of medical marijuana in place of pharmaceutical drugs, might report her to child protective services. The boy has intractable epilepsy and severe cognitive and physical delays. "There's no quality of life. This is like living death," the mother says later.

These parents are hoping pot can help where mainstream medicine has failed. Epilepsy costs individuals and institutions $15 billion a year. It is far more common than autism, multiple sclerosis or a host of other neurological disorders. And it kills more Americans every year than breast cancer—and yet the disease receives just 20 percent as much research funding from the National Institutes of Health. What's more, a third of people with epilepsy have an intractable drug-resistant type.

"We have been terribly and systematically misled for nearly 70 years in the United States, and I apologize for my own role in that," Dr. Gupta said in 2013.

http://edition.cnn.com/2013/08/08/health/gupta-changed-mind-marijuana (video)
http://america.aljazeera.com/watch/shows/live-news/2014/3/n-y-schools-mostsegregatedinamerica.html (video)
http://www.bbc.com/news/magazine-27299579 (video)

At least important parts of the establishment are listening. President Obama has said his administration has no interest in prosecuting doctors and patients who use marijuana — as long

as their state allows it. Attorney General Eric Holder formalized the policy with a memo to U.S. Attorneys in September 2009.

At the federal level, it's still 1985. Marijuana retains its status as a Schedule 1 controlled substance, the legal equivalent of heroin and LSD, with "a high potential for abuse" and "no currently accepted medical use."

The federal Drug Enforcement Agency (DEA) is estimated to have spent more than $10 million from 2005 to 2007 on raids on California dispensaries alone.

Federal law — in this case the ban on marijuana possession — always is supreme, but there are times states can choose to go their own way.

"What they're doing is perfectly legitimate," says Vanderbilt University law professor Rob Mikos. "It's just a passive form of resistance to federal authority."

Mikos says when it comes to using marijuana for medical purposes, our culture is changing and the states are leading the way.

But who is actually using medical marijuana?

No one doubts that medical marijuana has brought relief to the state's cancer patients, AIDS sufferers and MS victims. But these aren't the customers the industry is really serving. In 2010, Colorado health department records showed that only 2% of registered patients had cancer; 1% had HIV/AIDS. There were 94% who suffered "severe pain"—a catchall condition that can be entirely subjective and difficult for a doctor to measure or verify. Statewide, more than 70% of doctor recommendations were written by fewer than 15 physicians. Three out of four patients are men under 40. This patient profile—young males complaining of chronic pain—has been roughly the same in other medical-marijuana states like Montana and California.

Medical Marijuana Research

According to Dr. Sanjay Gupta, to do studies on marijuana in the United States today, you need two important things.

First of all, you need marijuana. And marijuana is illegal. You see the problem. Scientists can get research marijuana from a special farm in Mississippi, which is astonishingly located in the middle of the Ole Miss campus, but it is challenging.

The University of Mississippi was selected in 1968 as the United States' first, and only, legal marijuana farm. What makes the marijuana on the campus of the University of Mississippi unique is that it is grown, processed and sold by the federal government. This is the only such site under contract with the federal government. Marijuana is grown here legally for research being done by the National Institute on Drug Abuse in what is known as the Marijuana Research

Project. The stockpile represents the only source of pot allowed for researchers who want to conduct Food and Drug Administration-approved tests on using marijuana for medical purposes.

The DEA guards the 12-acre farm at Ole Miss as if it were plutonium. The entire complex is surrounded by multiple guard towers, two enormous barbed wire fences and countless security cameras. The marijuana grown here is for research, and it is where the federal government gets the marijuana it needs to supply the four current patients who are allowed by the federal government to use medical marijuana.

The second thing you need is approval, and the scientists I interviewed kept reminding me how tedious that can be. While a cancer study may first be evaluated by the National Cancer Institute, or a pain study may go through the National Institute for Neurological Disorders, there is one more approval required for marijuana: NIDA, the National Institute on Drug Abuse. It is an organization that has a core mission of studying drug abuse, as opposed to benefit.
