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.Notably, in a meta-analysis of 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.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.29 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, extensive pre-clinical research clearly indicates that cannabinoids can have tumor-reducing and anti-cancer properties.

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 and preclinical studies conducted over nearly three decades have consistently 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 noted that for “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.” 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.”

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.

The effects of cannabis may also provide an improvement in mood. In addition to THC, other cannabinoids on the plant such as CBD, can inhibit the side effects of THC, as well provide relief from anxiety and depression. By contrast, several conventional medications commonly prescribed for cancer patients, e.g. phenothiazines such as haloperidol (known as “major tranquillizers”) may produce unwanted side effects such as excessive sedation, flattening of mood, and/or distressing physical “extrapyramidal” symptoms such as uncontrolled or compulsive movements.

Anti-cancer potential of cannabis and cannabinoids

Recent scientific advances in the study of cannabinoid receptors and endocannabinoids have produced exciting new leads in the search for anti-cancer treatments. Several hundred research articles have been published on the effects of cannabinoids on cancer cells. We now know cannabinoids stop many kinds of cancers from growing and spreading, including brain, breast, leukemic, melanoma, phaeochromocytoma,

liver, and other kinds of cancer. Cannabinoids have been repeatedly shown in animal and other studies to promote apoptosis (programmed cell death of the tumor cells) and halt angiogenesis (blood vessel production to the tumor) in many types of human cancers.70-74 In one 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.

Scientists have established that 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. Research on the complex interactions of endogenous cannabinoids and receptors is leading to greater scientific understanding of the basic mechanisms by which cancers develop. Research studies on pituitary cancers suggest that cannabinoids may be the key to regulating human pituitary hormone secretion that affects tumor development.

The mechanism of the anti-cancer activity of cannabinoids has been repeatedly demonstrated with breast cancers, with numerous studies showing that cannabinoids are effective in fighting breast cancer tumors and metastization.

Recent research 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.

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.

Laboratory research on the effects on cancer tumors of the non-psychoactive cannabinoid cannabidiol (CBD) has found that it inhibits human glioma and glioblastoma multiforme cells, the most common and aggressive forms of brain cancer, in part by cutting of blood supply to tumors. 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.89 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.90 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.91 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.

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.93 This research confirms the findings of multiple studies which have indicated the effectiveness of cannabinoids in fighting gliomas.

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.102 One study found that 10-20 years of cannabis use significantly reduced the incidence of head, neck and throat cancers.103 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. A random-sample anonymous survey conducted by researchers at Harvard Medical School in 1990, years before any states had approved medical use, found that 44 percent of oncologists had recommended cannabis to at least some of their patients, and more said they would do so if the laws were changed. Of the oncologists expressing an opinion in 1990, a majority (54 percent) thought cannabis should be available by prescription.

According the American Cancer Society's data, 1,665,540 Americans will be diagnosed with cancer in 2014.105 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.

The authors of the 1999 Institute of Medicine report Marijuana and Medicine: Assessing the Science Base acknowledged that there are certain cancer patients for whom cannabis would be a valid medical option. Current research on cannabinoids has shown that activation of both cannabinoid receptors has a well-established 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 the toxic side effects associated with conventional treatments, more studies are warranted to develop a cannabis-based cancer treatment.

How cannabis compares to other medications

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

The newer antiemetics, Anzamet, Kytril and Zofran, are serotonin antagonists, blocking the neurotransmitter that sends a vomiting signal to the brain. Rare side effects of these drugs include fever, fatigue, bone pain, muscle aches, constipation, loss of appetite, inflammation of the pancreas, changes in electrical activity of heart, vivid dreams, sleep problems, confusion, anxiety and facial swelling.
Reglan, a substituted benzamide, increases emptying of the stomach, thus decreasing the chance of developing nausea and vomiting due to food remaining in the stomach. When given at high doses, it blocks the messages to the part of the brain responsible for nausea and vomiting resulting from chemotherapy. Side effects include sleepiness, restlessness, diarrhea and dry mouth. Rarer side effects are rash, hives and decreased blood pressure

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

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

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

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

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

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

THE EXPERIENCE OF PATIENTS

Judith Cushner, Breast Cancer

In 1989, I was diagnosed with breast cancer. After a brief period of recovery from the surgeries, I was placed on an aggressive protocol of chemotherapy, which lasted for eight months. That protocol was referred to as "CMF," because it consisted of heavy doses of 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 disruption; and eventually my withdrawal from social situations and interpersonal relationships. The cumulative effect of these symptoms often rendered it impossible (or painfully difficult) to take the huge number of medications essential to my treatment regimen.

Right from the start, I was given Compazine as part of my chemotherapy protocol. I took it both orally (in pill form) and intravenously, but it too caused severe adverse side effects, including neuropathy. Moreover, the Compazine provided little, if any, relief from the nausea that had persisted since my treatment began. Hoping for better results, my doctor discontinued the Compazine and prescribed Reglan. That, too, had no effect on the nausea and we decided to discontinue it after a fairly short time. By then, I had developed chronic mouth sores (also from the chemotherapy), which made it extremely painful to take pills or swallow anything. Rather than providing relief, the Reglan increased my discomfort and pain.

Yet another drug I tried was Marinol, which gave me no relief from the unrelenting nausea. If anything, taking yet another pill increased my discomfort. The pills themselves irritated the sores in my mouth. It also made me quite groggy, yet my sleep disturbance persisted, in part because my nausea and anxiety were so distracting. My doctor prescribed Lorazepam to help me sleep, but it was just one more medication with unpleasant effects of its own.

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

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

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

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

Jo Daly, Colon Cancer

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

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

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

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

I told my oncologist about how well marijuana quelled my nausea. My doctor was not surprised. In fact, he told me that many of his patients had made the same discovery. My doctor encouraged me to continue using marijuana if it worked. Although it occasionally produced a slight euphoria, it was not a painful sensation and I was careful never to leave the house during those rare moments.

My use of medical marijuana had a secondary, though by no means minor benefit: I was able to drastically reduce my dependence on more powerful prescription drugs that I was prescribed for pain and nausea. With the help of medical marijuana, which I ingest only occasionally and in small amounts, I no longer need the Compazine, Lorazepam, Ativan and Halcion. No combination of these medications provided adequate relief. They also caused serious side effects that I never experienced with marijuana.

- Jo Daly was formerly a San Francisco Police Commissioner

Anonymous, Breast Cancer

I have used medicinal cannabis legally in California for a year, after being diagnosed and treated for breast cancer. I have also been given prescription drugs that were not effective, that irritated my stomach, for which they wanted to prescribe more drugs. These medications were neither cost-effective nor useful, and I choose to use medicinal cannabis through a vaporizer as recommended by my physician, thereby bypassing the sometimes-harmful effects of smoking. I, personally, would rather the federal government use their resources to go after the true criminals and terrorists that we have in our country, as opposed to persecuting the sick for whatever relief they may have from medical cannabis.

Lyn Nofziger, Father of Cancer Patient

When our grown daughter was undergoing chemotherapy for lymph cancer, she was sick and vomiting constantly as a result of her treatments. No legal drugs, including Marinol, helped her. We finally turned to marijuana. With it, she kept her food down, was comfortable and even gained weight. Those who say Marinol and other drugs are satisfactory substitutes for marijuana may be right in some cases but certainly not in all cases. If doctors can prescribe morphine and other addictive medicines, it makes no sense to deny marijuana to sick and dying patients when it can be provided on a carefully controlled, prescription basis.

- Lyn Nofziger was formerly senior adviser to President Ronald Reagan

The Experience of Doctors

Howard D. Maccabee, M.D.

In my practice, I commonly use radiation therapy to treat the whole spectrum of solid malignant tumors. Radiation therapy is often used after surgery or chemotherapy, as a second stage in treatment. Sometimes, however, radiation therapy is used concurrently with chemotherapy, or even as the first or only modality of treatment.I treat approximately 20 patients each day and provide follow-up care and/or consultation with another 5 or so patients a day. I currently have approximately 2,000 patients in various stages of follow-up to their initial treatment. Most of these are long-term survivors. Because of the nature of some cancers, I must sometimes irradiate large portions of my patients' abdomens. Such patients often experience nausea, vomiting, and other side effects. Because of the severity of these side effects, some of my patients choose to discontinue treatment altogether, even when they know that ceasing treatment could lead to death.

During the 1980s, I participated in a state-sponsored study of the effects of marijuana and THC (an active ingredient in marijuana) on nausea. It was my observation during this time that some patients smoked marijuana while hospitalized, often with the tacit approval of physicians. I also observed that medical marijuana was clinically effective in treating the nausea of some patients. During my career as a physician, I have witnessed cases where patients suffered from nausea or vomiting that could not be controlled by prescription anti-emetics. I frequently hear similar reports from colleagues treating cancer and AIDS patients. As a practical matter, some patients are unable to swallow pills because of the side effects of radiation therapy or chemotherapy, or because of the nature of the cancer (for instance, throat cancer). For these patients, medical marijuana can be an effective form of treatment.

Debasish Tripathy, M.D.

Since 1993, I have been a physician at the UCSF Mount Zion Breast Care Center in San Francisco. My practice is devoted exclusively to breast cancer patients. I treat more than 1,000 patients. Approximately 100 of these patients are currently undergoing chemotherapy, a treatment utilizing various combinations of powerful medications. In some cases, the therapeutic dose of the medication we use is not far from the potentially lethal dose. Although chemotherapy is a widely used treatment in the treatment of many

cancers, it can also cause severe adverse affects, which some patients are simply unable to tolerate. The most common adverse effects of chemotherapy are nausea and retching.

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

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

Kate Scannell, MD

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

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

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

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

I winced. I knew about her wretched pain, her constant nausea and all the prescription drugs that had failed her - some of which also made her more constipated, less alert and even more nauseous. I knew about the internal derangements of chemotherapy, the terrible feeling that a toxic 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."

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 bedsies 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?