AGING
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:

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.

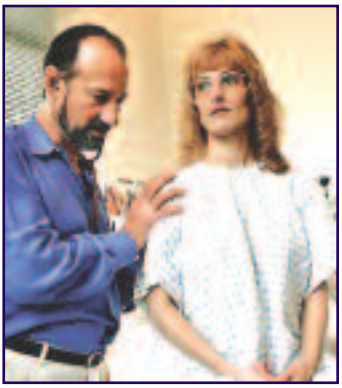
This brochure is intended to be a starting point for the consideration of applying cannabis therapies to specific conditions; it is not intended to replace the training and expertise of physicians with regard to medicine, or attorneys with regard to the law. But as patients, doctors and advocates who have worked intimately with these issues for many years, we have 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, please see **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 patient[9] 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

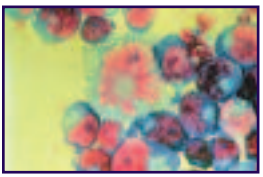
Patients protected under state, not federal, law. In June 2005, the U.S. Supreme Court overturned the Raich v. Ashcroft Ninth Circuit Court of Appeals decision. In reversing the lower court's ruling, Gonzales v. Raich established that it is legal under federal law to prosecute patients who possess, grow, 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.



T4 Immune 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 1991with 50 members; as of 2010, there are nearly 500 around the world. The International Association for Cannabis as Medicine (IACM), founded in March 2000, publishes a bi-weekly bulletin and holds international symposia 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 published double-blind, placebo-controlled studies studied pain relief; each showed cannabis to be effective.

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 opiods, 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 opioids.

CANNABIS AND AGING

Cannabis has been found to help many patients suffering from conditions that afflict older patients, including arthritis, chronic pain, cancer, Alzheimer's disease, diabetes, and spasticity associated with such diseases as Parkinson's.

Cannabis and Arthritis

More than 31 million Americans suffer from arthritis. There are two main types of arthritis: rheumatoid arthritis and osteoarthritis. Both affect the joints, causing pain and swelling, and limiting movement.

Rheumatoid arthritis (RA) is caused by a malfunction of the immune system. Instead of fighting off intruders such as bacteria or viruses, the body attacks the synovial membranes, which facilitate the movement of joints, eventually destroying cartilage and eroding bones. Rheumatoid arthritis is most common among the aged, whose immune systems are no longer as robust or efficient as they were when younger.

Osteoarthritis (OA), or arthritis of the bones, is also found primarily among the elderly, where cartilage has been worn away through many years of use. Arthritis may also manifest as chronic inflammation of the joints as the result of injuries. OA is the most common form of arthritis, affecting more than 10 million people worldwide. Currently, no drugs are available to treat or modify this disease, and treatment is primarily focused around the use of pain killers, which often have limited benefits and hazardous side effects.

An important aspect of arthritis pathology relates to maintaining healthy bone. As people age, bones undergo extensive remodelling, which can lead to destruction or functional degradation of synovial joints. Drugs which can not only modulate pain from arthritis but also protect bones are of great importance.

Cannabis and cannabinoids represent a promising treatment which can reduce arthritic pain and inflammation and positively modulate bone growth and maintenance. It has already been demonstrated that cannabinoids can effectively treat some types of arthritic pain, but recent evidence suggests that the cannabinoids are also important for bone growth and maintenance throughout life.[12-17]

The importance of cannabinoids in bone health has been established in trans-

genic mice that are missing either the CB1 or CB2 receptor. These mice develop osteoporosis much more quickly than normal or wild mice. Research has recently shown that mice missing both cannabinoid receptors have extremely weak bones, a condition that underlies osteoporosis and osteoarthritis pathology.[18-20]

Based on genetic screening techniques, a correlation between cannabinoids and bone is emerging in humans as well. Three studies in three distinct ethnic groups have demonstrated that mutations in the type 2 cannabinoid receptor correlate to bone diseases. One study even showed that hand bone strength weakness is very well correlated with dysfunctional/mutant CB2 receptors.

Arthritis of any type can be an extremely painful and debilitating condition that presents challenges for pain management. The use of cannabis as a treatment for musclo-skeletal pain in western medicine dates to the 1700s.[21-22] Evidence from recent research suggests that cannabis-based therapies are effective in the treatment of arthritis and the other rheumatic and degenerative hip, joint and connective tissue disorders. Since these are frequently extremely painful conditions, the well-documented analgesic properties of cannabis make it useful in treating the pain associated with arthritis, both on its own and as an adjunct therapy that substantially enhances the efficacy of opioid painkillers.

Cannabis has also been shown to have powerful immune-modulation and anti-inflammatory properties,[23-26] suggesting that it could play a role not just in symptom management but treatment of arthritis. In fact, one of the earliest records of medical use of cannabis, a Chinese text dating from ca. 2000 BC, notes that cannabis "undoes rheumatism," suggesting its anti-inflammatory and immune modulating effects were known even then.[27]

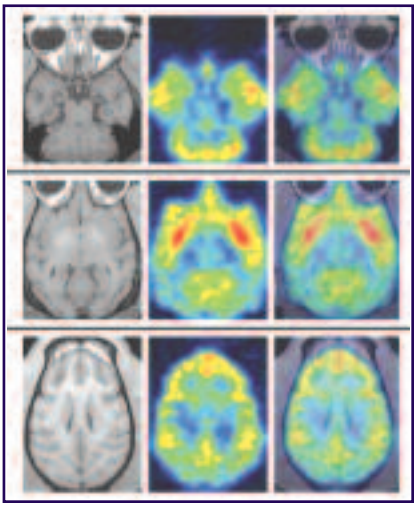
Modern research on cannabidiol (CBD), one of the non-psychoactive cannabinoid components of cannabis, has found that it suppresses the immune response in mice and rats that is responsible for a disease resembling arthritis, protecting them from severe damage to their joints and markedly improving their condition.[28-29]

Human studies have repeatedly shown cannabis to be an effective treatment for rheumatoid arthritis, and it is one of the enumerated conditions for which many states allow legal medical use. Cannabis has a demonstrated ability to improve mobility and reduce morning stiffness and inflammation. Research has also shown that patients are able to reduce their usage of potentially harmful Non-Steroidal Anti-Inflammatory drugs (NSAIDs) when using cannabis as an adjunct therapy.[30-31]

Medical researchers at Hebrew University in Jerusalem found that when cannabidiol is metabolized, one result is the creation of a compound with potent anti-inflammatory action comparable to the drug indomethacin, but without the considerable gastrointestinal side effects associated with that drug.[32]

In addition, when the body metabolizes tetrahydrocannabinol (THC), one of the primary cannabinoid components of cannabis, it produces a number of related chemicals. At least one of these metabolites has anti-inflammatory and pain-relieving effects. By modifying this metabolite, researchers have produced a synthetic carboxylic acid known as CT-3 (also calleddimethylheptyl-THC-11 oic acid

or DMH-11C), which is more powerful than the natural metabolite itself, and thus can be given in smaller doses. Animal tests found CT-3 effective against both chronic and acute inflammation, and it also prevented destruction of joint tissue from chronic inflammation.



Cannabinoid receptors in the brain

The remarkable 5,000-year safety record of cannabis—there has never been a recorded death from an overdose—and the fact that a metabolite with the desired anti-inflammatory effect is produced in the body when cannabis is used, indicates that the development of targeted, safe, and effective anti-inflammatory drugs in this class are possible.[33] CT3 has also demonstrated considerable analgesic effects in animals. In some cases, the dose-dependent effect of THC was equivalent to morphine, but with a much greater duration of action and far less toxicity.[34-35]

In contrast to the NSAIDs commonly prescribed arthritis sufferers, CT3 did not cause ulcers at therapeutically effective doses. Moreover, it does not depress respiration, produce dependence, induce body weight loss, or cause mutations, as many commonly prescribed drugs do. Studies on its mechanism of action are currently underway, with cytokine synthesis one of the pathways being studied.[36]

Cannabis may also help combat rheumatoid arthritis through its well-recognized immune-modulation properties.[37] Rheumatoid arthritis is characterized by dysregulation of the immune system in response to an initial infection or trauma. Over-activity of the immune system's B-cells causes antibodies to attack and destroy the synovial tissues located in the joint.

The immuno-modulatory properties of a group of fats found in cannabis, known as sterols and sterolins, have been used as natural alternatives to conventional rheumatoid arthritis treatments that employ highly toxic drugs to either suppress the entire immune response of the body or to palliate pain and the inflammatory process without correcting the underlying immune dysfunction.

Cytokines play a role in either fuelling or suppressing the inflammation that causes damage in rheumatoid arthritis and some other diseases. The release of selected cytokines is impaired by cannabis, but the findings differ by cell type, experimental conditions, and especially the concentration of the cannabinoids examined.[38-41] A sterol/sterolin combination has been experimentally demonstrated to reduce the secretion of the pro-inflammatory cytokines controlled by the TH2 helper cells and to increase the number of TH helper cells that regulate the secretion of antibodies from the B cells. This selective activation and inhibition of the immune system results is an effective control of the dysfunctional autoimmune response.

Similarly, ajulemic acid (another non-psychoactive cannabinoid) has been found

to reduce joint tissue damage in rats with adjuvant arthritis.[42] Tests on human tissue done in vitro showed a 50% suppression of one of the body's chemicals (interleukin-1beta) central to the progression of inflammation and joint tissue injury in patients with rheumatoid arthritis.[43]

Cannabis and Chronic Pain

Persistent and disabling pain can have numerous and sometimes multiple causes. Among them are cancer; AIDS; sickle cell anemia; multiple sclerosis; defects or injuries to the back, neck and spinal cord; arthritis and other rheumatic and degenerative hip, joint and connective tissue disorders; and severe burns. Pain is not a primary condition or injury, but rather a severe, frequently intolerable symptom that varies in frequency, duration, and severity according to the individual. The underlying condition determines the appropriate curative approach, but does not determine the proper symptom management. It is the character, severity, location and duration of the pain that determines the range of appropriate therapies

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"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

Chronic pain is a public health issue that is widespread across the aging populations of industrialized nations. Epidemiological statistics are alarming: In Europe, it is estimated that one in four adults has a chronic pain condition.[44] In the US, it is estimated that at least 38 million adults suffer from chronic pain, and at least 12 million have used cannabis as a treatment.

For patients in pain, the goal is to function as fully as possible by reducing their pain as much as possible, while minimizing the often-debilitating side effects of the pain therapies. Failure to adequately treat severe and/or chronic pain can have tragic consequences. Not infrequently, people in unrelieved pain want to die. Despair can also cause patients to discontinue potentially life-saving procedures (e.g., chemotherapy or surgery), which themselves cause severe suffering. In such dire cases, anything that helps to alleviate the pain will prolong these patients' lives.

Cannabis can serve at least two important roles in safe, effective pain management. It can provide relief from the pain itself (either alone or in combination with other analgesics), and it can control the nausea associated with taking opioid drugs, as well as the nausea, vomiting and dizziness that often accompany severe, prolonged pain.

Opioid therapy is often an effective treatment for severe pain, but all opiates have the potential to induce nausea. The intensity and duration of this nausea can cause enormous discomfort and additional suffering and lead to malnourishment, anorexia, wasting, and a severe decline in a patient's health. Some patients find the nausea so intolerable that they are inclined to discontinue the primary pain treatment, rather than endure the nausea.

Inhaled cannabis provides almost immediate relief for this with significantly fewer adverse effects than orally ingested Marinol. Inhalation allows the active compounds in cannabis to be absorbed into the blood stream with greater speed and efficiency. It is for this reason that inhalation is an increasingly common, and often preferable, route of administration for many medications. Cannabis may also be more effective than Marinol because it contains many more cannabinoids than just the THC that is Marinol's active ingredient. The additional cannabinoids may well have additional and complementary antiemetic qualities. They have been conclusively shown to have better pain-control properties when taken in combination than THC alone.

Research on cannabis and pain management

Cannabis has been used as an analgesic for thousands of years[45-47] and patients often report significant pain relief from cannabis, even in cases where conventional pain therapies have failed.[48-53]

After reviewing a series of trials in 1997, the U.S. Society for Neuroscience concluded that "substances similar to or derived from marijuana could benefit the more than 97 million Americans who experience some form of pain each year."[54] A 1999 study commissioned by the White House and conducted by the Institute of Medicine recognized the role that cannabis can play in treating chronic pain.[55] "After nausea and vomiting, chronic pain was the condition cited most often to the IOM study team as a medicinal use for marijuana." From 1975 to February 2011, there have been nearly 300 studies showing that cannabinoids and cannabis can help patients experiencing chronic pain.[56, 57]

Some of the most encouraging clinical data on effects of cannabinoids on chronic pain are from studies of intractable cancer pain and hard-to-treat neuropathic pain.[58] The effectiveness of cannabis and cannabinoids in relieving neuropathic pain has been demonstrated in more than three dozen preclinical and clinical trials.[59] A trial of cannabis cigarettes to treat HIV-associated daily neuropathic pain in 50 patients showed an average reduction of pain by 30% over a treatment course of only 5 days.[60] In 2001, researchers reported that cannabis extract sprayed under the tongue (Sativex®) was effective in reducing pain in patients suffering intractable neuropathic pain.[61] A review of over 20 clinical trials on cannabis and cannabinoids found that whole plant cannabis and extracts are superior to oral THC for the treatment of pain. Health Canada approved Sativex® for prescription in the treatment of HIV-associated neuropathic pain in 2005 and cancer pain in 2007.

The activity of the more than 100 cannabinoids and other components on the plant may explain its superiority in reducing pain when comparing whole plant cannabis and extracts to THC alone. For instance, the cannabinoid cannabichromene (CBC), the third most common ingredient on the plant, exhibits anti-inflammatory and analgesic actions, although weaker than THC.[62] Similarly, beta-sitosterol, a non-cannabinoid ingredient found in cannabis, was able to decrease inflammation and edema in skin treatment.[63] And a unique flavanoid found only in cannabis, cannaflavin A, inhibits the inflammatory molecule PGE-2, thirty times more potently than aspirin.[64] Lastly beta-caryophyllene, a cannabinoid found in many plants besides cannabis, has strong anti-inflamma-

tory properties but no noticeable side effects.[65] Beta-caryophyllen is the most commonly consumed FDA-approved cannabinoid in food.

The IOM report found that "basic biology indicates a role for cannabinoids in pain and control of movement, which is consistent with a possible therapeutic role in these areas. The evidence is relatively strong for the treatment of pain and intriguingly, although less well established, for movement disorder."

According to the IOM Report and numerous independent research articles, a number of areas in the brain that have an established role in sensing and processing pain respond to the analgesic effect of cannabis, adding that cannabinoids have been used successfully to treat cancer pain, which is often resistant to treatment with opiates. The effectiveness of cannabinoids in treating intractable cancer pain has been demonstrated in several subsequent clinical trials of a dosage-controlled sublingual spray.

Several studies have found that cannabinoids have analgesic effects in animal models, sometimes equivalent to codeine.[66-70] Cannabinoids also seem to synergize with opioids, which often lose their effectiveness as patients build up tolerance. One study found morphine was 15 times more active in rats with the addition of a small dose of THC. Codeine was enhanced on the order of 900 fold.[71] In 1990, researchers conducted a double-blind study comparing the antispasmodic and analgesic effects of THC, oral Codeine, and a placebo on a single patient suffering from a spinal cord injury.[72] Their findings confirmed the analgesic effects of THC being "equivalent to codeine." A 1997 study made similar findings related to morphine.[73]

A 1999 article reviewing the body of scientific animal research concerning the analgesic effects of marijuana concludes that "[t]here is now unequivocal evidence that cannabinoids are antinociceptive [capable of blocking the appreciation or transmission of pain] in animal models of acute pain."[74] The report notes that multiple cannabinoids and noncannabinoid components can serve as anti-inflammatory agents, and so have potential in preventing and reducing pain caused by swelling (such as arthritis). In short, the research community recognizes the potential benefits of cannabis for certain patients, including:

- Chemotherapy patients, especially those being treated for mucositis, nausea, and anorexia.
- Postoperative pain patients (using cannabinoids as an opioid adjunct to reduce the nausea and vomiting).
- Patients with spinal cord injury, peripheral neuropathic pain, or central post-stroke pain.
- Patients with chronic pain and insomnia.
- AIDS patients with cachexia, AIDS neuropathy, or any significant pain.

Britain's House of Lords reached similar conclusions and called for making cannabis available by prescription.[75]

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.[78] 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.[79] 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.[80] 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.[81]

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."[82] 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."[83-84]

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.[85]

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 gowing and spreading, including brain, breast, leukemic, melanoma, phaeochromocytoma, liver and other kinds of cancer.[86-103] Cannabinoids have been repeatedly shown to promote apoptosis (programmed cell death of the tumor cells) and halt angiogenesis (blood vessel production to the tumor).[104-108]

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.[109]

In multiple studies published between 2001 and 2003, cannabinoids inhibited tumor growth in laboratory animals.[110-113] 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.[114, 115] And, research on pituitary cancers suggest that cannabinoids may be the key to regulating human pituitary hormone secretion.[116-119] 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.[120]

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.[121] The mechanism of the anti-cancer activity of CBD and other cannabinoids has also been repeatedly demonstrated with breast cancers.[122-126]

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.[127] 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.[128] 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.[129] 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.[130]

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Marijuana and Medicine: Assessing the Science Base, 1999

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.[131] These recent studies confirm the findings of multiple studies that indicated the effectiveness of cannabinoids in fighting gliomas.[132-139]

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.[140] One study found that 10-20 years of cannabis use significantly reduced the incidence of head, neck and throat cancers.[141] Researchers suggest that cannabinoids my 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.[142] According the American Cancer Society's 2010 data, more than 1,529,000 Americans are diagnosed with cancer each year.[143] 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.

Authors of the Institute of Medicine report, "Marijuana and Medicine: Assessing the Science Base," acknowledged 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.[144]

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.

CANNABIS AND MOVEMENT DISORDERS

Movement disorders and neurodegenerative diseases, which are sometimes interlinked, are among the many conditions that cannabis and cannabinoids may be particularly well suited to treat.

The therapeutic use of cannabis for treating muscle problems and movement disorders has been known to western medicine for nearly two centuries. In reference to the plant's muscle relaxant and anti-convulsant properties, in 1839 Dr. William B. O'Shaughnessy wrote that doctors had "gained an anti-convulsive remedy of the greatest value."[145] In 1890 Dr. J. Russell Reynolds, physician to Queen Victoria, noted in an article in The Lancet that for "organic disease of a gross character in the nervous centers . . . India hemp (cannabis) is the most useful agent with which I am acquainted."[146]

Muscular spasticity is a common condition, affecting millions of people in the United States. It afflicts individuals who have suffered strokes, as well as those with multiple sclerosis, cerebral palsy, paraplegia, quadriplegia, and spinal cord injuries. Conventional medical therapy offers little to address spasticity problems. Phenobarbital and diazepam (Valium) are commonly prescribed, but they rarely provide complete relief, and many patients develop a tolerance, become addicted, or complain of heavy sedation. These drugs also cause weakness, drowsiness, and other side effects that patients often find intolerable.

Extensive modern studies in both animals and humans have shown that cannabis can treat many movement disorders affecting older patients, such as tremors and spasticity, because cannabinoids have antispasticity, analgesic, antitremor, and antiataxia properties.[147-158]

In the federal court brief filed in support of physicians' right to recommend cannabis, the American Public Health Association states that "marijuana is effective in treating muscle spasticity." They point out that the government's own Institutes of Medicine report on medical use of cannabis found that "current treatments for painful muscle spasms . . . have only limited effectiveness and their use is complicated by various adverse side effects."

They go on to note that "a survey of British and American MS patients reports that after ingesting marijuana a significant majority experienced substantial improvements in controlling muscle spasticity and pain. An extensive neurological study found that herbal cannabis provided relief from both muscle spasms and ataxia (loss of coordination), a multiple benefit not achieved by any currently available medications."[159]

Cannabis also has enormous potential for protecting the brain and central nervous system from the damage that leads to various movement disorders. Researchers have also found that cannabinoids can alleviate the damage caused by strokes, as well as brain trauma, spinal cord injury, and multiple sclerosis. More than 100 research articles have been published on how cannabinoids act as neuroprotective agents to slow the progression of such neurodegenerative diseases as Huntington's, Alzheimer's and particularly Parkinson's, which affects more than 52% of people over the age of 85.

An understanding of the actions of cannabis was spurred by the discovery of an endogenous cannabinoid system in the human body. This system appears to be intricately involved in normal physiology, specifically in the control of movement.[160-164] Central cannabinoid receptors are densely located in the basal ganglia, the area of the brain that regulates body movement.

Endogenous cannabinoids (which are those cannabinoids produced by our bodies) also appear to play a role in the manipulation of other transmitter systems within the basal ganglia—increasing transmission of certain chemicals, inhibiting the release of others, and affecting how others are absorbed. Research suggests that endogenous cannabinoids play a part in the body's control of movements.[165-169]

Endocannabinoids have paradoxical effects on the mammalian nervous system: sometimes they block neuronal excitability and other times they augment it. As scientists are developing a better understanding of the physiological role of the endocannabinoids, it is becoming clear that these chemicals may be involved in the pathology of several neurological diseases. Researchers are identifying an array of potential therapeutic targets within the human nervous system.

Movement disorders can be chronic disorders which arise from the loss or destruction of neurons and other structures in the brain. nterestingly, the activation of cannabinoid receptors was shown to trigger neuronal growth, suggest-

ing that a role in neuronal regeneration.[170] Various cannabinoids found in the cannabis plant can modulate the synthesis, uptake or metabolism of the endocannabinoids that are involved in the progression of Huntington's disease, Parkinson's disease, multiple sclerosis, and Alzheimer's disease.[171, 172]

Parkinson's disease has been linked to dysfunction in the body's dopamine system, specifically the production of too much of the neurotransmitter glutamate and oxidative damage to dopaminergic neurons. Studies have found a tight association between cannabinoids and dopamine, and recent research has produced anatomical, biochemical and pharmacological evidence supporting a role for the endogenous cannabinoid system in the modulation of dopaminergic transmission. Furthermore, the CB1 receptor appears to be deregulated in the basal ganglia of mice with this disease. Specifically, the down regulation of the CB1 receptor may be an early event in the beginning of Parkinson's disease. A profound up regulation of the CB1 receptor may occur after Parkinson's symptoms appear.[173-175]

Oxidative stress in the brain is a major hallmark of motor and neurological diseases such as Parkinson's and Alzheimer's disease. Cannabinoids are able to protect neurons from oxidative damage.[176] The neuroprotective action of cannabinoids appears to result from their ability to inhibit reactive oxygen species, glutamate, and tumour necrosis factor. THC, CBD, and synthetic AM404 all contain phenolic groups in their chemical structure and are thus able to reduce radical oxygen species. Notably CBD has extraordinary antioxidant properties and can effect Calcium homeostasis, both of which lead to positive effects against a wide range of neurodegenerative diseases.[177]

Few clinical trials have looked at Cannabinoids and Parkinson's disease. However, research has shown that 25% of Parkinson's patients smoke cannabis and 46% of these patients report improvement resulting from side effects of long term levodopa treatment.[178] A randomized placebo controlled study using extracts of cannabis produced significant improvements in patients' cognition. The authors note that they did not see improvements in pain or sleep disorders. They speculate that the oral route (versus inhaled) of cannabis ingestion leads to too much variability of cannabinoids in blood.[179]

Plant cannabinoids, such as CBD have been effective in experimental models of Alzheimer's, Parkinson's, and Huntington's disease. Hence, cannabinods represent an emerging therapeutic option that could be available in the near future. However, cannabinoids are still in an early phase of development but research suggest that they can be useful drugs for the treatment of many disease processes of the brain and central nervous system.

Cannabis and Neruodegenerative Disease

Age-related diseases of the brain are typically characterized through changes in inflammatory responses during disease progression. Inflammation in the brain is mediated by microglial cells and treatments which target these cells can protect neurons from damage that leads to degeneration Multiple Sclerosis, Parkinson's and Alzheimer's disease are neuro-degenerative conditions for which cannabis and cannabinoid therapies show promise, both for treating the symptoms and the

underlying disease by targeting microglial cells through cannabinoid receptors.[180]

Oxidative stress in the brain is a major hallmark of motor and neurological diseases such as Parkinson's and Alzheimer's disease. Cannabinoids are able to protect neurons from oxidative damage.[181] Alzheimer's disease, characterized in part by a decrease in the production of new neurons, and is also associated with oxidative stress due to the membrane action of beta-amyloid peptide aggregates. A laboratory study published in 2004 indicates that one of the cannabis plant's primary components, cannabidiol (CBD), exerts a combination of neuroprotective, anti-oxidative and anti-apoptotic effects by inhibiting the release of the toxic beta-amyloid peptide.[182]

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

Furthermore, recent studies suggest that endocannabinoids may control the growth and maturation of new neurons through the CB1 receptor. Therefore, cannabinoids could reduce inflammation and protect brains in age related neurodegenerative conditions such as Alzheimer's disease.[183] The neuroprotective action of cannabinoids appears to result from their ability to inhibit reactive oxygen species, glutamate, and tumour necrosis factor. THC, CBD, and synthetic AM404 all contain phenolic groups in their chemical structure and are thus able to reduce radical oxygen species. Notably CBD has extraordinary antioxidant properties and can effect Calcium homeostasis, both of which lead to positive effects against a wide range of neurodegenerative diseases.[184]

Another cannabinoid, THC, has also has been shown to reduce the agitation common to Alzheimer's sufferers, according to findings presented in 2003 at the American Society of Consultant Pharmacists' 34th annual meeting.[185] Agitation is the most common behavioural management problem in patients with Alzheimer's and affects an estimated 75 percent of people with the disease. It may lead to a variety of symptoms ranging from physical and/or verbal abusive postures, physically non-aggressive conduct including pacing and restlessness, as well as verbally disturbed behaviours such as screaming and repetitive requests for attention.

This study and the Institutes of Medicine report also show THC to be effective in combating the anorexia or wasting syndrome common to Alzheimer's sufferers, since food refusal is a common problem inpatients who suffer from Alzheimer's type dementia. The appetite-stimulation properties of cannabis are some of the most well-established in clinical research.[186]

Few clinical trials have looked at Cannabinoids and Parkinson's disease. However, research has shown that 25% of Parkinson's patients smoke cannabis and 46% of these patients report improvement resulting from side effects of

long term levodopa treatment. [187] A randomized placebo controlled study using extracts of cannabis produced significant improvements in patients' cognition. The authors note that they did not see improvements in pain or sleep disorders. They speculate that the oral route (versus inhaled route) of cannabis ingestion leads to too much variability of cannabinoids in blood.[188]

Cannabinods represent an emerging therapeutic option that could be available in the near future. Plant cannabinoids such as CBD have been effective in experimental models of Alzheimer's, Parkinson's, and Huntington's disease.[189, 190] Cannabinoid therapies are still in an early phase of development, but research suggests that they can be useful drugs for the treatment of many diseases.

This new research on cannabis and neurodegenerative diseases, coupled with the extensive work done on other neuroprotective and neurogenic qualities of cannabis and its components, indicates that cannabis may become the source of the most effective treatments for battling the Central Nervous System diseases that afflict millions of elderly Americans.

HOW CANNABIS COMPARES TO OTHER TREATMENTS

Arthritis Medications

Nearly 100 medications are listed by the Arthritis Foundation website for use with arthritis or other related conditions, such as fibromyalgia, psoriasis, osteoporosis and gout. These medicines include aspirin, ibuprofen and other oral and topical analgesics that dull pain. The most commonly used analgesic, **acetaminophen** (aspirin-free Anacin, Excedrin, Panadol, Tylenol) is usually not associated with side effects, though long-term use of acetaminophen is thought to be one of the common causes of end-stage renal disease. To effectively control arthritis, **aspirin** must be taken in large, continuous doses (1000-5400 mg daily), which can cause stomach pain or damage; it is believed to cause more than 1,000 deaths annually in the United States. For that reason, some doctors prescribe one of several chemical variations referred to as nonacetylated salicylates, such as CMT, Tricosal, and Trilisate, which can cause deafness or ringing in the ears in large doses.

Much stronger analgesics are also prescribed for arthritis, sometimes along with acetominophen. These are: **codeine** (Dolacet, Hydrocet, Lorcet, Lortab, Vicodin); **morphine** (Avinza, Oramorph); **oxycodone** (Oxycontin, Roxicodone); **propoxyphene** (Percocet, Darvon, Darvocet) and **tramadol** (Ultram, Ultracet). These medicines can cause psychological and physical dependence, as well as constipation, dizziness, lightheadedness, mood changes, nausea, sedation, shortness of breath and vomiting. Taking high doses or mixing with alcohol can slow down breathing, a potentially fatal condition.

Analgesics don't treat the inflammation that can cause severe arthritis pain. For inflammation, steroids, nonsteroidal anti-inflammatory drugs (NSAIDs) and newer COX-2 inhibitors are prescribed. **Corticosteroids** such as cortisone, prednisone, and related medications can cause bruising, cataracts, elevated blood sugar, hypertension, increased appetite, indigestion, insomnia, mood swings, muscle weakness, nervousness or restlessness, osteoporosis, susceptibility to infection, and thin skin.

Twenty NSAIDs are available with a doctor's prescription, with three of those also available over the counter. They are **diclofenac** (Arthrotec, Cataflam, Voltaren); **diflunisal** (Dolobid); **etodolac** (Lodine); **fenoprofen calcium** (Nalfon); **flurbiprofen** (Ansaid); **ibuprofen** (Advil, Motrin IB, Nuprin); **indomethacin** (Indocin); **ketoprofen** (Orudis); **meclofenamate sodium** (Meclomen); **mefenamic acid** (Ponstel); **meloxicam** (Mobic); **nabumetone** (Relafen); **naproxen** (Naprosyn, Naprelan); **naproxen sodium** (Anaprox, Aleve); **oxaprozin** (Daypro); **piroxicam** (Feldene); **sulindac** (Clinoril); and **tolmetin sodium** (Tolectin).

Side effects of NSAIDs include abdominal or stomach cramps, edema (swelling of the feet), pain or discomfort, diarrhea, dizziness, drowsiness or lightheadedness, headache, heartburn or indigestion, nausea or vomiting, gastric ulcers, stomach irritation, bleeding, fluid retention, and decreased kidney function. This is because NSAIDs act on arthritis by inhibiting prostaglandins, which protect the stomach lining, promote clotting of the blood, regulate salt and fluid balance, and maintain blood flow to the kidneys. The gastrointestinal complications of NSAIDS are the most commonly reported serious adverse drug reaction, though NSAIDs cause more than 7,600 annual deaths and 70,000 hospitalizations.

The newer group of arthritis drugs is known as cyclo-oxygenase-2 inhibitors (COX-2), which include **Celebrex**, **Bextra** and **Vioxx**. These medications have the same side effects as NSAIDS, except they are less likely to cause bleeding stomach ulcers and susceptibility to bruising or bleeding.

Non-selective NSAIDS have been associated with an increased risk of congestive heart failure. Less is known or has been concluded about the cardiovascular effects of COX-2 inhibitors, though a retrospective analysis of the risk of hospital admission for heart failure done by the Institute for Clinical Evaluative Sciences in Toronto, Canada suggests some may have serious side effects. The study of 130,000 older patients found that those using Vioxx had an 80% increased risk of hospital admission for congestive heart failure. Those using non-selective NSAIDS had a 40% increased risk, and those using Celebrex had the same rate of heart failure as people who had never used NSAIDS.

Antipyretic and anti-inflammatory effects of NSAIDs can mask the signs and symptoms of infection. Their use can interfere with the pharmacologic control of hypertension and cardiac failure in patients who take beta-adrenergic antagonists, angiotensin-converting enzyme inhibitors, or diuretics. Long-term use may damage chondrocyte (cartilage) function.

Only about 60% of patients will respond to any single NSAID. Approx-imately 10% of rheumatoid arthritis patients will not respond to any NSAID.

Biologic response modifiers such as **adalimumab** (Humira); **etanercept** (Enbrel); **infliximab** (Remicade), and **anakinra** (Kineret)) are prescribed to either inhibit or the supplement the immune system components called cytokines. Rare reports of lupus (with symptoms such as rash, fever and pleurisy) have been linked to treatment with adalimumab, etanercept and infliximab. Lupus symptoms resolve when the medication is stopped. Multiple sclerosis has rarely developed in

patients receiving biologic response modifiers. Seizures have been reported with etanercept.

Chronic Pain Medications

According to the Institute of Medicine, "All of the currently available analgesic (pain-relieving) drugs have limited efficacy for some types of pain. Some are limited by dose-related side effects and some by the development of tolerance or dependence."

The opioid analgesics commonly used to combat pain include **codeine** (Dolacet, Hydrocet, Lorcet, Lortab); **morphine** (Avinza, Oramorph); **oxycodone** (Vicodin, Oxycontin, Roxicodone, Percocet, Roxicet); **propoxyphene** (Darvon, Darvocet) and **tramadol** (Ultram, Ultracet). These medicines can cause psychological and physical dependence, as well as constipation, dizziness, lightheadedness, mood changes, nausea, sedation, shortness of breath and vomiting. Taking high doses or mixing with alcohol can slow down breathing, a potentially fatal condition.

In addition, patients in pain are often prescribed muscle relaxants such as Robaxin and Flexeril; anti-anxiety agents such as Valium, Sinequan, Vistaril, Ativan and Xanax; hypnotics such as Halcion, Restoril, Chloralhydrate, Dalmane and Doral and anti-emetics such as Zofran, Compazine, Phenergan, Tigan and Marinol.

Robaxin's side effects include abnormal taste, amnesia, blurred vision, confusion, dizziness, drop in blood pressure and fainting, drowsiness, fever, flushing, headache, hives, indigestion, insomnia, itching, light-headedness, nasal congestion, nausea, pinkeye, poor coordination, rash, seizures, slowed heartbeat, uncontrolled eye movement, vertigo, vomiting and yellow eyes and skin.

Flexeril can cause abnormal heartbeats, aggressive behavior, agitation, anxiety, bloated feeling, blurred vision, confusion, constipation, convulsions, decreased appetite, depressed mood, diarrhea, difficulty falling or staying asleep, difficulty speaking, disorientation, double vision, excitement, fainting, fatigue, fluid retention, gas, hallucinations, headache, heartburn, hepatitis, hives, increased heart rate, indigestion, inflammation of the stomach, itching, lack of coordination, liver diseases, loss of sense of taste, low blood pressure, muscle twitching, nausea, nervousness, palpitations, paranoia, rash, ringing in the ears, severe allergic reaction, stomach and intestinal pain, sweating, swelling of the tongue or face, thirst, tingling in hands or feet, tremors, unpleasant taste in the mouth, urinating more or less than usual, vague feeling of bodily discomfort, vertigo, vomiting, weakness, and yellow eyes and skin

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.

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. 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.

Benzodiazepine drugs **Ativan** and **Xanax** are prescribed to combat the anxiety associated with chronic pain. 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.

Cancer Medications

The American Cancer Society lists 269 medicines 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 13 drugs are currently prescribed to treat nausea, including Marinol, a synthetic form of delta-9-THC, one of the active ingredients in cannabis.

Antiemetic medications used for treating nausea, and medications such as antihitamines that are sometimes prescribed in combination with antiemetics, are all discussed above, under pain medications.

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 and diarrhea.

Spasticity And Movement Medications

Benzodiazepines, levedopa, baclofen, dantrolene sodium, and tizanidine are the most widely used agents for reduction of spasticity. At high dosages, oral medications can cause unwanted side effects that include sedation, as well as changes in mood and cognition.

Benzodiazepines, which include Diazepam (Valium) and Clonazepam (Klonopin, Rivotril) are centrally acting agents that increase the affinity of GABA to its receptor. Diazepam is the oldest and most frequently used oral agent for managing spasticity. Benzodiazepine side effects include sedation, weakness, hypotension, GI symptoms, memory impairment, incoordination, confusion, depression and ataxia. Tolerance and dependency may occur and withdrawal on cessation. Tolerance may also lead to unacceptable dosage escalation.

Levedopa is common long-term treatment option for Parkinson's disease. Long-term use can result in diskynesia and is often a reason for not taking the drug. Diskynesia can lead to less control of voluntary movements and can result in tics or chorea. Dikynesia can result in excessive tongue rolling and after years of use it can manifest as "jerky" movements of the head and arms.

Baclofen (Lioresal) has been widely used for spasticity since 1967. It is a GABA agonist. Tolerance to the medication may develop. Baclofen must be slowly weaned to prevent withdrawal effects such as seizures, hallucinations and increased spasticity. It must be used with care in patients with renal insufficiency as its clearance is primarily renal. Side effects are predominantly from central depressant properties including sedation, ataxia, weakness and fatigue. May cause depression when combined with tizanidine or benzodiazepines.

Dantrolene Sodium (Dantrium) acts peripherally at the level of the muscle fiber and works best for cerebral palsy and traumatic brain injury. Because the action of dantrolene sodium is not selective for spastic muscles, it may cause generalized weakness, including weakness of the respiratory muscles. The side effects include drowsiness, dizziness, weakness, fatigue and diarrhea. In addition, hepatotoxicity (liver damage) occurs in < 1% of patients who take dantrolene sodium.

Tizanidine (Zanaflex) facilitates short-term vibratory inhibition of the H-reflex.

Tizanidine in conjunction with baclofen or benzodiazepines has potential additive effects, including sedation and the possibility of liver toxicity. Dry mouth, somnolence, asthenia and dizziness are the most common side effects. Liver function problems and hallucinations may also occur.

Cannabis vs. Other Medications

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."[191]

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. 39 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.[192] 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.[193]

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 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 60 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.

Clinical research on Marinol vs. cannabis has been limited by federal restrictions, but a review of state clinical trials conducted in the 70's and 80's published in 2001 reports that "…the data reviewed here suggested that the inhalation of THC appears to be more effective than the oral route... Patients who smoked marijuana experienced 70-100% relief from nausea and vomiting, while those who used THC capsules experienced 76-88% relief."[194] 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 states, "Some users of both find cannabis itself more effective."[195]

THE EXPERIENCE OF PATIENTS

Dorothy Gibbs

In 1911, at the age of one, I contracted the polio virus. The early onset of polio caused permanent damage in my legs, spine, and back, resulting in significant weakness and atrophy in my legs. As a result, I have never been able to walk without the assistance of crutches and braces or a wheelchair. Approximately 30 years ago, my condition began to deteriorate. I began to suffer from increasing

levels of pain and weakness in my legs and back as well as severe osteoarthritis in my hands, arms, and joints. Over time, my deteriorating medical condition has been exacerbated by my pain, leaving me increasingly immobilized..

Angel Raich using a vaporizer in the hospital

By May, 1996, my physician [Dr. Arnold Leff, M.D.] had tried various prescription medications to relieve my pain, including: Tylenol #3, Ultram, Daypro, Tegretol, Soma, Valium, steroid injections into the trigger point, Dilantin, Duragesic, Zofran and Comapazine for the nausea caused by the opioid pain relievers, and Doloboid and Lodine as nonsteroids. Nothing seemed to work, and the pain persisted. I was growing increasingly depressed by the inability of anything to relieve my pain. During this period it was clear to me, my caretaker and my physician that nothing was working to combat my pain. My caretaker, Pat, had heard of the success some people experience with the medicinal use of marijuana for pain management. Sometime during the end of 1997, she obtained a sample for me. Although I had never used marijuana in my previous eighty-seven years of life, I was willing to try anything that could alleviate even part of the pain.

The relief I experienced from medical marijuana was almost immediate. I was so pleased with the result that I wrote to Dr. Leff about my use of medical marijuana and we talked about the benefits of the medicine. Dr. Leff examined me and noted that medical marijuana helped me experience less chronic pain and nausea, leading him to recommended medical marijuana as part of my daily pain care regimen.... I strongly feel that I should have the right to use anything that may relieve any or some of my pain, and my last days should not be spent suffering. . . . Ever since trying medical marijuana, my life has drastically improved. Although chronic pain, related to my post-polio syndrome will always be a part of my life, medical marijuana had helped me manage this pain by providing fast and effective relief for my muscle spasms, acute pains, and arthritis..

Since I began using medical marijuana, my pain is no longer persistent or debilitating. When I do suffer from pain, I am usually able to "get ahead of it" by using medical marijuana and make it manageable..

Judith Cushner

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 Cytoxan, methotraxate, 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 dis-

ruption; 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.

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.

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.

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 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

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. . . . 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 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.

THE EXPERIENCE OF DOCTORS

Harvey L. Rose, M.D.

Both my research and my many years as a clinician have convinced me that marijuana can serve at least two important roles in safe and effective pain management. Ample anecdotal evidence and clinical observations, as well as significant research findings, strongly indicate that marijuana, for whatever reason, is often effective in relieving pain. This is true across a range of patient populations, including the elderly, the terminally ill seeking comfort in their final days, young adults stricken with life-threatening conditions, and cancer patients unable to tolerate the devastating effects of potentially life-saving therapies. Marijuana is also widely recognized as an antiemetic that reduces the nausea and vomiting often

induced by powerful opioid analgesics prescribed for chronic, severe pain, as well as the nausea, vomiting and dizziness which often accompany severe and/or prolonged pain. I have had the benefit of consultations on this subject over many years with a range of treatment providers, including physicians, oncologists, pharmacologists, family practitioners, hospice workers, and pain specialists..

Specifically, I have found that cannabis can have an important opioid-sparing effect for pain patients. That is to say, that patients who are prescribed high doses of opioid analgesics can significantly reduce their reliance on these medications and improve their daily functioning by incorporating cannabis into their pain care regimen.

Marijuana not only has important analgesic properties but it also is an effective and important adjuvant therapy for patients suffering acute and/or chronic pain. No experienced and respected physician will deny that for such patients opioid therapy is central to palliative care. By the same token, the same experienced physicians will readily acknowledge that opioids often induce nausea and vomiting. For a number of pain patients, standard prescription antiemetics (e.g., Compazine, Zofran and Reglan) simply do not substantially reduce their nausea. For many, those medications are substantially less effective, or produce more debilitating side effects, than marijuana..

Quite simply, marijuana can serve much the same function for pain patients undergoing opiate therapy that it does for cancer patients undergoing chemotherapy: it suppresses the nausea and vomiting associated with treatment, and reduces the pain associated with prolonged nausea and retching, thereby increasing the chances that the patient will remain compliant with the primary treatment. With both chemotherapy and long-term pain management, failure to obtain and continue proper palliative and adjutant care can have dire, even fatal, consequences..

Finally, it is important to note that in my clinical experience observing patients who ingest cannabis for relief from pain and nausea and/or to stimulate appetite, I have witnessed no adverse complications. By contrast, many of the first-line pharmaceuticals used to combat cancer, HIV/AIDS, and pain associated with these and other illnesses can induce a variety of iatrogenic effects, including, in some instances, death. While patients may face serious legal implications related to their use of medical marijuana, as a physician I have yet to encounter a medical downside to their cannabinoid therapy. . . .

[A]gainst the backdrop of a growing body of scientific research, the reports of myriad pain patients, and the burgeoning clinical experience of physicians like myself, it is my considered opinion that cannabis can constitute an acceptable and sometimes necessary medicine to alleviate the immediate suffering of certain patients.

Dr. Rose has served as a medical officer in the Air Force, taught at UC Davis School of Medicine, and consulted with state legislative bodies.

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.

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.

Kate Scannell, M.D.

Because I was a cancer patient receiving chemotherapy at the same hospital where I worked, the elderly 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 suitemates was also one of my patients.

I braced myself for this woman's question, both wanting to make my-self 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 swill 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."

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

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

Denis Petro, M.D.

As a practicing neurologist, I saw many patients for whom uncontrollable spasticity was a major problem. Unfortunately, there are very few drugs specifically designed to treat spasticity. Moreover, these drugs often cause very serious side effects. Dantrium or dantrolene sodium carries a boxed warning in the Physician's Desk Reference because of its very high toxicity…The adverse effects

associated with Lioresal Baclofen are somewhat less severe, but include possibly lethal consequences, even when the drug is properly prescribed and taken as directed. Unfortunately, neither Dantrium or Lioresal are very effective spasm control drugs. Their marignal medical utility, high toxicity, and potential for serious adverse effects, make these drugs difficult to use in spasticity therapy.

[Dr. Petro then related his experience with a patient who was smoking cannabis for his symptoms. Dr. Petro and colleagues examined the patient and then asked him to refrain from smoking for six weeks. He continues:]

After six weeks he returned for another examination. At this time, he reported an increase in his symptoms to the point where he had leg pains, increased clonic activity, and uncontrolled leg spasms every night. More disturbing to him was urinary incontinence, which occurred on two occasions during leg spasms. On objective examination, in layman's terms, this patient's spasticity had increased dramatically in six weeks. This spasticity made his legs extremely rigid, he was finding it increasingly difficult to walk or sleep, and he was losing bladder control.

Following our examination, and at the patient's request, he left the clinic then returned one hour later to be examined for a second time. This second examination was remarkable. The earlier findings of moderate to severe spasticity could not be elicited. Deep tendon reflexes were brisk, but without spread, ankle clonus was absent, and the plantar response was flexor on the left and equivocal on the right.

In short, this patient had undergone a stunning transformation. Moreover, this unmistakable improvement had occurred in an incredibly brief period of time. Less than an hour separated the two examinations. On questioning, the patient informed us he had smoked part of one marijuana cigarette in the interval between examinations.

Denis Petro, M.D is a former FDA Review Officer and principal investigator on spasticity and cannabis.

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."[196]

The American Medical Association opposed the first federal law against cannabis with an article in its leading journal.[197] 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 substantially helped by it.

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

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

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, 18 states and the District of Columbia have removed criminal penalties for their citizens who use cannabis on the advice of a physcian. Voters have passed medical cannabis ballot initiatives in 10 states plus the District of Columbia, while the legislatures in Connecticut, Delaware, Hawaii, Maryland, New Jersey, New Mexico, Rhode Island, and Vermont 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, Connecticut, Delaware, Hawaii, Maine, Massachusetts, Michigan, 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 affect individual states' medical marijuana programs, and only applies to prosecution in federal, not state, court.

Petition for legal prescriptions under appeal

ASA is suing the federal Drug Enforcement Administration over the denial of a petition to reclassify cannabis as having medical use. The Department of Health and Human Services (HHS) and the DEA stalled for nine years before rejecting the petition, saying there are no scientific studies that show cannabis has medical use, despite the hundreds of peer-reviewed published scientific findings that show otherwise. ASA is appealing the decision, arguing that the DEA is acting arbitrarily and capriciously in applying a more stringent standard to cannabis than other drugs.

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 "insome 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).

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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 50,000 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.

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