



CANCER **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. This brochure is intended to help doctors, patients and policymakers better understand how marijuana—or "cannabis" as it is more properly called—may be used as a treatment for people with serious medical conditions. This booklet contains information about using cannabis as medicine. In it you'll find information on:

- Why Cannabis is Legal to Recommend 3**
- Overview of the Scientific Research on Medical Cannabis 4**
- Research on Cannabis and Cancer 6**
- Comparison of Medications: Efficacy and Side-Effects 10**
- Why Cannabis is Safe to Recommend 12**
- Testimonials of Patients and Doctors 13**
- History of Cannabis as Medicine 20**
- Scientific and Legal References 24**

We recognize that information about using cannabis as medicine has been difficult to obtain. The federal prohibition on cannabis has meant that modern clinical research has been limited, to the detriment of medical science and the wellness of patients. But the documented history of the safe, medical use of cannabis dates to 2700 B.C. Cannabis was part of the American pharmacopoeia until 1942 and is currently available by prescription in the Netherlands and Canada.

Testimonials from both doctors and patients reveal valuable information on the use of cannabis therapies, and supporting statements from professional health organizations and leading medical journals support its legitimacy as a medicine. In the last few years, clinical trials in Great Britain, Canada, Spain, Israel, and elsewhere have shown great promise for new medical applications.

This brochure is intended to be a starting point for the consideration of applying cannabis therapies to specific conditions; it is not intended to replace the training and expertise of physicians with regard to medicine, or attorneys with regard to the law. But as patients, doctors and advocates who have been working intimately with these issues for many years, Americans for Safe Access has seen firsthand how helpful cannabis can be for a wide variety of indications. We know doctors want the freedom to practice medicine and patients the freedom to make decisions about their healthcare.

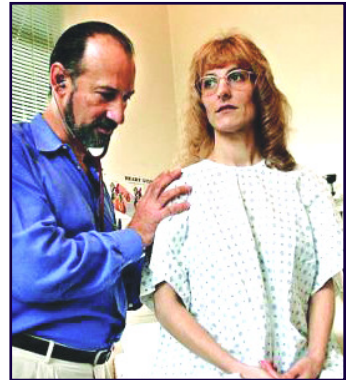
For more information about ASA and the work we do, please see our website at **AmericansForSafeAccess.org** or call **1-888-929-4367**.

Is Cannabis Legal to Recommend?

In 2004, the United States Supreme Court upheld earlier federal court decisions that doctors have a fundamental Constitutional right to recommend cannabis to their patients.

The history. Within weeks of California voters legalizing medical cannabis in 1996, federal officials had threatened to revoke the prescribing privileges of any physicians who recommended cannabis to their patients for medical use.¹ In response, a group of doctors and patients led by AIDS specialist Dr. Marcus Conant filed suit against the government, contending that such a policy violates the First Amendment.² The federal courts agreed at first the district level,³ then all the way through appeals to the Ninth Circuit and then the Supreme Court.

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 a physician may discuss the pros and cons of medical cannabis with any patient, and issue a written or oral recommendation to use cannabis without fear of legal reprisal.⁷ This is true regardless of whether the physician anticipates that the patient will, in turn, use this recommendation to obtain cannabis.⁸ What physicians may not do is actually prescribe or dispense cannabis to a patient⁹ or tell patients how to use a written recommendation to procure it from a cannabis club or dispensary.¹⁰ Doctors can tell patients they may be helped by cannabis. They can put that in writing. They just can't help patients obtain the cannabis itself.



Angel Raich & Dr. Frank Lucido

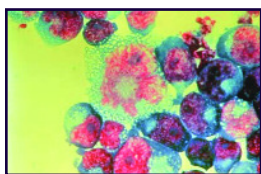
Patients protected under state, not federal, law. In June 2005, the U.S. Supreme Court overturned the *Raich v. Ashcroft* Ninth Circuit Court of Appeals decision. In reversing the lower court's ruling, *Gonzales v. Raich* established that it is legal under federal law to prosecute patients who possess, grow, or consume medical cannabis in medical cannabis states. However, this Supreme Court decision does not overturn or supersede the laws in states with medical cannabis programs.

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

Scientific Research Supports Medical Cannabis

Between 1840 and 1900, European and American medical journals published more than 100 articles on the therapeutic use of the drug known then as Cannabis Indica (or Indian hemp) and now simply as cannabis. Today, new studies are being published in peer-reviewed journals that demonstrate cannabis has medical value in treating patients with serious illnesses such as AIDS, glaucoma, cancer, multiple sclerosis, epilepsy, and chronic pain.

The safety of the drug has been attested to by numerous studies and reports, including the LaGuardia Report of 1944, the Schafer Commission Report of 1972, a 1997 study conducted by the British House of Lords, 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.



T cells

Recent published research on CD4 immunity in AIDS patients found no compromise to the immune systems of patients undergoing cannabis therapy in clinical trials.¹¹

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.

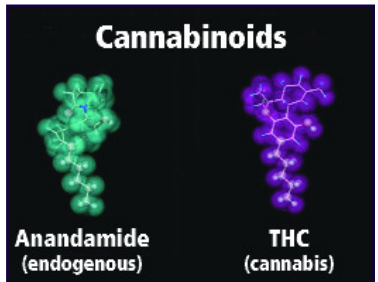
Recent Research Advances

While research has until recently been sharply limited by federal prohibition, the last few years have seen rapid change. The International Cannabinoid Research Society was formally incorporated as a scientific research organization in 1991. Membership in the Society has more than tripled from about 50 members in the first year to over 500 in 2010. The International Association for Cannabis as Medicine (IACM) was founded in March 2000. It publishes a bi-weekly newsletter and the IACM-Bulletin, and holds a bi-annual symposium to highlight emerging research in cannabis therapeutics. In 2001, the State of California established the Center for Medicinal Cannabis Research to coordinate an \$8.7-million research effort at University of California campuses. As of 2010, the CMCR had completed six of 14 approved studies. Of those, five were double-blind, placebo-controlled studies that showed cannabis to be effective for pain relief.

In the United Kingdom, GW Pharmaceuticals has been conducting clinical

trials with its cannabis-based medicine for the past decade. GW's Phase II and Phase III trials of cannabis-based medicine 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.

As of December 2010, the company has obtained regulatory approval in Spain, New Zealand, and the UK for Sativex® Oromucosal Spray, a controlled-dose whole-plant extract. 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 opioids, and in 2010 for spasticity related to multiple sclerosis. Sativex has been made available either for named patient prescription use or for clinical trials purposes in a total of 22 countries. 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 strong opioids.



CANNABIS AND CANCER

Cannabis has been found to help cancer patients with the symptoms that usually accompany cancer such as pain, nausea, wasting, and loss of appetite.¹² Notably, in a meta-analysis of 30 clinical studies on the therapeutic use of cannabis for chemotherapy-induced nausea and vomiting, Delta9-THC (dronabinol AKA marinol) proved superior to modern anti-emetics.¹³ Additionally, patients showed a clear preference for cannabinoids as anti-emetic medication over conventional drugs, when receiving chemotherapy.

Only one clinical trial has ever been published on the effects of Delta9-THC on cancer growth in humans.¹⁴ Doctors administered oral Delta 9-THC to nine patients who experienced tumor progression despite surgical therapy and radiation treatments. The major finding of the study was that Delta 9-THC was safe and did not cause any obvious psychoactive effects in a clinical setting. Furthermore, current research clearly indicates that cannabinoids can have tumor-reducing and anti-cancer properties.¹⁵

Research on cannabis and chemotherapy

One of the most widely studied therapeutic applications for cannabis and the pharmaceutical drugs derived from cannabinoids is in the treatment of nausea and vomiting associated with cancer chemotherapy.. Numerous clinical studies have reported that the use of cannabis reduces pain, nausea, vomiting, and stimulates appetite, thereby reducing the severity of cachexia, or wasting syndrome, in patients receiving chemotherapy treatment.



The 1999 Institutes of Medicine report suggested: "In patients already experiencing severe nausea or vomiting, pills are generally ineffective, because of the difficulty in swallowing or keeping a pill down, and slow onset of the drug effect. Thus an inhalation (but, preferably not smoking) cannabinoid drug delivery system would be advantageous for treating chemotherapy-induced nausea."¹⁶ For certain individuals unresponsive to conventional anti-emetic drugs, the use of smoked or vaporized cannabis can provide relief more effectively than oral THC (Marinol) which may be difficult to swallow or be vomited before taking effect. The IOM

report concluded, "nausea, appetite loss, pain and anxiety ... all can be mitigated by marijuana."

A 1997 inquiry by the British Medical Association found cannabis more effective than Marinol, and a 1998 review by the House of Lords Science & Technology Select Committee concluded that "Cannabinoids are undoubtedly effective as anti-emetic agents in vomiting induced by anti-cancer drugs. Some users of both find cannabis itself more effective."¹⁷⁻¹⁸

In 2009, a clinical trial involving 177 patients, with intractable cancer pain and experienced inadequate relief from opiates, showed remarkable reductions in pain scores from using a cannabis extract which contained THC and CBD. This THC:CBD extract was more effective than an extract containing only THC.¹⁹

The effects of cannabis may also provide an improvement in mood. In addition to THC, other cannabinoids on the plant such as CBD, can inhibit the side effects of THC, as well provide relief from anxiety and depression. By contrast, several conventional medications commonly prescribed for cancer patients, e.g. phenothiazines such as haloperidol (known as "major tranquillizers") may produce unwanted side effects

such as excessive sedation, flattening of mood, and/or distressing physical “extrapyramidal” symptoms such as uncontrolled or compulsive movements.

Anti-cancer potential of cannabis and cannabinoids

Recent scientific advances in the study of cannabinoid receptors and endocannabinoids have produced exciting new leads in the search for anti-cancer treatments. Several-hundred research articles have been published on the effects of cannabinoids on cancer cells. We now know cannabinoids stop many kinds of cancers from growing and spreading, including brain, breast, leukemic, melanoma, pheochromocytoma, liver and other kinds of cancer.²³⁻⁴⁰ Cannabinoids have been repeatedly shown to promote apoptosis (programmed cell death of the tumor cells) and halt angiogenesis (blood vessel production to the tumor).⁴¹⁻⁴⁵

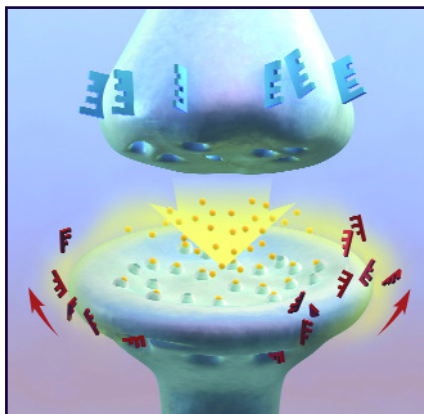
The anti-cancer properties of cannabinoids are mediated through cannabinoid receptors. CB1 and CB2 cannabinoid receptors are abundantly expressed throughout the human body, making them an excellent target for disease treatment.

Indeed, research on the complex interactions of endogenous cannabinoids and receptors is leading to greater scientific understanding of the basic mechanisms by which cancers develop.⁴⁶

In multiple studies published between 2001 and 2003, cannabinoids inhibited tumor growth in laboratory animals.⁴⁷⁻⁵⁰ In another study, injections of synthetic THC eradicated malignant brain tumors in one-third of treated rats, and prolonged life in another third by as much as six weeks.^{51, 52} And, research on pituitary cancers suggest that cannabinoids may be the key to regulating human pituitary hormone secretion.⁵³⁻⁵⁶

A 2009 review of recent studies that have focused on the role of cannabinoids and cannabinoid receptors in the treatment of breast cancer notes that cannabinoids have been shown in laboratory models to be effective fighting many types of cancers.⁵⁷

Recent research published in 2009 has found that the non-psychoactive cannabinoid cannabidiol (CBD) inhibits the invasion of both human cervical cancer and human lung cancer cells. By manipulating cannabidiol's up-regulation of a tissue inhibitor, researchers may have revealed the mechanism of CBD's tumor-fighting effect. A further in vivo study demonstrated "a significant inhibition" of lung cancer metastasis in mice treated with CBD.⁵⁸ The mechanism of the anti-cancer activity of CBD and other cannabinoids has



CB1 receptor

also been repeatedly demonstrated with breast cancers.⁵⁹⁻⁶³

Also in 2009, scientists reported on the anti-tumor effects of the cannabinoid THC on cholangiocarcinoma cells, an often-fatal type of cancer that attacks the liver's bile ducts. They found that "THC inhibited cell proliferation, migration and invasion, and induced cell apoptosis." At low levels, THC reduced the migration and invasion of cancer cells, while at high concentrations, THC triggered cell-death in tumors. In short, THC reduced the activity and number of cancer cells. This dose-dependent action of cannabinoids on tumors has also been demonstrated in animal studies.

Research on cannabinoids and gliomas, a type of aggressive brain cancer for which there is no cure, holds promise for future treatments. A study that examined both animal and human glioblastoma multiforme (GBM) tumors, the most common and aggressive form of brain cancer, describes how cannabinoids controlled glioma growth by regulating the blood vessels that supply the tumors.⁶⁴ In another study, researchers demonstrated that the administration of the non-psychoactive cannabinoid cannabidiol (CBD) significantly inhibited the growth of subcutaneously implanted U87 human glioma cells in mice. The authors of the study noted that "... CBD was able to produce a significant antitumor activity both in vitro and in vivo, thus



suggesting a possible application of CBD as an antineoplastic agent.⁶⁵ The targeted effects of cannabinoids on GBM were further demonstrated in 2005 by researchers who showed that the cannabinoid THC both selectively inhibited the proliferation of malignant cells and induced them to die off, while leaving healthy cells unaffected.⁶⁶ While CBD and THC have each been demonstrated to have tumor-fighting

properties, research published in 2010 shows that CBD enhances the inhibitory effects of THC on GBM cell proliferation and survival.⁶⁷

Similarly, researchers reported in 2010 that the way cannabinoid and cannabinoid-like receptors in brain cells "regulate these cells' differentiation, functions and viability" suggests cannabinoids and other drugs that target cannabinoid receptors can "manage neuroinflammation and eradicate malignant astrocytomas," a type of glial cancer.⁶⁸ These recent studies confirm the findings of multiple studies that indicated the effectiveness of cannabinoids in fighting gliomas.⁶⁹⁻⁷⁶

Indications of the remarkable potential of cannabinoids to fight cancer in humans have also been seen in three large-scale population studies done

recently. The studies were designed to find correlations between smoking cannabis and cancers of the lung, throat, head and neck. Instead, the researchers discovered that the cancer rates of cannabis smokers were at worst no greater than those who smoked nothing at all or even better.⁷⁷ One study found that 10-20 years of cannabis use significantly reduced the incidence of head, neck and throat cancers.⁷⁸

Researchers suggest that cannabinoids may produce a prophylactic effect against cancer development, as seen in the anti-proliferation effect that has been demonstrated in vitro and in vivo.

While clinical research on using cannabis medicinally has been severely limited by federal restrictions, the accumulated data speaks strongly in favour of considering it as an option for most cancer patients, and many oncologists do. Survey data from a Harvard Medical School study in 1990, before any states had approved medical use, shows that 44% of oncologists had recommended cannabis to at least some of their patients, and more said they would do so if the laws were changed.⁷⁹ According to the American Cancer Society's 2010 data, more than 1,529,000 Americans are diagnosed with cancer each year.⁸⁰ At least 400,000 of them will undergo chemotherapy, meaning as many as 200,000 patients annually may have cannabis recommended to them to help fight the side effects of conventional treatments.



Radiation Therapy

Authors of the Institute of Medicine report, *Marijuana and Medicine: Assessing the Science Base*, acknowledge that there are certain cancer patients for whom cannabis should be a valid medical option. A random-sample anonymous survey was conducted in the spring of 1990 measuring the attitudes and experiences of oncologists concerning the antiemetic use of cannabis in cancer chemotherapy patients. Of the respondents expressing an opinion, a majority (54%) thought cannabis should be available by prescription.⁸¹

Current research on cannabinoids has shown that activation of both cannabinoid receptors has a well known anti-proliferative effect on cancer cells and may also have anti-angiogenic, anti-adhesive, anti-invasive, and anti-metastatic properties. Since cannabinoids are generally well tolerated and patients do not develop toxic side effects of conventional treatments, more studies are warranted to develop a cannabis-based cancer treatment.

How cannabis compares to other medications

The American Cancer Society lists more than 300 medications currently prescribed to treat cancer and its symptoms, and to treat the side effects of other cancer drugs. Some drugs are prescribed for pain caused by cancer, and cancer patients report pain relief with cannabis therapy. Many chemotherapy agents cause severe nausea and more than a dozen drugs are currently prescribed to treat nausea, including **Marinol**, a synthetic form of delta-9-THC, one of the active ingredients in cannabis.

The newer antiemetics, **Anzamet**, **Kytril** and **Zofran**, are serotonin antagonists, blocking the neurotransmitter that sends a vomiting signal to the brain. Rare side effects of these drugs include fever, fatigue,

bone pain, muscle aches, constipation, loss of appetite, inflammation of the pancreas, changes in electrical activity of heart, vivid dreams, sleep problems, confusion, anxiety and facial swelling.

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**

Reglan, a substituted benzamide, increases emptying of the stomach, thus decreasing the chance of developing nausea and vomiting due to food remaining in the stomach. When given at high doses, it blocks the messages to the part

of the brain responsible for nausea and vomiting resulting from chemotherapy. Side effects include sleepiness, restlessness, diarrhea and dry mouth. Rarer side effects are rash, hives and decreased blood pressure

Haldol and **Inapsine** are tranquilizers that block messages to the part of the brain responsible for nausea and vomiting. Possible side effects include decreased breathing rate, increased heart rate, decrease in blood pressure when changing position and, rarely, change in electrical activity of the heart.

Compazine and **Torecan** are phenothiazines, the first major anti-nausea drugs. Both have tranquilizing effects. Common side effects include dry mouth and constipation. Less common effects are blurred vision, restlessness, involuntary muscle movements, tremors, increased appetite, weight gain, increased heart rate and changes in electrical activity of

heart. Rare side effects include jaundice, rash, hives and increased sensitivity to sunlight.

Benadryl, an antihistamine, is given along with Reglan, Haldol, Inapsine, Compazine and Torecan to counter side effects of restlessness, tongue protrusion, and involuntary movements. Its side effects include sedation, drowsiness, dry mouth, dizziness, confusion, excitability and decreased blood pressure.

Decadron (dexamethasone), a corticosteroid, is given with other chemotherapy drugs as an adjunct medication. Common side effects include increased appetite, irritation of stomach, euphoria, difficulty sleeping, mood changes, flushing, increased blood sugar, decreased blood potassium level. Possible side effects upon discontinuing the drug include adrenal insufficiency, weakness, aches, fever, dizziness, lowering of blood pressure when changing position, difficulty breathing, and low blood sugar.



Benzodiazepine drugs **Ativan** and **Xanax** are also prescribed to combat the effects of chemotherapy. Ativan causes amnesia. Abruptly stopping the drug can cause anxiety, dizziness, nausea and vomiting, and tiredness. It can cause drowsiness, confusion, weakness, and headache when first starting the drug. Nausea, vomiting, dry mouth, changes in heart rate and blood pressure, and palpitations are possible side effects.

In addition, in April 2003 the FDA approved the drug **Emend** (aprepitant) to help control delayed-onset nausea. It is given along with two other anti-nausea drugs. A regimen of three pills costs \$250. The most common side effects with Emend are fatigue, nausea, loss of appetite, constipation, diarrhea.

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.

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.”⁸²

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.⁸³ 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 cancer, lung disease, or other respiratory problems.

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 another 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 by use of inhaled cannabis.



Angel Raich using a vaporizer in the hospital

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."⁸³ 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 observed, "Some users of both find cannabis itself more effective."

THE EXPERIENCE OF PATIENTS

Judith Cushner, Breast Cancer

In 1989, I was diagnosed with breast cancer. After a brief period of recovery from the surgeries, I was placed on an aggressive protocol of chemotherapy, which lasted for eight months. That protocol was referred to as "CMF," because it consisted of heavy doses of Cytosan, methotrexate, and 5 fluorouracil.

The treatment caused severe and persistent side effects which were thoroughly disabling: chronic nausea, joint pain and weakness; a debilitating lack of energy and motivation; loss of appetite and a resulting unwanted weight loss; sleep disruption; and eventually my withdrawal from social situations and interpersonal relationships. The cumulative effect of these symptoms often rendered it impossible (or painfully difficult) to take the huge number of medications essential to my treatment regimen.

Right from the start, I was given Compazine as part of my chemotherapy protocol. I took it both orally (in pill form) and intravenously, but it too caused severe adverse side effects, including neuropathy. Moreover, the Compazine provided little, if any, relief from the nausea that had persisted since my treatment began. Hoping for better results, my doctor discontinued the Compazine and prescribed Reglan. That, too, had no effect on the nausea and we decided to discontinue it after a fairly

short time. By then, I had developed chronic mouth sores (also from the chemotherapy), which made it extremely painful to take pills or swallow anything. Rather than providing relief, the Reglan increased my discomfort and pain.

Yet another drug I tried was Marinol, which gave me no relief from the unrelenting nausea. If anything, taking yet another pill increased my discomfort. The pills

themselves irritated the sores in my mouth. It also made me quite groggy, yet my sleep disturbance persisted, in part because my nausea and anxiety were so distracting. My doctor prescribed Lorazepam to help me sleep, but it was just one more medication with unpleasant effects of its own.

During this time, a friend of mine (who happened to be a nurse) gave me a marijuana cigarette. She had seen my suffering and thought it might help. I took her advice and it worked. I took just a few puffs and within minutes, the nausea dissipated. For the first time in several months, I felt relief. I also felt hope. I smoked small amounts of marijuana for the remainder of my chemotherapy and radiation treatment. It was not a regular part of my day, nor did it become a habit. Each time I felt nausea coming on, I inhaled just two or three puffs and it subsided.

As my nausea decreased, my ability to eat and retain food increased. I saw a marked weight gain and my energy increased. As my general health improved, my sleeping habits also improved. In retrospect, one of the greatest benefits from the marijuana was that it decreased my use of other, more disabling and toxic medications, including the Compazine, Reglan and Lorazepam.

My cancer has been in remission now for just under a year. I lived to see

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

my son's Bar Mitzvah, and I am proud to say that the risks I took to save my life, while technically illegal, have earned me the respect of both my children. They have learned the difference between therapeutic treatment and substance abuse, and (unlike many of their peers) that knowledge has helped them resist the temptations of recreational drugs.

My decision to use marijuana and save my own life has educated many, including my rabbi and my congregation.

Jo Daly, Colon Cancer

In 1980, I was appointed by Dianne Feinstein, then Mayor of San Francisco, to serve as police commissioner for the city of San Francisco, an office which I held for six years. On May 24, 1988, I was diagnosed with Phase IV cancer of the colon. By the time it was diagnosed, it had already spread to my ovaries and lymph nodes. My oncologist at the UCSF Hospital prescribed an aggressive regimen of chemotherapy, which lasted six months. I was given large doses of the chemicals, four hours a day, five days a week in the first week of each month.

Each day, when I returned home from the hospital following treatment, at about 5:00 p.m., my whole body turned quite warm, as if a fever were coursing through me. My fingernails even burned with heat. Invariably, I was overcome by a sudden wave of intense nausea—like a nuclear implosion in my solar plexus—and I rushed desperately for the bathroom where I would remain for hours, clutching the toilet and retching my guts out. I had no appetite. I could not hold down what little food that I managed to swallow. And I could not sleep at night.

This intense nausea persisted for the two weeks following the treatment. By the third week after treatment, the side effects of the chemicals began to wear off, and I started to feel better. The next week, however, I had to return to the hospital where the chemicals were administered once more, beginning my hell all over again.

To combat the nausea, I tried Marinol, a synthetic version of THC, one of the primary chemicals found in marijuana. However, I was often unable to swallow the Marinol capsule because of my severe nausea and retching. A friend then gave me a marijuana cigarette, suggesting that it might help quell my nausea. I took three puffs from the cigarette. One-half hour later, I was calm, my nausea had disappeared, my appetite returned, and I slept that evening.

I told my oncologist about how well marijuana quelled my nausea. My doctor was not surprised. In fact, he told me that many of his patients had made the same discovery. My doctor encouraged me to continue using marijuana if it worked. Although it occasionally produced a slight

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.

euphoria, it was not a painful sensation and I was careful never to leave the house during those rare moments.

My use of medical marijuana had a secondary, though by no means minor benefit: I was able to drastically reduce my dependence on more powerful prescription drugs that I was prescribed for pain and nausea.

With the help of medical marijuana, which I ingest only occasionally and in small amounts, I no longer need the Compazine, Lorazepam, Ativan and Halcion. No combination of these medications provided adequate relief. They also caused serious side effects that I never experienced with marijuana.

—Jo Daly was formerly a San Francisco Police Commissioner

Anonymous, Breast Cancer

I have used medicinal cannabis legally in California for a year, after being diagnosed and treated for breast cancer. I have also been given prescription drugs that were not effective, that irritated my stomach, for which they wanted to prescribe more drugs. These medications were neither cost-effective nor useful, and I choose to use medicinal cannabis through a vaporizer as recommended by my physician, thereby bypassing the sometimes-harmful effects of smoking.

I, personally, would rather the federal government use their resources to go after the true criminals and terrorists that we have in our country, as opposed to persecuting the sick for whatever relief they may have from medical cannabis.

Lyn Nofziger, Father of Cancer Patient

When our grown daughter was undergoing chemotherapy for lymph cancer, she was sick and vomiting constantly as a result of her treatments. No legal drugs, including Marinol, helped her. We finally turned to marijuana. With it, she kept her food down, was comfortable and even gained weight. Those who say Marinol and other drugs are satisfactory substitutes for marijuana may be right in some cases but certainly not in all cases.

If doctors can prescribe morphine and other addictive medicines, it

makes no sense to deny marijuana to sick and dying patients when it can be provided on a carefully controlled, prescription basis.

—Lyn Nofziger was formerly senior adviser to President Ronald Reagan

THE EXPERIENCE OF DOCTORS

Howard D. Maccabee, M.D.

In my practice, I commonly use radiation therapy to treat the whole spectrum of solid malignant tumors. Radiation therapy is often used after surgery or chemotherapy, as a second stage in treatment. Sometimes, however, radiation therapy is used concurrently with chemotherapy, or even as the first or only modality of treatment.

I treat approximately 20 patients each day and provide follow-up care and/or consultation with another 5 or so patients a day. I currently have approximately 2,000 patients in various stages of follow-up to their initial treatment. Most of these are long-term survivors.

Because of the nature of some cancers, I must sometimes irradiate large portions of my patients' abdomens. Such patients often experience nausea, vomiting, and other side effects. Because of the severity of these side effects, some of my patients choose to discontinue treatment altogether, even when they know that ceasing treatment could lead to death.

During the 1980s, I participated in a state-sponsored study of the effects of marijuana and THC (an active ingredient in marijuana) on nausea. It was my observation during this time that some patients smoked marijuana while hospitalized, often with the tacit approval of physicians. I also observed that medical marijuana was clinically effective in treating the nausea of some patients.

During my career as a physician, I have witnessed cases where patients suffered from nausea or vomiting that could not be controlled by prescription anti-emetics. I frequently hear similar reports from colleagues treating cancer and AIDS patients. As a practical matter, some patients are unable to swallow pills because of the side effects of radiation therapy or chemotherapy, or because of the nature of the cancer (for instance, throat cancer). For these patients, medical marijuana can be an effective form of treatment.

Debasish Tripathy, M.D.

Since 1993, I have been a physician at the UCSF Mount Zion Breast Care Center in San Francisco. My practice is devoted exclusively to breast can-

cer patients. I treat more than 1,000 patients. Approximately 100 of these patients are currently undergoing chemotherapy, a treatment utilizing various combinations of powerful medications. In some cases, the therapeutic dose of the medication we use is not far from the potentially lethal dose. Although chemotherapy is a widely used treatment in the treatment of many cancers, it can also cause severe adverse affects, which some patients are simply unable to tolerate. The most common adverse effects of chemotherapy are nausea and retching.

The nausea and retching associated with chemotherapy are often disabling and intractable. The severity of the symptoms and their medical consequences vary from patient to patient. In many cases, the immediate results are weight loss, fatigue, and chronic discomfort. The consequences can be far graver in patients whose health and functioning is already compromised. For example, the dangers associated with weight loss and malnutrition are greater in patients whose cancer has metastasized and attacked other parts of the body.

... I have prescribed Marinol to some of my patients and it has proven effective in some cases. However, scientific and anecdotal reports consistently indicate that smoking marijuana is a therapeutically preferable means of ingestion. Marinol is available in pill form only. Moreover, Marinol contains only one of the many ingredients found in marijuana (THC). It may be that the beneficial effects of THC are increased by the cumulative effect of additional substances found in cannabis. That is an area for future research. For whatever reason, smoking appears to result in faster, more effective relief, and dosage levels are more easily titrated and controlled in some patients.

Kate Scannell, MD

Because I was a cancer patient receiving chemotherapy at the same hospital where I worked, the women with whom I shared the suite quickly surmised that I was also a doctor. The clues were obvious: the colleagues dropping by, the "doctor" salutations from co-workers and the odd coincidence that one of my suite mates was also one of my patients.

I braced myself for this woman's question, both wanting to make myself available to her but also wishing that the world could forget that I was a doctor for the moment. After receiving my cancer diagnosis, dealing with surgery and chemo-therapy and grappling with insistent reminders of my mortality, I had no desire to think about medicine or to experience myself as a physician in that oncology suite. And besides, the chemotherapy, anti-nauseants, sleep medications and prednisone were hampering my ability to think clearly.

So, after a gentle disclaimer about my clinical capabilities, I said I'd do my best to answer her question. She shoved her IV line out of the way and, with great effort and discomfort, rolled on her side to face me. Her belly was a pendulous sack bloated with ovarian cancer cells, and her eyes were vacant of any light. She became short of breath from the task of turning toward me.

"Tell me," she managed, "Do you think marijuana could help me? I feel so sick."

I winced. I knew about her wretched pain, her constant nausea and all the prescription drugs that had failed her —some of which also made her more constipated, less alert and even more nauseous. I knew about the internal derangements of chemotherapy, the terrible feeling that a toxic swirl is invading your bones, destroying your gut and softening your brain. I knew this woman was dying a prolonged and miserable death.

And, from years of clinical experience, I —like many other doctors — also knew that marijuana could actually help her. 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. I could firmly attest to its benefits and wager the likelihood that it would decrease her suffering.

Still, federal law has forbidden doctors to . . . prescribe marijuana to patients [though doctors may legally recommend it.] In fact, in 1988 the Drug Enforcement Agency even rejected one of its own administrative law judge's conclusions supporting medicinal marijuana, after two full years of hearings on the issue.

Judge Francis Young recommended the change on grounds that "marijuana, in its natural form, is one of the safest therapeutically active substances known to man," and that it offered a "currently accepted medical use in treatment."

Doctors see all sorts of social injustices that are written on the human

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**

body, one person at a time. But this one —the rote denial of a palliative care drug like marijuana to people with serious illness —smacks of pure cruelty precisely because it is so easily remediable, precisely

AMERICAN ACADEMY OF FAMILY PHYSICIANS

"The American Academy of Family Physicians [supports] the use of marijuana ... under medical supervision and control for specific medical indications."

1996-1997 AAFP Reference Manual

because it prioritizes service to a cold political agenda over the distressed lives and deaths of real human beings.

Washington bureaucrats — far removed from the troubled bedsides of sick and dying patients —are ignoring what patients and doc-

tors and health care workers are telling them about real world suffering. The federal refusal to honor public referendums like California's voter-approved Medical Marijuana Initiative is bewildering. Its refusal to listen to doctors groups like the California Medical Association that support compassionate use of medical marijuana is chilling.

In a society that has witnessed extensive positive experiences with medicinal marijuana, as long as it is safe and not proven to be ineffective, why shouldn't seriously ill patients have access to it? Why should an old woman be made to die a horrible death for a hollow political symbol?

—Dr. Scannell is co-director of the Ethics Department of Kaiser-Permanente.

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."⁶⁵

The American Medical Association opposed the first federal law against cannabis with an article in its leading journal.⁶⁶ 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. But the U.S. federal government also 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 helped by it substantially.

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 pro-

gram 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

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**

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

Public opinion is clearly in favor of ending the prohibition of medical cannabis and has been for some time. A CNN/Time poll in November 2002 found that 80% of Americans support medical cannabis. The AARP, the national association whose 35 million members are over the age of fifty, released a national poll in December 2004 showing that nearly two-thirds of older Americans support legal access to medical marijuana. Support in the West, where most states that allow legal access are located, was strongest, at 82%, but at least 2 out of 3 everywhere agreed that "adults should be allowed to legally use marijuana for medical purposes if a physician recommends it."

The refusal of the federal government to act on this support has meant that patients have had to turn to the states for action. Since 1996, 15 states have removed criminal penalties for their citizens who use cannabis on the advice of a physician. Voters have passed medical cannabis ballot initiatives in 10 states plus the District of Columbia, while the legislatures in Hawaii, Maryland, New Jersey, New Mexico, Rhode Island, and Vermont and have enacted similar bills. Approximately one third of the U.S. population resides in a state that permits medical use, and medical cannabis legislation is introduced in more states every year.

Currently, laws that effectively remove state-level criminal penalties for growing and/or possessing medical cannabis are in place in Alaska, Arizona, California, Colorado, Hawaii, Maine, Montana, Nevada, New Jersey, New Mexico, Oregon, Rhode Island, Vermont, Washington, and the District of Columbia. Maryland has reduced the criminal penalty for medical use to a maximum \$100 fine. Thirty-six states have symbolic medical cannabis laws (laws that support medical cannabis but do not provide patients with legal protection under state law).

2005 U.S. Supreme Court ruling

In June 2005, the U.S. Supreme Court overturned a decision by a U.S. appeals court (*Raich v. Ashcroft*) that had exempted medical marijuana from federal prohibition. The 2005 decision, now called *Gonzales v. Raich*, ruled that federal officials may prosecute medical marijuana patients for possessing, consuming, and cultivating medical cannabis. But according to numerous legal opinions, that ruling does not

PROFESSIONAL ORGANIZATION ENDORSEMENTS

AIDS Action Council	French Ministry of Health
Alaska Nurses Association	Hawaii Nurses Association
American Academy of Family Physicians	Health Canada
American Medical Student Association	Kaiser Permanente
American Nurses Association	Lymphoma Foundation of America
American Preventive Medical Association	Mississippi Nurses Association
American Public Health Association	Multiple Sclerosis Society (Canada)
American Society of Addiction Medicine	National Acad. of Sciences Inst. of Medicine
Arthritis Research Campaign (UK)	National Association for Public Health Policy
Australian Medical Association	National Nurses Society on Addictions
Australian National Task Force on Cannabis	Netherlands Ministry of Health
Belgian Ministry of Health	New Jersey State Nurses Association
British House of Lords Select Committee	New Mexico Medical Society
British Medical Association	New Mexico Nurses Association
California Academy of Family Physicians	New York State Nurses Association
California Nurses Association	North Carolina Nurses Association
California Pharmacists Association	San Francisco Mayor's Summit on AIDS
Colorado Nurses Association	San Francisco Medical Society
Federation of American Scientists	Virginia Nurses Association
Florida Governor's Red Ribbon Panel on AIDS	Whitman-Walker Clinic
Florida Medical Association	Wisconsin Nurses Association

affect individual states' medical marijuana programs, and only applies to prosecution in federal, not state, court.

Petitions for legal prescriptions pending

The federal Department of Health and Human Services (HHS) and the FDA are currently reviewing two legal petitions with broad implications for medical marijuana. The first, brought by ASA under the Data Quality Act, says HHS must correct its statements that there is no medical use for marijuana to reflect the many studies which have found it helpful for many conditions. Acknowledging legitimate medical use would then force the agency to consider allowing the prescribing of marijuana as they do other drugs, based on its relative safety.

A separate petition, of which ASA is a co-signer, asks the Drug Enforcement Administration for a full, formal re-evaluation of marijuana's medical benefits, based on hundreds of recent medical research studies and two thousand years of documented human use.

Legal Citations

1. See "The Administration's Response to the Passage of California Proposition 215 and Arizona Proposition 200" (Dec. 30, 1996).
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).

Research Citations

11. Abrams D et al. 2003. Short-Term Effects of Cannabinoids in Patients with HIV-1 Infection: A Randomized, Placebo-Controlled Clinical Trial. *Ann Intern Med.* Aug 19;139(4):258-66.
12. Tramer et al. 2001. Cannabinoids for control of chemotherapy induced nausea and vomiting: quantitative systematic review. *BMJ* Jul 7;323(7303):16-21.
13. Machado. 2008. Therapeutic use of Cannabis sativa on chemotherapy-induced nausea and vomiting among cancer patients: systematic review and meta-analysis. *Eur J cancer Care Sep*;17(5):431-43
14. Guzman M et al. 2007. A pilot clinical study of Delta9-tetrahydrocannabinol in patients with recurrent glioblastoma multiforme. *Br J Cancer.* Jul 17;95(2):197-203
15. Alexander A et al. 2009. Cannabinoids in the Treatment of Cancer. *Cancer Lett* Nov 18;285(1):6-12.
16. Joy J et al. 1999. *Marijuana and Medicine: Assessing the Science Base.* Washington, DC: Institute of Medicine.
17. British Medical Association. 1997. *Therapeutic Uses of Cannabis.* Harwood.
18. House of Lords, Select Committee on Science and Technology, (1998). *Cannabis: The Scientific and Medical Evidence.* London, England: The Stationery Office, Parliament.
19. Johnson J et al. 2009. Multicenter, Double Blind, Randomized, Placebo-Controlled, Parallel-Group Study of the Efficacy, Safety, and Tolerability of THC:CBD Extract and THC Extract in Patients with Intractable Cancer Related pain. *J of Pain and Symptom Management.*
23. Sarfaraz et al. 2005. Cannabinoid receptors as a novel target for the treatment of prostate cancer. *Cancer Research* 65: 1635-1641.
24. Mimeault et al. 2003. Anti-proliferative and apoptotic effects of anandamide in human prostatic cancer cell lines. *Prostate* 56: 1-12.
25. Ruiz et al. 1999. Delta-9-tetrahydrocannabinol induces apoptosis in human prostate PC-3 cells via a receptor-independent mechanism. *FEBS Letters* 458: 400-404.

26. Pastos et al. 2005. The endogenous cannabinoid, anandamide, induces cell death in colorectal carcinoma cells: a possible role for cyclooxygenase-2. *Gut* 54: 1741-1750.
27. Casanova et al. Inhibition of skin tumor growth and angiogenesis in vivo by activation of cannabinoid receptors. 2003. *Journal of Clinical Investigation* 111: 43-50.
28. Powles et al. 2005. Cannabis-induced cytotoxicity in leukemic cell lines. *Blood* 105: 1214-1221
29. Guzman et al. 2003. Inhibition of tumor angiogenesis by cannabinoids. *The FASEB Journal* 17: 529-531.
30. Jia et al 2006. Delta-9-tetrahydrocannabinol-induced apoptosis is jurkat leukemic T cells in regulated by translocation of Bad to mitochondria. *Molecular Cancer Research* 4: 549-562.
31. Preet et al. 2008. Delta9-Tetrahydrocannabinol inhibits epithelial growth factor-induced lung cancer cell migration in vitro as well as its growth and metastasis in vivo. *Oncogene* 10: 339-346.
32. Baek et al. 1998. Antitumor activity of cannabigerol against human oral epitheloid carcinoma cells. *Archives of Pharmacal Research*: 21: 353-356.
33. Carracedo et al. 2006. Cannabinoids induce apoptosis of pancreatic tumor cells via endoplasmic reticulum stress-related genes. *Cancer Research* 66: 6748-6755.
34. Michalski et al. 2008. Cannabinoids in pancreatic cancer: correlation with survival and pain. *International Journal of Cancer* 122: 742-750.
35. Ramer and Hinz. 2008. Inhibition of cancer cell invasion by cannabinoids via increased cell expression of tissue inhibitor of matrix metalloproteinases-1. *Journal of the National Cancer Institute* 100: 59-69.
36. Whyte et al. 2010. Cannabinoids inhibit cellular respiration of human oral cancer cells. *Pharmacology* 85: 328-335.
37. Leelawat et al. 2010. The dual effects of delta(9)-tetrahydrocannabinol on cholangiocarcinoma cells: anti-invasion activity at low concentration and apoptosis induction at high concentration. *Cancer Investigation* 28: 357-363.
38. Gustafsson et al. 2006. Cannabinoid receptor-mediated apoptosis induced by R(+)-methanandamide and Win55,212 is associated with ceramide accumulation and p38 activation in Mantle Cell Lymphoma. *Molecular Pharmacology* 70: 1612-1620.
39. Gustafsson et al. 2008. Expression of cannabinoid receptors type 1 and type 2 in non-Hodgkin lymphoma: Growth inhibition by receptor activation. *International Journal of Cancer* 123: 1025-1033.
40. Liu et al. 2008. Enhancing the in vitro cytotoxic activity of Δ9-tetrahydrocannabinol in leukemic cells through a combinatorial approach. *Leukemia and Lymphoma* 49: 1800-1809.
41. Torres S, et al. *Mol Cancer Ther* 2011;10(1):90-103. THC and cannabidiol (CBD) remarkably reduced the growth of gliomas.
42. Guzman et al. 1998. Delta-9-tetrahydrocannabinol induces apoptosis in C6 glioma cells. *FEBS Letters* 436: 6-10.
43. Guzman et al. 2000. Anti-tumoral action of cannabinoids: involvement of sustained ceramide accumulation and extracellular signal-regulated kinase activation. *Nature Medicine* 6: 313-319.
44. Guzman et al. 2003. Inhibition of tumor angiogenesis by cannabinoids. *The FASEB Journal* 17: 529-531.
45. Alexander A et al. 2009. Cannabinoids in the Treatment of Cancer. *Cancer Lett Nov* 18:285(1):6-12.

46. Olea-Herrero N et al. 2009. Inhibition of human tumour prostate PC-3 cell growth by cannabinoids R(+)-Methanandamide and JWH-015: Involvement of CB2. *British Journal of Cancer*. 101, 940-950.
47. Blazquez C et al (2003) Inhibition of tumor angiogenesis by cannabinoids. *FASEB J*. 17(3): 529-31. Epub 2003 Jan 02.
48. Sanchez C et al. 2001. Inhibition of glioma growth in vivo by selective activation of the CB(2) cannabinoid receptor. *Cancer Res*. 61(15): 5784-9.
49. Casanova ML et al. 2003. Inhibition of skin tumor growth and angiogenesis in vivo by activation of cannabinoid receptors. *J Clin Invest*. 111(1): 43-50
50. Jacobsson SO, et al. 2001. Inhibition of rat C6 glioma cell proliferation by endogenous and synthetic cannabinoids. Relative involvement of cannabinoid and vanilloid receptors. *J Pharmacol Exp Ther*. Dec;299(3): 951-9.
51. Galve-Roperph I et al. 2000. Antitumoral action of cannabinoids: involvement of sustained ceramide accumulation of ERK activation. *Nature Medicine* 6: 313-319
52. ACM Bulletin. "THC destroys brain cancer in animal research." <http://www.acmed.org/english/2000/eb000305.html>
53. Gonzalez S et al. 2000. Decreased cannabinoid CB1 receptor mRNA levels and immunoreactivity in pituitary hyperplasia induced by prolonged exposure to estrogens. *Pituitary*. 3(4):221-6.
54. Pagotto U et al. 2001. Normal human pituitary gland and pituitary adenomas express cannabinoid receptor type 1 and synthesize endogenous cannabinoids: first evidence for a direct role of cannabinoids on hormone modulation at the human pituitary level. *J Clin Endocrinol Metab*. 86(6):2687-96
55. Bifulco M et al. 2001. Control by the endogenous cannabinoid system of ras oncogene-dependent tumor growth. *FASEB J*. 15(14): 2745-7.
56. Rubovitch V et al. 2002. The cannabinoid agonist DALN positively modulates L-type voltage-dependent calcium-channels in N18TG2 neuroblastoma cells. *Brain Res Mol Brain Res*. 101(1-2):93-102.
57. *Cancer Lett*. 2009 May 11.
58. Ramer R. 2010. Cannabidiol inhibits cancer cell invasion via upregulation of tissue inhibitor of matrix metalloproteinases-1. *Biochem Pharmacol*. Apr 1;79(7):955-66.
59. McAllister et al. 2007. Cannabidiol as a novel inhibitor of Id-1 gene expression in aggressive breast cancer cells. *Molecular Cancer Therapeutics* 6: 2921-2927.
60. Cafferal et al. 2010. Cannabinoids reduce ErbB2-driven breast cancer progression through Akt inhibition. *Molecular Cancer* 9: 196.
61. De Petrocellis et al. 1998. The endogenous cannabinoid anandamide inhibits human breast cancer cell proliferation. *Proceedings of the National Academy of Sciences of the United States of America* 95: 8375-8380.
62. Cafferal et al. 2006. Delta-9-Tetrahydrocannabinol inhibits cell cycle progression in human breast cancer cells through Cdc2 regulation. *Cancer Research* 66: 6615-6621.
63. Di Marzo et al. 2006. Anti-tumor activity of plant cannabinoids with emphasis on the effect of cannabidiol on human breast carcinoma. *Journal of Pharmacology and Experimental Therapeutics Fast Forward* 318: 1375-1387.
64. Guzman et al. 2004. Cannabinoids inhibit the vascular endothelial growth factor pathways in gliomas (PDF). *Cancer Research* 64: 5617-5623.
65. Massi P et al. 2004. Antitumor effects of cannabidiol, a nonpsychoactive cannabinoid, on human glioma cell lines. *JPET* 308:838-845.

66. Allister et al. 2005. Cannabinoids selectively inhibit proliferation and induce death of cultured human glioblastoma multiforme cells. *Journal of Neurooncology* 74: 31-40.
67. Marcu J et al (2010). Cannabidiol enhances the inhibitory effects of Delta9-tetrahydrocannabinol on human glioblastoma cell proliferation and survival. *Molecular Cancer Therapeutics* 9(1):180-9
68. Stella N. 2010. Cannabinoid and cannabinoid-like receptors in microglia, astrocytes, and astrocytomas. *Glia*. Jul;58(9):1017-30.
69. Guzman et al. 1998. Delta-9-tetrahydrocannabinol induces apoptosis in C6 glioma cells. *FEBS Letters* 436: 6-10.
70. Massi et al. 2004. Antitumor effects of cannabidiol, a non-psychotropic cannabinoid, on human glioma cell lines. *Journal of Pharmacology and Experimental Therapeutics Fast Forward* 308: 838-845.
71. Guzman et al. 2004. Cannabinoids inhibit the vascular endothelial growth factor pathways in gliomas (PDF). *Cancer Research* 64: 5617-5623.
72. Allister et al. 2005. Cannabinoids selectively inhibit proliferation and induce death of cultured human glioblastoma multiforme cells. *Journal of Neurooncology* 74: 31-40.
73. Guzman et al. 2006. A pilot clinical study of delta-9-tetrahydrocannabinol in patients with recurrent glioblastoma multiforme. *British Journal of Cancer* (E-pub ahead of print).
74. Parolaro and Massi. 2008. Cannabinoids as a potential new drug therapy for the treatment of gliomas. *Expert Reviews of Neurotherapeutics* 8: 37-49
75. Galanti et al. 2007. Delta9-Tetrahydrocannabinol inhibits cell cycle progression by downregulation of E2F1 in human glioblastoma multiforme cells. *Acta Oncologica* 12: 1-9.
76. Calatozzolo et al. 2007. Expression of cannabinoid receptors and neurotrophins in human gliomas. *Neurological Sciences* 28: 304-310.
77. Tashkin D. 2006. Paper presented at American Thoracic Society 102nd International Conference, San Diego, May 23, 2006.
78. Lang C et al. 2009. A population-based case-control study of marijuana use and head and neck squamous cell carcinoma. *Cancer Prev Res (Phila Pa)*. 2009 Aug;2(8):759-68.
79. Doblin R, Kleiman MAR (1991). Marijuana as Antiemetic Medicine: A Survey of Oncologists' Experiences and Attitudes. *J Clin Oncol*; 9: 1275-1290.
80. American Cancer Society (2010). *Cancer Facts and Figures 2010*. <http://www.cancer.org/acs/groups/content/@epidemiologysurveillance/documents/document/acspc-026238.pdf>.
81. Doblin R (1991). Op cit.
82. Grinspoon L (1995). Marijuana as medicine: a plea for reconsideration. *JAMA* 273(23):1875-1876.
83. Hazekamp A et al (2006). Evaluation of a vaporizing device (Volcano(R)) for the pulmonary administration of tetrahydrocannabinol. *J Pharm Sci* 95 (6) Apr 24: 1308-1317.
84. Musty R, Rossi R (2001). Effects of smoked cannabis and oral delta-9-tetrahydrocannabinol on nausea and emesis after cancer chemotherapy: a review of state clinical trials. *Journal of Cannabis Therapeutics*. 1: 29-56.
85. *Lancet* 1; 1823.
86. 108 J.A.M.A. 1543-44; 1937.

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

Advancing Legal Medical Marijuana Therapeutics and Research

888-929-4367 www.AmericansForSafeAccess.org
1322 Webster Street, Suite 402, Oakland, California 94612