GASTRO-INTESTINAL DISORDERS AND MEDICAL CANNABIS

AmericansFor SafeAccess
Advancing Legal Medical Marijuana Therapeutics and Research

A Note from Americans for Safe Access

We are committed to ensuring safe, legal availability of marijuana for medical uses. Today over one million Americans are legally using medical marijuana—or "cannabis," as it is more properly called—under the care of their medical professional, and nearly half the country lives in a state where this treatment is an option. This publication series is intended to help medical professionals, patients and policymakers better understand how cannabis may be used safely and effectively as a treatment for many medical conditions. You will find information on:

While the federal prohibition of cannabis has limited modern clinical research and resulted in considerable misinformation, a scientific consensus on its therapeutic value has emerged, based on a growing body of successful clinical trials and preclinical research. The experience of patients, medical professionals and research has revealed that cannabis can safely treat a remarkably broad range of medical conditions, often more effectively than conventional pharmaceutical drugs. For some of the most difficult to treat conditions, such as multiple sclerosis and neuropathic pain, cannabis often works when nothing else does.

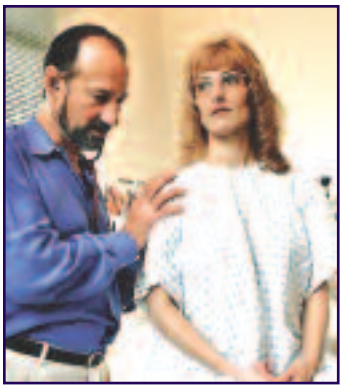
Many of its therapeutic uses are well known and documented, and medical researchers are learning more each day. Cannabis and its constituent components show potential to fight tumors, autoimmune disorders, and serious neurological conditions for which treatment options are limited. As of July 2014, 23 states and the District of Columbia have laws allowing its use under a doctor's supervision, and cannabis or a dose-controlled whole-plant extract of it is available by prescription in 11 countries and approved for 13 more.

This brochure is only a starting point for the consideration of applying cannabis therapies to specific conditions; it is not intended to replace the training and expertise of medical professionals with regard to medicine, or attorneys with regard to the law. But as advocates for the hundreds of thousands of patients who have found relief with cannabis, we know there are millions more for whom it may be the best medicine. For more information, see **AmericansForSafeAccess.org** or call **1-888-929-4367**.

Why Cannabis is Legal to Recommend

Medical professionals have a legal right to recommend cannabis as a treatment in any state, as protected by the First Amendment. That was established by a 2004 United States Supreme Court decision to uphold earlier federal court rulings that doctors and their patients have a fundamental Constitutional right to freely discuss treatment options. State rules for qualifying an individual patient for legal protections when using medical cannabis differ as to who may make the recommendation and for what conditions, as well as how that recommendation is communicated to state authorities. Medical professionals and patients should familiarize themselves with the laws and regulations in their state. ASA provides state-by-state resources at: AmericansForSafeAccess.org/state_by_state_recommending_cannabis.

Under federal law, cannabis may not be prescribed, but its therapeutic use can be recommended without any legal jeopardy. The court rulings that protect medical professionals stem from a lawsuit brought by a group of doctors and patients led by AIDS specialist Dr. Marcus Conant. The suit was filed in response to federal officials who, within weeks of California voters legalizing medical cannabis in 1996, had threatened to revoke the prescribing privileges of any physicians who recommended cannabis to their patients for medical use.[1] Dr. Conant contended that such a policy would violate the First Amendment, and the federal courts agreed.[2,3]



Angel Raich & Dr. Frank Lucido

What doctors may and may not do. In *Conant v. Walters*,[4] the Ninth Circuit Court of Appeals held that the federal government could neither punish nor threaten a doctor merely for recommending the use of cannabis to a patient.[5] But it remains illegal for a doctor to "aid and abet" a patient in obtaining cannabis.[6] This means physicians and other medical professionals may discuss the pros and cons of medical cannabis with any patient, and recommend its use whenever appropriate. They may put that in writing or otherwise participate in state medical cannabis programs without fear of legal reprisal.[7] This is true even when the recommending medical professional knows the patient will use the recommendation to obtain cannabis through a state program.[8] What physicians may not do is prescribe or provide cannabis directly to a patient[9] or say where or how to obtain it.[10]

Patients protected under state law, not federal. As of July 2014, 23 states and the District of Columbia provide legal protections for qualified individuals participating in their state medical cannabis program. However, all use of cannabis remains illegal under federal law, and in June 2005, the U.S. Supreme Court in *Gonzales v. Raich* ruled that state medical cannabis laws do not provide protections for patients and providers from federal pros-

ecution.[11] Under the Obama Administration, the Department of Justice has issued three memos providing guidance to federal prosecutors, each indicating that individual patients and caregivers should not be federal enforcement priorities. The latest memo indicates enforcement should be left to states so long as they have effective regulations in place for use and distribution. An analysis by ASA of existing state laws and local regulations found that all reflect the same general enforcement priorities as the 2013 federal guidelines.[12]

For assistance with determining how best to write or obtain a legal recommendation for cannabis, please contact ASA at 1-888-929-4367.

Medical Professionals Say Cannabis is Medicine

Thousands of studies published in peer-reviewed journals indicate cannabis has medical value in treating patients with such serious conditions as AIDS, glaucoma, cancer, epilepsy, and chronic pain, as well as a variety of such neurological disorders as multiple sclerosis, Parkinsonism, and ALS.

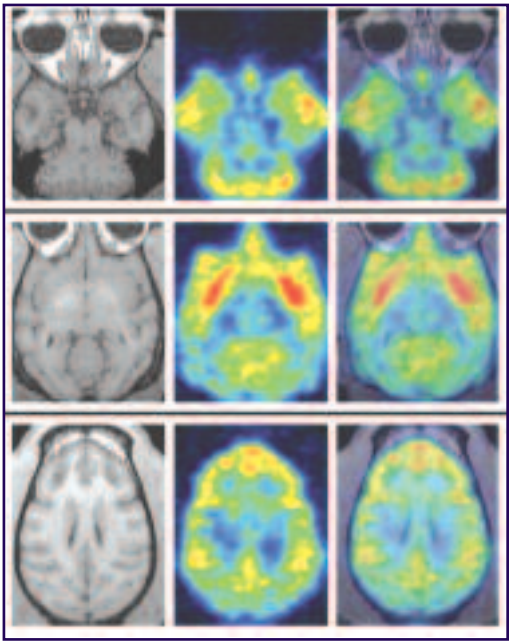
A 2013 poll conducted by the *New England Journal of Medicine* found that three out of four clinicians would recommend the use of medical cannabis for a hypothetical cancer patient.[13] The use of medical cannabis has been endorsed by numerous professional organizations, including the American Academy of Family Physicians, the American Public Health Association, and the American Nurses Association. Its use is supported by such leading medical publications as *The New England Journal of Medicine* and *The Lancet*. The International Cannabinoid Research Society was formally incorporated as a scientific research organization in 1991 with 50 members; as of 2014, there are nearly 500 around the world. The International Association for Cannabinoid Medicines (IACM), founded in 2000, publishes a bi-weekly bulletin and holds international symposia to highlight emerging research in cannabis therapeutics.

The safety and efficacy of cannabis has been attested to by numerous government studies and reports issued over the past 70 years. These include the 1944 LaGuardia Report, the Schafer Commission Report in 1972, a review commissioned by the British House of Lords in 1997, the Institutes of Medicine report of 1999, research sponsored by Health Canada, and numerous studies conducted in the Netherlands, where cannabis has been quasi-legal since 1976 and is currently available from pharmacies by prescription.

Scientific Research Advances

While modern research has until recently been sharply limited by federal prohibition, the last few decades have seen rapid change. More than 15,000 modern peer-reviewed scientific articles on the chemistry and pharmacology of cannabis and cannabinoids have been published, as well as more than 2,000 articles on the body's natural cannabinoids and the receptors they attach to.[14] The discovery of the endocannabinoid system (ECS) opened a door

to new understandings of how the body regulates internal systems and how the phytocannabinoids found in the cannabis plant interact with it. Endocannabinoids are crucial to bioregulation, and evidence suggests they play a role in inflammation, insulin sensitivity, and fat and energy metabolism, as well as chronic neurologic and immune conditions. The cannabinoid receptors CB1 and CB2 are identified targets for treating a remarkable variety of serious medical conditions.[15-18]



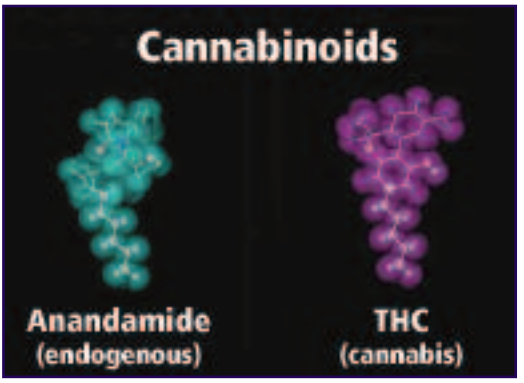
Cannabinoid receptors in the brain

A 2009 review of controlled clinical studies with medical cannabis conducted over a 38-year period found that "nearly all of the 33 published controlled clinical trials conducted in the United States have shown significant and measurable benefits in subjects receiving the treatment."[19] The review's authors note that the more than 100 different cannabinoids in cannabis have the capacity for analgesia through neuromodulation in ascending and descending pain pathways, neuroprotection, and anti-inflammatory mechanisms. Research into the therapeutic potential of cannabis and cannabinoids has expanded considerably in the past decade. As of May 2014, the Center for Medicinal Cannabis Research, a state-funded $8.7-million research effort at University of California campuses, had completed 13 approved studies. Of those, seven published double-blind, placebo-controlled studies examined pain relief, and each showed cannabis to be effective.[20]

No adverse health effects related to medical cannabis use have been reported, even among the most seriously ill and immune-compromised patients. Research on CD4 immunity in AIDS patients found no negative effects to the immune systems of patients undergoing cannabis therapy in clinical trials.[21] A complete health assessment in 2002 of four of the patients enrolled in the U.S. Investigational New Drug program who had used cannabis daily for between 11 and 27 years found cannabis to be clinically effective for each with no negative health consequences.[22]

In the United Kingdom, GW Pharmaceuticals has been conducting clinical trials for more than a decade with its cannabis medicine, Sativex® Oromucosal Spray, a controlled-dose whole-plant extract. GW's Phase II and Phase III trials

show positive results for the relief of neurological pain related to: multiple sclerosis (MS), spinal cord injury, peripheral nerve injury (including peripheral neuropathy secondary to diabetes mellitus or AIDS), central nervous system damage, neuroinvasive cancer, dystonias, cerebral vascular accident, and spina bifida. They have also shown cannabinoids to be effective in clinical trials for the relief of pain and inflammation in rheumatoid arthritis and also pain relief in brachial plexus injury.[23-26]



Plant and endogneous cannabinoids are similar

Sativex® was approved in Canada for symptomatic relief of neuropathic pain in 2005, in 2007 for patients with advanced cancer whose pain is not fully alleviated by opiates, and in 2010 for spasticity related to multiple sclerosis. As of 2014, Sativex has been made available or approved for named patient prescription use in 24 countries, including the UK, Spain, Italy and Germany.

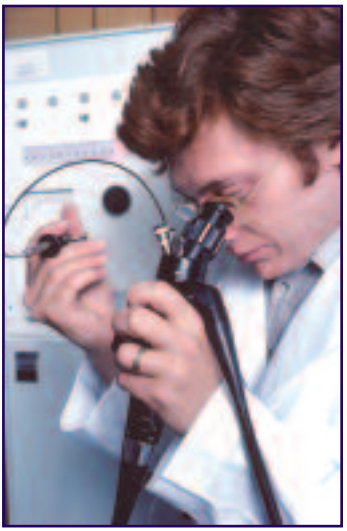
In the US, GW was granted an import license for Sativex® by the DEA following meetings in 2005 with the FDA, DEA, the Office for National Drug Control Policy, and the National Institute for Drug Abuse. Sativex® is currently an investigational drug in FDA-approved clinical trials as an adjunctive analgesic treatment for patients with advanced cancer whose pain is not relieved by opioids. In 2013, GW Pharmaceuticals received FDA approval to test a highly purified cannabinoid extract (cannabidiol or CBD) named Epidiolex® on a limited number of US children with seizure disorders. As of January 2014, seven US pediatric epilepsy specialists have been approved to treat 125 children with Dravet syndrome, Lennox-Gastaut syndrome, and other pediatric epilepsy syndromes.

CANNABIS AND GI DISORDERS

The effectiveness of cannabis and its derivatives for treating gastrointestinal disorders has been known for centuries. Recently, its value as an anti-emetic and analgesic has been proven in numerous studies and has been acknowledged by several comprehensive, government-sponsored reviews, including those conducted by the Institute of Medicine (IOM), the U.K. House of Lords Science and Technology Committee, the Australian National Task Force on Cannabis, and others.

The IOM concluded, "For patients . . . who suffer simultaneously from severe pain, nausea, and appetite loss, cannabinoid drugs might offer broad-spectrum relief not found in any other single medication."[27]

The most common gastrointestinal disorders—Irritable Bowel Syndrome and Inflammatory Bowel Disease—affect millions of people. The disorders are different, but they each cause a great deal of discomfort and distress and both can be disabling. Painful cramping, chronic diarrhea or constipation, nausea, and inflammation of the intestines are all symptoms of these GI disorders that can be alleviated by cannabis.



A doctor performing an endoscopy

Irritable Bowel Syndrome (IBS) is a common disorder of the intestines that leads to stomach pain, gassiness, bloating, constipation, diarrhea or both. Chronic, painful abdominal cramping is common. The cause of IBS is not known, and there is no cure. Researchers have found that the colon muscle of a person with IBS begins to spasm after only mild stimulation. IBS is at least partly a disorder affecting colon motility and sensation.

Inflammatory Bowel Disease (IBD) refers to both Ulcerative Colitis and Crohn's Disease. Ulcerative colitis causes inflammation of the lining of the large intestine, while Crohn's disease causes inflammation of the lining and wall of the large and/or small intestine. The causes of IBD are not known, but there are indications that the disease has a genetic component. The immune system changes that accompany IBD suggest that it may be an immune disorder.

The most common symptoms of Crohn's Disease are pain in the abdomen, diarrhea, and weight loss. There may also be rectal bleeding and fever. The most common complications of Crohn's Disease are blockage of the intestine and ulceration that breaks through into surrounding tissues. Surgery is sometimes required.

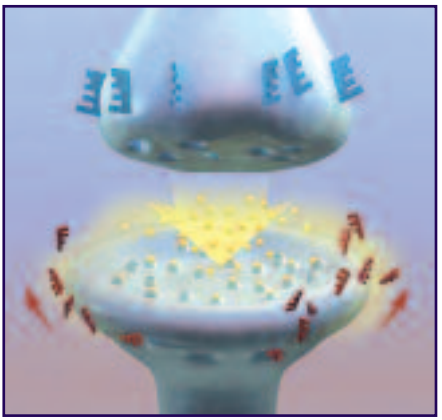
The symptoms of Ulcerative Colitis include diarrhea, abdominal cramps, and rectal bleeding. Some people may be very tired and have weight loss, loss of appetite, abdominal pain, and loss of body fluids and nutrients. Joint pain, liver problems, and redness and swelling of the eyes can also occur. Hospitalization and surgery are sometimes needed.

Research on cannabis and GI disorders

Research demonstrates that cannabis and cannabinoids are effective in treating the symptoms of these GI disorders in part because it interacts with the endogenous cannabinoid receptors in the digestive tract, which can result in calming spasms, assuaging pain, and improving motility. Cannabis has also been shown to have anti-inflammatory properties[28-30] and recent

research has demonstrated that cannabinoids are immune system modulators, either enhancing or suppressing immune response.[31,32]

Cannabis has a long documented history of use in treating GI distress, going back more than a century in western medicine, and far longer in the east. While clinical studies on the use of cannabis for the treatment of gastrointestinal disorders have been largely limited to investigations on nausea suppression and appetite stimulation—two conditions for which cannabis has been consistently shown to be highly effective[33-44]—the evidence in support of cannabis therapy for other gastrointestinal diseases and disorders is also strong. There is now extensive anecdotal evidence from patients with IBS, Crohn's disease and other painful GI disorders that cannabis eases cramping and helps modulate diarrhea, constipation and acid reflux. Recent laboratory research on the endogenous cannabinoid system in humans has identified that there are many cannabinoid receptors located in both the large and small intestine.[45-50]



CB1 receptor

Cannabis and new cannabinoid drugs are attractive for GI treatment because they can address a number of symptoms at once with minimal side-effects. Cannabinoids alter how the gut feels, affect the signals the brain sends back and forth to the gut, and modulate the actions of the GI tract itself.[51-53] For instance, cannabidiol (CBD), the second most abundant cannabinoid on the plant, has been shown to reduce hypermotility, inflammation, and tissue damage in experimental models of GI diseases.[54, 55]

Beginning in the 1970s, a series of human clinical trials established cannabis' ability to stimulate food intake and weight gain in healthy volunteers. In a randomized trial, THC significantly improved appetite and nausea in comparison with placebo. There were also trends towards improved mood and weight gain. Unwanted effects were generally mild or moderate in intensity.

Cannabis helps combat the painful and often debilitating cramping that accompanies many GI disorders because cannabinoids relax contractions of the smooth muscle of the intestines. In fact, the smooth muscle-relaxant properties of cannabinoids are so well established that preparations of guinea-pig intestine are routinely used as an in vitro screening tool to test the potency and function of synthetic cannabinoids.

Research on a variety of rodents has shown that endogenous cannabinoids

play crucial neuromodulatory roles in controlling the operation of the gastrointestinal system, with synthetic and natural cannabinoids acting powerfully to control gastrointestinal motility and inflammation. Cannabinoid receptors comprise G-protein coupled receptors that are predominantly in enteric and central neurones (CB1R) and immune cells (CB2R). The digestive tract contains endogenous cannabinoids (anandamide and 2-arachidonylglycerol) and cannabinoid CB1 receptors can be found on myenteric and submucosal nerves. Activating cannabinoid receptors has been demonstrated to inhibit gastrointestinal fluid secretion and inflammation in animal models.[56-67]

In the last decade, evidence obtained from the use of selective agonists and inverse agonists/antagonists indicates that manipulation of CB1R can have significant results.[68] Research has also shown that in the case of intestinal inflammation, the body will increase the number of cannabinoid receptors in the area in an attempt to regulate the inflammation by processing more cannabinoids.[69] The abundant cannabinoid receptors in the gut represent an excellent target to treat GI disorders, as the receptors are shown to be up-regulated in the intestinal tissue of patients suffering from IBD.[70] The activation of these hyper-expressed cannabinoid receptors can have protective and therapeutic effects against disorders of the GI tract.[71]

INSTITUTE OF MEDICINE

"Nausea, appetite loss, pain and anxiety . . all can be mitigated by marijuana.... For patients, such as those with AIDS or undergoing chemotherapy, who suffer simultaneously from severe pain, nausea, and appetite loss, cannabinoid drugs might offer broad spectrum relief not found in any other single medication."

Marijuana and Medicine: Assessing the Science Base, 1999

Cannabinoids have a demonstrated ability to block spinal, peripheral and gastrointestinal mechanisms that promote pain in IBS and related disorders.[72] Animal research also indicates that cannabinoids work well in controlling gastroesophageal reflux disease, a condition in which gastric acids attack the esophagus and for which commonly prescribed medications, such as atropine, have serious, adverse side effects.[73-75]

From this evidence, many researchers have concluded that pharmacological modulation of the endogenous cannabinoid system provides new treatment options for a number of gastrointestinal diseases, including nausea and vomiting, gastric ulcers, irritable bowel syndrome, Crohn's disease, secretory diarrhea, paralytic ileus and gastroesophageal reflux disease.[76-79] The experience of patients with these GI disorders shows that for broad-spectrum relief, cannabis is highly effective and frequently helps when other treatment options prove ineffective.[80]

How Cannabis Compares to Other Treatments

The medications currently employed to fight chronic GI disorders include many that produce serious side effects. These side effects frequently threaten the health of the patient and require other medications to combat them. Drugs commonly prescribed to combat GI disorders include:

Megestrol acetate (Megace), an anticachectic. Serious side effects of this medicine include high blood pressure, diabetes, inflammation of the blood vessels, congestive heart failure, seizures, and pneumonia. Less serious side effects of this medicine include diarrhea, flatulence, nausea, vomiting, constipation, heartburn, dry mouth, increased salivation, and thrush; impotence, decreased libido, urinary frequency, urinary incontinence, urinary tract infection, vaginal bleeding and discharge; disease of the heart, palpitation, chest pain, chest pressure, and edema; pharyngitis, lung disorders, and rapid breathing; insomnia, headache, weakness, numbness, seizures, depression, and abnormal thinking.

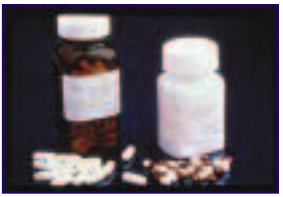
Prednisone (Delatasone), like all steroids, can have serious adverse musculoskeletal, gastrointestinal, dermatologic, neurological, endocrine, and ophthalmic side effects. These include: congestive heart failure in susceptible patients, potassium loss, hypokalemic alkalosis, sodium retention, and hypertension. Muscle weakness, steriod myopathy, loss of muscle mass, osteoporosis, tendon rupture, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, and pathologic fracture of long bones. Peptic ulcer with possible perforation and hemorrhage; pancreatitis; abdominal distention; ulcerative esophagitis. Impaired wound healing, thin fragile skin, petechiae and ecchymoses, facial erythema. Increased intracranial pressure (pseudo-tumor cerebri) usually after treatment, convulsions, vertigo, and headache. Menstrual irregularities; development of Cushingoid state; secondary adrenocortical and pituitary unresponsiveness; decreased carbohydrate tolerance; manifestations of latent diabetes mellitus. Posterior subcapsular cataracts, increased intraocular pressure, glaucoma, and exophthalmos.

Metronidazole (Flagyl) has been shown to be carcinogenic in mice and rats. Two serious adverse reactions reported in patients treated with Metronidazole have been convulsive seizures and peripheral neuropathy, the latter characterized mainly by numbness or paresthesia of an extremity. The most common adverse reactions reported have been referable to the gastrointestinal tract, particularly nausea reported by about 12% of patients, sometimes accompanied by headache, anorexia, and occasionally vomiting; diarrhea; epigastric distress, and abdominal cramping. Constipation has been reported.

Sulfasalazine (Azulfidine)—The most common adverse reactions associated with sulfasalazine are anorexia, headache, nausea, vomiting, gastric

distress, and apparently reversible oligospermia. These occur in about one-third of the patients. Less frequent adverse reactions are pruritus, urticaria, fever, Heinz body anemia, hemolytic anemia and cyanosis, which may occur at a frequency of one in every thirty patients or less.

Chlordiazepoxide/Clidinium (Librax)—Drowsiness, ataxia and confusion have been reported in some patients, particularly the elderly and debilitated. Adverse effects reported with use of Librax are those typical of anticholinergic agents, i.e., dryness of the mouth, blurring of vision, urinary hesitancy and constipation. Withdrawal symptoms, similar in character to those noted with barbiturates and alcohol (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating), have occurred following abrupt discontinuance of chlordiazepoxide.



Hyoscyamine Sulfate (Levsin)—Adverse reactions may include dryness of the mouth; urinary hesitancy and retention; blurred vision; tachycardia; palpitations; mydriasis; cycloplegia; increased ocular tension; loss of taste; headache; nervousness; drowsiness; weakness; dizziness; insomnia; nausea; vomiting; impotence; suppression of lactation; constipation; bloated feeling; allergic reactions or drug idiosyncrasies; urticaria and other dermal manifestations; ataxia; speech disturbance; some degree of mental confusion and/or excitement (especially in elderly persons); and decreased sweating.

Mesalamine CR (Pentasa)—The most common side effects are diarrhea, headache, nausea, abdominal pain, dyspepsia, vomiting, and rash.

Phosphorated carbohydrate (Emetrol)—Side effects include: fainting; swelling of face, arms, and legs; unusual bleeding; vomiting; weight loss; yellow eyes or skin. Less common-more common with large doses: Diarrhea; stomach or abdominal pain.

Dicyclomine (Bentyl)—The most common side effects occurring with dicyclomine are due to its anticholinergic activity: dry mouth, blurred vision, confusion, agitation, increased heart rate, heart palpitations, constipation, difficulty urinating, and occasionally seizures can occur. Other potential side effects include changes in taste perception, difficulty swallowing, headache, nervousness, drowsiness, weakness, dizziness, impotence, flushing, difficulty falling asleep, nausea, vomiting, rash, and a bloated feeling.

Ciprofloxacin (Cipro)—The most frequent side effects include nausea, vomiting, diarrhea, abdominal pain, rash, headache, and restlessness. Rare allergic reactions have been described, such as hives and anaphylaxis.

Methotrexate (Rheumatrex, Trexall)—can cause severe toxicity when taken

in high doses. The most frequent reactions include mouth sores, stomach upset, and low white blood counts. Methotrexate can cause severe toxicity of the liver and bone marrow, which require regular monitoring with blood testing. It can cause headache and drowsiness, which may resolve if the dose is lowered. Methotrexate can cause itching, skin rash, dizziness, and hair loss. A dry, non-productive cough can be a result of a rare lung toxicity.

Diphenoxylate and **atropine** (Lotomil)—The most common side effects include drowsiness, dizziness, and headache, nausea or vomiting, and dry mouth. Euphoria, depression, lethargy, restlessness, numbness of extremities, loss of appetite, and abdominal pain or discomfort have been reported less frequently. Although the dose of atropine in Lomotil is too low to cause side effects when taken in the recommended doses, side effects of atropine (including dryness of the skin and mucous membranes, increased heart rate, urinary retention, and increased body temperature) have been reported, particularly in children under two.

Cannabis—By comparison, the side effects associated with cannabis are typically mild and are classified as "low risk." Euphoric mood changes are among the most frequent side effects. Cannabinoids can exacerbate schizophrenic psychosis in predisposed persons. Cannabinoids impede cognitive and psychomotor performance, resulting in temporary impairment. Chronic use can lead to the development of tolerance. Tachycardia and hypotension are frequently documented as adverse events in the cardiovascular system. A few cases of myocardial ischemia have been reported in young and previously healthy patients. Inhaling the smoke of cannabis cigarettes induces side effects on the respiratory system. Cannabinoids are contraindicated for patients with a history of cardiac ischemias. In summary, a low risk profile is evident from the literature available. Serious complications are very rare and are not usually reported during the use of cannabinoids for medical indications.

Angel Raich using a vaporizer in the hospital

Is cannabis safe to recommend?

"The smoking of cannabis, even long term, is not harmful to health...." So began a 1995 editorial statement of Great Britain's leading medical journal, The Lancet. The long history of human use of cannabis also attests to its safety—nearly 5,000 years of documented use without a single death. In

the same year as the Lancet editorial, Dr. Lester Grinspoon, a professor emeritus at Harvard Medical School who has published many influential books and articles on medical use of cannabis, had this to say in an article in the *Journal of the American Medical Association* (1995):

> One of marihuana's greatest advantages as a medicine is its remarkable safety. It has little effect on major physiological functions. There is no known case of a lethal overdose; on the basis of animal models, the ratio of lethal to effective dose is estimated as 40,000 to 1. By comparison, the ratio is between 3 and 50 to 1 for secobarbital and between 4 and 10 to 1 for ethanol. Marihuana is also far less addictive and far less subject to abuse than many drugs now used as muscle relaxants, hypnotics, and analgesics. The chief legitimate concern is the effect of smoking on the lungs. Cannabis smoke carries even more tars and other particulate matter than tobacco smoke. But the amount smoked is much less, especially in medical use, and once marihuana is an openly recognized medicine, solutions may be found; ultimately a technology for the inhalation of cannabinoid vapors could be developed.

The technology Dr. Grinspoon imagined in 1995 now exists in the form of "vaporizers," (which are widely available through stores and by mail-order) and recent research attests to their efficacy and safety.[81] Additionally, pharmaceutical companies have developed sublingual sprays and tablet forms of the drug. Patients and doctors have found other ways to avoid the potential problems associated with smoking, though long-term studies of even the heaviest users in Jamaica, Turkey and the U.S. have not found increased incidence of lung disease or other respiratory problems. A decade-long study of 65,000 Kaiser-Permanente patients comparing cancer rates among non-smokers, tobacco smokers, and cannabis smokers found that those who used only cannabis had a slightly lower risk of lung and other cancers as compared to non-smokers.[82] Similarly, a study comparing 1,200 patients with lung, head and neck cancers to a matched group with no cancer found that even those cannabis smokers who had consumed in excess of 20,000 joints had no increased risk of cancer.[83]

As Dr. Grinspoon notes, "the greatest danger in medical use of marihuana is its illegality, which imposes much anxiety and expense on suffering people, forces them to bargain with illicit drug dealers, and exposes them to the threat of criminal prosecution." This was the same conclusion reached by the House of Lords, which recommended rescheduling and decriminalization.

Cannabis or Marinol?

Those committed to the prohibition on cannabis frequently cite Marinol, a Schedule III drug, as the legal means to obtain the benefits of cannabis. However, Marinol, which is a synthetic form of THC, does not deliver the same therapeutic benefits as the natural herb, which contains at least 100

cannabinoids in addition to THC. Recent research conducted by GW Pharmaceuticals in Great Britain has shown that Marinol is simply not as effective for pain management as the whole plant; a balance of cannabinoids, specifically CBC and CBD with THC, is what helps patients most. In fact, Marinol is not labeled for pain, only appetite stimulation and nausea control. But studies have found that many severely nauseated patients experience difficulty in getting and keeping a pill down, a problem avoided with inhaled cannabis.

Clinical research on Marinol vs. cannabis has been limited by federal restrictions, but a 2001 review of clinical trials conducted in the 70's and 80's reports that "…the inhalation of THC appears to be more effective than the oral route."[67] Additionally, patients frequently have difficulty getting the right dose with Marinol, while inhaled cannabis allows for easier titration and avoids the negative side effects many report with Marinol. As the House of Lords report states, "Some users of both find cannabis itself more effective."

THE EXPERIENCE OF PATIENTS

Bruce Buckner

My name is Bruce Buckner. I am a 48-year old computer pre-press technician and webmaster from Seattle, WA. I play music with a couple different bands for fun and profit as well.

I remember my first bouts of abdominal cramping and diarrhea around the age of nine or ten. I was told I was suffering from colitis, that it was just a "nervous stomach." It was always particularly bad on days I woke early to go somewhere, so the "nervous stomach" diagnosis kind of made sense. The cramping and frequent bowel movements continued. I was going to the bathroom a dozen times a day. I was always of slight build but by the age of twelve my weight had dropped off the "low normal" range of the height/weight charts. I became drastically underweight (I am a 48-year-old male who weighs 114 lbs.)

While attending the University of Oregon in Eugene, I was suffering from a particularly bad flare-up. I developed psoriasis, and started getting little red bumps on my lower legs, which I scratched into sores. I was very fortunate that the young doctor I saw was very familiar with Crohn's (his wife had it). He was able to diagnose it right away, although he still made me undergo a colonoscopy the following week, which confirmed his diagnosis. He started me on sulfasalazine. This caused severe nausea and vomiting. The cure was much worse than the disease. The doctor gave me steroids (prednisone). This made me lay awake all night sweating. I was making all kinds of stupid mistakes—I backed my car into a light post, I lost my temper easily, I couldn't handle the sleep deprivation and stopped taking the steroids. In 1972 my doctor told me his wife found that smoking pot helped. Whenever I was

cramping, I smoked a couple joints from that point on.

Through the seventies and eighties, I worked in the music business. My occupations allowed me to wake slowly, work late hours, and smoke lots of pot. Coincidentally, my Crohn's was in almost total remission. I still had occasional bouts of leg sores and cramping and diarrhea, but the cramping and bowel movements would subside after a couple hours and I would be OK the rest of the day. I was still underweight, but I could eat two or three times a day.

FEDERATION OF AMERICAN SCIENTISTS

"Based on much evidence, from patients and doctors alike, on the superior effectiveness and safety of whole cannabis compared to other medications,... the President should instruct the NIH and the FDA to make efforts to enroll seriously ill patients whose physicians believe that whole cannabis would be helpful to their conditions in clinical trials"

FAS Petition on Medical Marijuana, 1994

After changing jobs and suffering through several years of flare ups, I realized smoking a little pot helped lessen the cramping, increased my appetite and helped me feel a little better. But smoking a lot of pot (a big joint every hour and a half) would keep the disease in a state of almost total remission. I would have only one to three bowel movements in the morning, minimal morning cramping, I could eat any food I wanted; even my leg sores would go away.

I have several relatives with Crohn's Disease. Every one of them has had major surgery. Every one of them has had complications from the steroids and immune suppressors they have been prescribed. Most no longer have functioning excretory systems and are wearing pouches.

I went to a specialist who stated "Frankly, I can't believe you could have gone thirty years with Crohn's without major medical intervention, I have to question whether you really have Crohn's." He ordered an "enteroclysis" (a horrible procedure that I wouldn't wish on anyone) which showed definite scarring and narrowing in my terminal ileum. The doctor had to admit that I did have Crohn's and that I had kept the disease in control with marijuana.

I am firmly convinced that I would be in the same condition as my relatives with Crohn's, if I hadn't used pot. The medical use of marijuana has saved my colon and my quality of life.

Fernando Mosquera

I have personally been waging a lifelong battle with Crohn's disease, a battle in which medical marijuana has proven to be a great ally. Crohn's disease causes inflammation affecting the entire gastrointestinal tract. During flare-

ups, the symptoms can be paralyzing; over the past ten years my life has been brought to a stop by sharp, debilitating stomach pain, constant diarrhea (at its worst I spent entire days on the toilet screaming in pain), blood in the stool and severe weight loss. Medicine has made little progress in the search for a cure and doesn't even fully understand the cause of the illness. The most popular way to control Crohn's is with Prednisone, a multi-purpose steroid drug that can cause psychosis, stunted growth, high blood pressure, weak bones and glaucoma.

The manufacturer of Prednisone recommends it be used in short spurts to minimize side effects, but during my adolescence I was kept on high doses of the drug for prolonged periods of time. Prednisone couldn't control my illness, and even worse it went to work on my body and mind, stunting my growth, causing mood shifts and water retention, and putting me at risk for osteoporosis. I tried all the treatments available, even attempting an "elemental diet:" breakfast, lunch and dinner served through a tube that ran up my nose and down to my stomach. This failed too, and I had to be home-schooled through high school, spending my days lying in bed clutching my stomach in agony, hoping the constant diarrhea would stop.

AMERICAN NURSES ASSOCIATION

In 2003 the American Nurses Association passed a resolution that supports those health care providers who recommend medicinal use, recognizes "the right of patients to have safe access to therapeutic marijuana/cannabis," and calls for more research and education, as well as a rescheduling of marijuana for medical use.

A writing career led me to California, where I discovered a medical marijuana regimen of smoking before and after meals made the symptoms of my Crohn's disease disappear. Under California's Proposition 215, I had the legal right to use a medicine that proved far more effective than anything my doctors had tried.

The alternative is Marinol, a legal prescription medicine that contains a synthetic version of tetrahydrocannabinol (THC), the main active ingredient in natural marijuana. Marinol has several disadvantages: 1) It takes much longer to work, especially after meals when I need relief the most; 2) It is difficult to have the right amount. I either end up being too stoned to function or not medicated enough; and 3) THC is not the only active compound in marijuana, and research shows the anti-inflammatory effect of marijuana is likely a result not of THC, but of cannabidiol, a separate chemical not contained in Marinol.

Rose Wheeler

I'm a 40-year-old wife and mother of two young boys who was diagnosed with Crohn's disease in September of 1993, while my husband was stationed

in Austria. The best way I could describe my symptoms was that food was POISON to me. When I ate or drank ANYTHING, within 5 minutes I was on the toilet bent over in severe pain and experiencing hot flashes. I spent more time in the bathroom than any other place in my home. I was very weak, nauseated. With every bowel movement there was much blood and mucus, and I became seriously depressed. It was very difficult for me to care for my children.

At this time, not knowing what was wrong with me, I could only think that I was actually going to die. My abdomen felt bruised all the time, and the last thing I wanted to do was eat. I then began what seemed a roller coaster ride of seeing different doctors and having different tests done, which to say the least made me in more pain than ever. The doctors told me the small bowel series revealed findings consistent with Crohn's disease. I was still not prescribed any meds for my symptoms. The doctors felt it was better to give me a consult to see a doctor for further testing, and to begin my treatment after our return to the States.

I then was introduced to marijuana before leaving Austria, and within 1 hour I could not believe that the pain, bowel movements and ALL my other symptoms were relieved. Now my major concern was the illegality of marijuana, and putting my husband at risk in his military career. I had serious thoughts of getting busted and my children being taken from me. I quit the marijuana after a week of smoking it, only to have all those terrible symptoms return.

Once we returned to the states I began taking 750mg of flagyl,1500mg of azulfidine, and 1mg of folic acid per day. My life started to turn for the better. But after two years, I began experiencing migraines and feeling as though I was going to pass out at times. I then chose to try smoking marijuana. I felt no one could know I was smoking, not even my husband. I wanted to so badly tell my doctor how much smoking marijuana had relieved my symptoms, but knew I couldn't. I will never forget my last visit to my doctor, telling him that my symptoms were gone and I wanted to quit the meds. He agreed with me that the migraines and dizzy spells were a side effect of the meds. I have not taken any prescription meds for my Crohn's since 1995.

Erin Hildebrandt

My name is Erin Hildebrandt, and I'm a 34-year-old wife and stay-at-home mom to five kids, ages 3 to 9. I suffer from Crohn's Disease, a disease for which there is no known cure; therefore, symptom control is the goal of treatment. Marijuana is not a panacea, but it's the only medicine I've found that controls a large number of my most debilitating symptoms. Compared to the dozens of truly dangerous pharmaceuticals first given to me by doctors, the cannabis recommended by a friend, and subsequently endorsed by

my doctor, is more effective and has fewer side-effects. For me, Crohn's Disease produces severe nausea, vomiting, diarrhea, intractable pain, cramping, fever, sweating, chills, bloating, and weight loss. I can only compare it to the worst case of food poisoning I can imagine, except that it doesn't just go away after a day or two. It comes back again and again, varying in both intensity and duration. During the worst attacks, proper nutrition and exercise are an often insurmountable challenge. However, through the use of marijuana, I feel well enough to function more normally. In addition, with consistent therapeutic use, the inflammation in my digestive tract stays under control, and I'm able to bring my disease into remission.

THE EXPERIENCE OF DOCTORS

Kate Scannell, M.D.

From working with AIDS and cancer patients, I repeatedly saw how marijuana could ameliorate a patient's debilitating fatigue, restore appetite, diminish pain, remedy nausea, cure vomiting and curtail down-to-the-bone weight loss. The federal obsession with a political agenda that keeps marijuana out of the hands of sick and dying people is appalling and irrational.

Kate Scannell, M.D. is Co-Director, Kaiser-Permanente, Northern California Ethics Department.

Marcus A. Conant, M.D.

Medical marijuana. . . stimulates the appetite and promotes weight gain, in turn strengthening the body, combating chronic fatigue, and providing the stamina and physical well-being necessary to endure or withstand both adverse side effects of ongoing treatment and other opportunistic infections. It has been shown effective in reducing nausea, neurological pain and anxiety, and in stimulating appetite. When these symptoms are associated with (or caused by) other therapies, marijuana has been useful in facilitating compliance with more traditional therapies. It may also allow individual patients to engage in normal social interactions and avoid the despair and isolation which frequently accompanies long-term discomfort and illness. …

I was one of the principal investigators of an FDA-supervised trial conducted by Unimed, Inc. on the safety and efficacy of Marinol as an appetite stimulant in HIV/AIDS patients suffering from wasting syndrome. Marinol is a form of THC, one of the key active components of marijuana; it is essentially a marijuana extract. It was approved by the FDA five years ago, and has been widely prescribed by physicians treating both AIDS and cancer patients. …I am aware, however, that Marinol (like any medication) is not effective in treating all patients. In some cases, the reason is simple: Marinol is taken orally, in pill form. Patients suffering from severe nausea and retching cannot tolerate the pills and thus do not benefit from the drug. There are likely other reasons why smoked marijuana is sometimes more effective than Marinol. The body's absorption of the chemical may be faster or more

complete when inhaled. Means of ingestion is often critical in understanding treatment efficacy.

Dr. Marcus Conant has practiced medicine for 33 years. He is Professor at University of California San Francisco and is author of over 70 publications.

Neil M. Flynn, M.D., MPH

If I am unable to relieve the patient's nausea with [conventional] remedies, I next prescribe Marinol, a synthetic version of THC, one of the main active compounds found in marijuana. Marinol is also helpful in stimulating appetite in patients suffering from AIDS wasting, as are other drugs, Megace, anabolic steroids, and human growth hormone.

NEW ENGLAND JOURNAL OF MEDICINE

"A federal policy that prohibits physicians from alleviating suffering by prescribing marijuana to seriously ill patients is misguided, heavy-handed, and inhumane.... It is also hypocritical to forbid physicians to prescribe marijuana while permitting them to prescribe morphine and meperidine to relieve extreme dyspnea and pain…there is no risk of death from smoking marijuana.... To demand evidence of therapeutic efficacy is equally hypocritical"

Jerome P. Kassirer, MD, editor
N Engl J Med 336:366-367, 1997

If Marinol does not provide adequate relief from nausea and/or wasting, I may suggest that the patient try a related remedy, marijuana. I firmly believe that medical marijuana is medically appropriate as a drug of last resort for a small number of seriously ill patients. Over 20 years of clinical experience persuade me of this fact. The anecdotal evidence is overwhelming. Almost every patient I have known to have tried marijuana achieved relief from symptoms with it. That success rate far surpasses that for Compazine.

Accordingly, as with any other medication that I consider potentially beneficial to my patients, I must discuss the option of medical marijuana in detail when appropriate. Anything less is malpractice. ... I have seen marijuana restore patients' will to live by restoring their ability to eat, gain strength, and perform simple, daily activities free from crippling nausea or pain.

Dr. Neil M. Flynn is a Professor of Clinical Medicine at the University of California, Davis School of Medicine and is the author of numerous articles.

THE HISTORY OF CANNABIS AS MEDICINE

The history of the medical use of cannabis dates back to 2700 B.C. in the pharmacopoeia of Shen Nung, one of the fathers of Chinese medicine. In the west, it has been recognized as a valued, therapeutic herb for centuries. In 1823, Queen Victoria's personal physician, Sir Russell Reynolds, not only

prescribed it to her for menstrual cramps but wrote in the first issue of The Lancet, "When pure and administered carefully, [it is] one of the of the most valuable medicines we possess." (Lancet 1; 1823).

The American Medical Association opposed the first federal law against cannabis with an article in its leading journal (108 J.A.M.A. 1543-44; 1937). Their representative, Dr. William C. Woodward, testified to Congress that "The American Medical Association knows of no evidence that marihuana is a dangerous drug," and that any prohibition "loses sight of the fact that future investigation may show that there are substantial medical uses for Cannabis." Cannabis remained part of the American pharmacopoeia until 1942 and is currently available by prescription in the Netherlands and Canada.

Federal policy is contradictory

Federal policy on medical cannabis is filled with contradictions. Cannabis was widely prescribed until the turn of the century. Now cannabis is a Schedule I drug, classified as having no medicinal value and a high potential for abuse, yet its most psychoactive component, THC, is legally available as Marinol and is classified as Schedule III. And the U.S. federal government grows and provides cannabis for a small number of patients today.

In 1976 the federal government created the Investigational New Drug (IND) compassionate access research program to allow patients to receive medical cannabis from the government. The application process was extremely complicated, and few physicians became involved. In the first twelve years the government accepted about a half dozen patients. The federal government approved the distribution of up to nine pounds of cannabis a year to these patients, all of whom report being substantially helped by it.

In 1989 the FDA was deluged with new applications from people with AIDS, and 34 patients were approved within a year. In June 1991, the Public Health Service announced that the program would be suspended because it undercut the administration's opposition to the use of illegal drugs. The program was discontinued in March 1992 and the remaining patients had to sue the federal government on the basis of "medical necessity" to retain access to their medicine. Today, a few surviving patients still receive medical cannabis from the federal government, grown under a doctor's supervision at the University of Mississippi and paid for by federal tax dollars.

Despite this successful medical program and centuries of documented safe use, cannabis is still classified in America as a Schedule I substance. Healthcare advocates have tried to resolve this contradiction through legal and administrative channels. In 1972, a petition was submitted to reschedule cannabis so that it could be prescribed to patients.

The DEA stalled hearings for 16 years, but in 1988 their chief administrative law judge, Francis L. Young, ruled that, "Marijuana, in its natural form, is one of the safest therapeutically active substances known... It would be unreasonable, arbitrary and capricious for the DEA to continue to stand between those sufferers and the benefits of this substance." The DEA refused to implement this ruling based on a procedural technicality and continues to classify cannabis as a substance with no medical use.

Widespread public support; state laws passed; new policy

Public opinion is strongly in favor of ending the prohibition of medical cannabis and has been for some time, with every national poll conducted over the past two decades showing a substantial majority in support. A CBS News national poll in January 2014 found that 86 percent of Americans think doctors should be allowed to prescribe cannabis for patients suffering from serious illnesses. In 2004, the 35 million-member American Association of Retired Persons (AARP) released a national poll of older Americans showing 72 percent of seniors agreed that "adults should be allowed to legally use marijuana for medical purposes if a physician recommends it." Every national poll for more than a decade has found similar super-majorities of support.

The refusal of the federal government to act on this widespread public support has meant that advocates have had to turn to the states for action. Currently, laws that effectively remove state-level criminal penalties for growing and/or possessing medical cannabis are in place in Alaska, Arizona, California, Colorado, Connecticut, Delaware, Hawaii, Illinois, Maine, Maryland, Massachusetts, Michigan, Minnesota, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, Oregon, Rhode Island, Vermont, Washington, and the District of Columbia. Another ten states have established limited laws that allow the legal medical use of a cannabis plant extract. Thirty-six states have symbolic medical cannabis laws (laws that support medical cannabis but do not provide patients with legal protection under state law).

On August 29, 2013, the U.S. Department of Justice issued new guidance to federal prosecutors, telling them medical cannabis dispensaries should no longer automatically be considered targets for prosecution. The memo from Deputy Attorney General James M. Cole to all U.S. Attorneys reverses previous federal policy on prosecuting medical cannabis providers and businesses. The new guidance says state and local officials can avoid federal interference in their medical cannabis programs if they "implement strong and effective regulatory and enforcement systems" that reflect eight federal enforcement priorities.

The memo does not change federal law, nor does it preclude prosecution of any individual or business, as the U.S. Attorneys' offices are autonomous, and federal prosecutors make independent decisions about which cases to pursue.

Legal Citations

1. See "The Administration's Response to the Passage of California Proposition 215 and Arizona Proposition 200" (Dec. 30, 1996). https://www.ncjrs.gov/txtfiles/215rel.txt
2. See *Conant v. McCaffrey*, 172 F.R.D. 681 (N.D. Cal. 1997).
3. See id.; *Conant v. McCaffrey*, 2000 WL 1281174 (N.D. Cal. 2000); Conant v. Walters, 309 F.3d 629 (9th Cir. 2002).
4. 309 F.3d 629 (9th Cir. 2002).
5. Id. at 634-36.
6. Criminal liability for aiding and abetting requires proof that the defendant "in some sort associate[d] himself with the venture, that he participate[d] in it as something that he wishe[d] to bring about, that he [sought] by his action to make it succeed."*Conant v. McCaffrey*, 172 F.R.D. 681, 700 (N.D. Cal. 1997) (quotation omitted). A conspiracy to obtain cannabis requires an agreement between two or more persons to do this, with both persons knowing this illegal objective and intending to help accomplish it. Id. at 700-01.
7. 309 F.3d at 634 & 636.
8. *Conant v. McCaffrey*, 2000 WL 1281174, at *16 (N.D. Cal. 2000).
9. 309 F.3d at 634.
10. See id.. at 635; *Conant v. McCaffrey*, 172 F.R.D. 681, 700-01 (N.D. Cal. 1997).
11. *Gonzales v. Raich*, 545 U.S. 1 (2005) 352 F.3d 1222.
12. *Third Time the Charm? State Laws on Medical Cannabis Distribution and Department of Justice Guidance on Enforcement*. Americans for Safe Access. November 25, 2013. http://americansforsafeacess.org/dojwhitepaper.

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DEA CHIEF ADMINISTRATIVE LAW JUDGE

Marijuana, in its natural form, is one of the safest therapeutically active substances known... It would be unreasonable, arbitrary and capricious for the DEA to continue to stand between those sufferers and the benefits of this substance.

The Honorable Francis L. Young,
Ruling on DEA rescheduling hearings, 1988

ADDITIONAL RESOURCES

Americans for Safe Access maintains a website with additional resources for doctors and patients. There you will find the latest information on legal and legislative developments, new medical research, and what you can do to help protect the rights of patients and doctors.

With more than 45,000 active members and chapters and affiliates in all 50 states, ASA is the largest national member-based organization of patients, medical professionals, scientists, and concerned citizens promoting safe and legal access to cannabis for therapeutic uses and research.

AmericansFor SafeAccess
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