CANNABIS AND GI DISORDERS

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

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

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

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

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

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

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

Research on cannabis and GI disorders

Research demonstrates that cannabis and cannabinoids are effective in treating the symptoms of these GI disorders in part because it interacts with the endogenous cannabinoid receptors in the digestive tract, which can result in calming spasms, assuaging pain, and improving motility. Cannabis has also been shown to have anti-inflammatory properties and recent research has demonstrated that cannabinoids are immune system modulators, either enhancing or suppressing immune response.

Cannabis has a long documented history of use in treating GI distress, going back more than a century in western medicine, and far longer in the east. While clinical studies on the use of cannabis for the treatment of gastrointestinal disorders have been largely limited to investigations on nausea suppression and appetite stimulation - two conditions for which cannabis has been consistently shown to be highly effective the evidence in support of cannabis therapy for other gastrointestinal diseases and disorders is also strong. There is now extensive anecdotal evidence from patients with IBS, Crohn's disease and other painful GI disorders that cannabis eases cramping and helps modulate diarrhea, constipation and acid reflux. Recent

laboratory research on the endogenous cannabinoid system in humans has identified that there are many cannabinoid receptors located in both the large and small intestine.

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

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

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

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

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

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

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

How Cannabis Compares to Other Treatments

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

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

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

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

Sulfasalazine (Azulfidine) - The most common adverse reactions associated with sulfasalazine are anorexia, headache, nausea, vomiting, gastric distress, and apparently reversible oligospermia. These occur in about one-third of the patients. Less frequent adverse reactions are pruritus, urticaria, fever, Heinz body anemia, hemolytic anemia and cyanosis, which may occur at a frequency of one in every thirty patients or less.

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

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

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

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

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

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

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

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

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

THE EXPERIENCE OF PATIENTS

Bruce Buckner

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

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

While attending the University of Oregon in Eugene, I was suffering from a particularly bad flare-up. I developed psoriasis, and started getting little red bumps on my lower legs, which I scratched into sores. I was very fortunate that the young doctor I saw was very familiar with Crohn's (his wife had it). He was able to diagnose it right away, although he still made me undergo a colonoscopy the following week, which

confirmed his diagnosis. He started me on sulfasalazine. This caused severe nausea and vomiting. The cure was much worse than the disease. The doctor gave me steroids (prednisone). This made me lay awake all night sweating. I was making all kinds of stupid mistakes - I backed my car into a light post, I lost my temper easily, I couldn't handle the sleep deprivation and stopped taking the steroids. In 1972 my doctor told me his wife found that smoking pot helped. Whenever I was cramping, I smoked a couple joints from that point on.

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

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

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

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

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

Fernando Mosquera

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

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

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

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

Rose Wheeler

I'm a 40-year-old wife and mother of two young boys who was diagnosed with Crohn's disease in September of 1993, while my husband was stationed in Austria. The best way I could describe my symptoms was that food was POISON to me. When I ate or drank ANYTHING, within 5 minutes I was on the toilet bent over in severe pain and experiencing hot flashes. I spent more time in the bathroom than any other place in my home. I was very weak, nauseated. With every bowel movement there was much blood and mucus, and I became seriously depressed. It was very difficult for me to care for my children.

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

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

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

Erin Hildebrandt

My name is Erin Hildebrandt, and I'm a 34-year-old wife and stay-at-home mom to five kids, ages 3 to 9. I suffer from Crohn's Disease, a disease for which there is no known cure; therefore, symptom control is the goal of treatment. Marijuana is not a panacea, but it's the only medicine I've found that controls a large number of my most debilitating symptoms. Compared to the dozens of truly dangerous pharmaceuticals first given to me by doctors, the cannabis recommended by a friend, and subsequently endorsed by my doctor, is more effective and has fewer side-effects. For me, Crohn's Disease produces severe nausea, vomiting, diarrhea, intractable pain, cramping, fever, sweating, chills, bloating, and weight loss. I can only compare it to the worst case of food poisoning I can imagine, except that it doesn't just go away after a day or two. It comes back again and again, varying in both intensity and duration. During the worst attacks, proper nutrition and exercise are an often insurmountable challenge. However, through the use of marijuana, I feel well enough to function more normally. In addition, with consistent therapeutic use, the inflammation in my digestive tract stays under control, and I'm able to bring my disease into remission.

THE EXPERIENCE OF DOCTORS

Kate Scannell, M.D.

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

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

Marcus A. Conant, M.D.

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

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

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

Neil M. Flynn, M.D., MPH

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

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

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

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