

## **MEDICAL CANNABIS AND MULTIPLE SCLEROSIS**

An estimated 350,000 people in the United States are living with multiple sclerosis (MS), a debilitating and sometimes fatal disorder of the central nervous system. Because physicians are not required to report new cases, and because symptoms can go undetected for some time, the prevalence and incidence rate of MS can only be estimated. Nonetheless, MS is the most common debilitating neurological disease of young people, typically appearing between the ages of 20 and 40, affecting approximately twice as many women as men. Veterans appear to be significantly more likely to develop MS than the general population.

Members of the US military who served in the Gulf War era have one of the highest incidence rates of MS ever found (between 9.6 per 100,000 per year), according to a 2012 study of all military medical records from the time period. Researchers discovered that those who served in the Air Force and Army have double the rate of those who served in the Marines, and women in all services have more than triple the rate of their male counterparts.

Another 2012 study of US military medical records from 2000-2009 found an even higher incidence rate of MS among service members of 12.9 per 100,000 person-years, the highest disease rate ever reported for MS. Researchers note that the increase incidence of MS among military personnel have manifested over the past two to three generations, speculating that “there may be unique environmental exposures within the military that increase ones risk for multiple sclerosis above that of the general population.”

MS is a disease of the central nervous system (CNS) that manifests due to the immune system attacking the myelin, the protective covering around nerve fibers such as neurons and dendrites. As the disease progresses, normal neurotransmission is inhibited and additional symptoms develop, such as pain, spasms, muscle spasticity, limb tremor, fatigue, and incontinence. All of the disease symptoms have a large negative impact on the quality of life of MS patients. MS most frequently presents at onset as a relapsing and remitting disorder, where symptoms come and go.

MS exacerbations appear to result from abnormal immune activity that causes inflammation and the destruction of myelin in the brain or spinal cord. After repeated attack from the immune system, nerves lose plasticity, which creates stress in nerve tissue. This stress leaves nerve tissue vulnerable to progressive damage and death.

Current treatment of MS is primarily symptomatic, focusing on such problems as spasticity, pain, fatigue, bladder problems and depression. Although symptom-specific treatments exist, these are often associated with adverse side effects. This has prompted many people who suffer from MS to seek alternative therapies. Cannabinoids, the active ingredients in cannabis, have demonstrated the ability to control aspects of MS disease progression.

Anecdotal reports on the self medication of cannabis to treat the symptoms of MS are supported by recent advances in the understanding of the biology of cannabis and the cannabinoid receptors. Controlled studies have found that cannabis and cannabinoids can help manage such symptoms as pain, spasms, spasticity, and incontinence.

The leading effects of prolonged neurodegeneration in MS cause permanent disabilities. This neurodegeneration has yet to be effectively treated. Initial neurodegeneration occurs with inflammation, cannabis and cannabinoids have been shown to have neuroprotective effects during immune attacks on the CNS.

### **Surveys and Clinical Research on Marijuana Use for Multiple Sclerosis**

Numerous case studies, surveys and double-blind studies have reported improvement in patients treated with cannabinoids for symptoms including spasticity, chronic pain, tremor, sexual dysfunction, bowel and bladder dysfunctions, vision dimness, dysfunctions of walking and balance (ataxia), and memory loss.

A 1998 House of Lords report concludes, "We have seen enough evidence to convince us that a doctor might legitimately want to prescribe cannabis to relieve...the symptoms of multiple sclerosis and that the criminal law ought not to stand in the way." Many of those who testified for that report shared the British Medical Association's view that "[a] high priority should be given to carefully controlled trials of cannabinoids in patients with chronic spastic disorders."<sup>50</sup> The British Medical Association has requested that the synthetic cannabinoids Nabilone and Dronabinol be officially licensed for use in MS and other spastic disorders.

A 2005 survey of MS patients in the UK found that 43 percent of respondents used cannabis therapeutically. Among them, nearly three quarters said that cannabis mitigated their spasms, and more than half said it alleviated their pain.<sup>51</sup> A Canadian survey published in August 2003 in the Canadian Journal of Neurological Sciences reported that 96 percent of MS patients believe that cannabis is therapeutically useful for treating the disease. Of those who admitted using cannabis medicinally, the majority found it to be beneficial, particularly in the treatment of chronic pain, spasticity, and depression.<sup>52</sup> The accompanying editorial states, "This is an exciting time for cannabinoid research. There is a growing amount of data to suggest that cannabis (marijuana) can alleviate symptoms like muscle spasticity and pain in patients with MS.

The published results of a number of GW Pharmaceuticals Phase III studies show that pain relief was significantly superior to placebo and there were subjective improvements in spasm frequency, bladder control, spasticity and sleep. The authors of one such trial concluded that "the results of this study suggest that Sativex® is an effective treatment for spasticity associated with MS." In April 2005, GW announced that it had received approval to distribute Sativex in Canada for the symptomatic relief of neuropathic pain in adults with Multiple Sclerosis.

A U.K. study published in the journal Lancet looked at 630 multiple sclerosis patients after 15 weeks of orally delivered treatment. Fifty-seven percent of the patients taking a whole cannabis extract said their pain had eased, compared with 50 percent who took capsules containing THC and 37 percent who were given placebo capsules. Patients also reported improved sleep and fewer or less intense muscle spasms and stiffness. Those who could walk were significantly more mobile as measured by a walking test. The investigators also noted there were fewer relapses in the treatment groups; however, the study was not designed to investigate impact on relapses. An accompanying editorial suggests that current data supporting the benefit of cannabinoid treatment of spasticity in MS is now as strong as for any available pharmaceutical agent.

Pain is a common problem in MS, and many patients who report using cannabis say it helps. In clinical trials, an oral cannabis extract was not initially shown not to be effective; however, pain relief became evident after long-term treatment. This may be due to the neuroprotective effects of plant cannabinoids that promote the repair of damaged pathways.

Studies have described the role of CB1 and CB2 cannabinoid receptors in regulating CNS autoimmune inflammation and other factors that can contribute to MS symptoms.<sup>59,60</sup> Researchers have an animal model for MS, called experimental allergic encephalomyelitis (EAE), that allows testing for symptom suppression and disease progression. Animal studies in transgenic mice without cannabinoid receptors has shown that the cannabinoid system play an important role in MS. Mice lacking the CB1 receptor, experience rapid neurodegeneration in a model of MS. Pre-clinical reports have found that cannabinoids lessened both tremor and spasticity in mice with EAE. The CB2 receptor also influences inflammatory events in animal models. Mice lacking the CB2 receptor exhibit increased severity of MS compared to normal mice.<sup>61</sup> It is thought the CB2 receptor may control the production of inflammatory signals and immune cell migration into tissue that are part of MS. These studies of animal models of MS have greatly

expanded our understanding of MS and cannabinoid biology. Emerging research suggests that cannabinoids have the potential to measurably lessen MS symptoms and may also slow the progression of the disease.

In addition to studying the potential role of marijuana and its derivatives in the treatment of MS-related symptoms, scientists are exploring the potential of cannabinoids to inhibit neurodegeneration. A study that the American MS Society called "interesting and potentially exciting" demonstrated that cannabinoids were able to slow the disease process in mice by offering neuroprotection against EAE. After analyzing the findings, authors at London's Institute of Neurology concluded, "In addition to symptom management, cannabis may also slow down the neurodegenerative processes that ultimately lead to chronic disability in multiple sclerosis and probably other diseases."

## **Efficacy and side effects: how cannabis compares**

A recent review of all available medications for MS concluded that "forthcoming information relating to the use of cannabinoids in MS may result in there being better evidence of the effectiveness of new treatments than of any of the currently used drugs."

Over 40 medicines are listed by the Multiple Sclerosis Society as commonly used by MS patients. Symptoms and medications prescribed include "acute exacerbations" (Decadron, Solu-Medrol); depression (Effexor, Paxil, Prozac, Wellbutrin, Zoloft); erectile dysfunction (Papaverine, Levitra, MUSE, Prostin VR, Viagra); fatigue (Amantadine, Cylert, Provigil, Prozac); itching (Atarax); nausea (Antivert); pain (Aventyl, Dilantin, Elvail, Neurontin, Gabapentin, Pamelor, Tegretol); urinary tract infections (Bacrim, Cipro, Hiprex, Macrochantin, Nitrofurantoin, Pyridium); and urinary frequency or bladder dysfunction (DDAVP, Ditropan, Oxytrol, Pro-Banthine, Tofranil). Interferon-based medicines are also prescribed as "disease-modifying agents."

Drugs commonly prescribed for muscle spasticity and tremor include **Klonopin**, **Dantrium**, **Baclofen** (Medtronic), **Zanaflex** and **Valium**. Klonopin (Clonazepam) and Valium (diazepam) are both benzodiazepines, central nervous system (CNS) depressants manufactured by Roche. Overdoses of these medications, especially when taken with alcohol, may lead to unconsciousness and death. They frequently cause people to become drowsy, dizzy, lightheaded, clumsy, or unsteady. Other common side effects include slurred speech; abdominal cramps or pain; blurred vision or other changes in vision; changes in sexual drive or performance; gastrointestinal changes, including constipation or diarrhea; dryness of mouth; fast or pounding heartbeat; muscle spasm; trouble with urination; trembling. Studies in animals have shown that clonazepam and diazepam can cause birth defects or other problems, including death of the animal fetus. Overuse of clonazepam during pregnancy may cause the baby to become dependent on it and it may pass into breast milk and cause drowsiness, slow heartbeat, shortness of breath, or troubled breathing in nursing babies.

**Dantrium** is a muscle relaxant manufactured by Proctor & Gamble. It has been shown to cause cancer and non-cancerous tumors in animals, can cause liver damage, and should not be taken with alcohol. Common side effects include diarrhea, dizziness, drowsiness, weakness, nausea, unusual tiredness, abdominal cramps, blurred or double vision, chills and fever; constipation, frequent urination, headache, loss of appetite, speech difficulties, sleep difficulties and nervousness.

**Baclofen** (Medtronic) may be administered orally or with a surgically implanted pump in the spine. Its side effects include high fever, altered mental status, spasticity that is worse than was experienced prior to starting ITB Therapy, and muscle rigidity. Symptoms of overdose include shortness of breath or troubled breathing, vomiting, seizures, loss of consciousness and coma. Abruptly stopping implanted baclofen has been fatal.

**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**

### **Greg Paufler**

Some days I would be semi-ambulatory. Most days I was completely bedridden. My eyesight became very blurred and I lost all ability to focus. Unable to walk, read, or be with my family, I became very depressed. . . One evening some old friends came to visit and we smoked several joints. When my friends got up to leave, I stood up to say goodbye. Everybody in the room suddenly stopped talking and stared at me. At first I could not understand what was wrong. Then I realized I was standing, I had spontaneously stood up, unassisted, as if standing up was a perfectly natural. . . .

I quickly discovered that when I did not smoke marijuana my condition worsened, I suffered more frequent spasms, and the spasms were more intense. When I smoked marijuana my condition stabilized, then dramatically improved. After smoking marijuana my spasms were much more controlled and less severe. Marijuana caused me to feel better. I regained control over my limbs and could walk totally unaided. My vision, often blurred and unfocused, [now] improved. . . . I do not like breaking the law. I do not like being forced to pay terribly inflated prices for an unregulated, uncontrolled product. I do not like having to purchase marijuana from drug dealers and I do not like having to use marijuana without medical supervision. However, I do like to walk, talk, read, and see. Marijuana allows me to do these simple, human things by controlling the symptoms of my MS. If I am forced to choose between maintaining my health with an illegal drug or obeying the law, I would choose to maintain my health.

- Greg Paufler, May 11, 1987, Testimony submitted to the DEA In the Matter of Marijuana Rescheduling and in Idaho v. Hastings.

### **B.D.**

I was diagnosed with multiple sclerosis in 1988. Prior to that, I was an active person with ballet and swimming. I now have a swimming pool, so I swim each and every day, and smoke marijuana. The government has given me the marijuana to smoke. Each month I pick up a can filled with the marijuana cigarettes rolled by the government.

At one time I weighed 85 lb. and I now weigh 105. Twenty pounds is quite a bit to put on. I could not walk. I did not have the appetite. I use a scooter now for distance. I can get around the house. I have a standard poodle who is kind of like an assistant dog. She is good at it. She helps me.

When I found out that there was a program to get marijuana from the government, I decided that was the answer. I was not a marijuana smoker before that. In fact, I used to consider the people I knew who smoked the marijuana as undesirables. Now, I myself am an undesirable.

But it works. It takes away the backache. With multiple sclerosis, you can get spasms, and your leg will just go straight out and you cannot stop that leg. You may have danced all of your life and put the leg where you wanted it to be, but the MS takes that from you. So I use the swimming pool, and that helps a lot. The kicks are much less when I have smoked a marijuana cigarette. Since 1991, I've smoked 10 cigarettes a day.

I do not take any other drugs. Marijuana seems to have been my helper. At one time, I did not think much of the people who smoke it. But when it comes to your health, it makes a big difference.

- B.D. was one of the patients legally allowed to use cannabis as part of the Compassionate IND program.

### **Nathaniel**

I am a patient suffering from multiple sclerosis, and have found amazing amounts of relief from marijuana. I have been through Rebif, Amantadine, Baclofen, Ultram, Provigil, Soma, and Prednisone. All of these medications either provided little or no relief, or had very undesirable side effects for me. Before learning that I had MS, I had used marijuana maybe 10 times in my whole life. I started using it more regularly, and noticed that I was feeling much better all around when smoking marijuana. I could get around better, I felt better, I was in a better mood, and I ate (something that is often very difficult for me).

Marijuana is now the only medication I am using to treat my condition, and I would be so much less functional without it that I don't know what I would do (or COULD do, for that matter). Being a California resident, I obtained a doctor's recommendation, and am now legal to use medical marijuana in California.

### **Missi**

I had done much research into the helpful benefits of the medicinal use of marijuana, but I did have my doubts since I felt that maybe many of the people who claimed its benefits just really wanted to get 'high'. Well, as God as my witness, (something I don't ever say lightly because I am a born-again Christian), I was totally amazed at the results.

Everyone around me had witnessed my daily life. They had finally seen firsthand that I had problems just walking across the room. Well, anyway, I smoked a joint with my relative and I am telling you, I was up and about walking everywhere. She has a 3000sq ft house and I walked around it like I was an Olympic athlete. OK, maybe not that great but that is what I felt like. I was happy, moving all over the place, and most importantly I did not need to take my next dosage of Oxycontin! I had no pain at all or any of the associated problems. Not only was I able to go with out that dosage but the next morning dosage as well and I did not experience any withdrawal symptoms either.

I really could not believe it. I had hoped to receive some help but I honestly did not think it would be THAT helpful THAT fast. I was very happy that I had witnesses to this seemingly miraculous recovery. But the sad thing is that I am not using it now and cannot get it. I asked my military Neurologist about medical marijuana and was surprised to hear him say (he is very strict) that if he were not a military doctor that is what he would have me on now. It is safer by far than the other meds I am currently on.

### **Anonymous**

This is just another letter from a fellow MS sufferer vouching for how effective I find cannabis in relieving some of the unpleasant symptoms of MS. I was first told of the diagnosis of MS in 1991 (on my 35th birthday) this was just a few weeks following an unbelievably acrimonious divorce, my wife having thrown me out claiming that she was sick of me being tired all the time, and then telling her solicitor that I was a heroin addict, a totally fabricated claim which I, staggering and slurring my speech like a vaudeville drunk, did a very poor job of denying. Realising that the vicious cycle of anger and frustration in which I found myself caught, was exacerbating my symptoms I decided to try smoking some pot, after a three year period of abstinence, as to quote Ken Kesey, "it makes you feel pretty philosophical about most things". I was totally unprepared for the way in which the sensation of 'tight bands and writhing rats' in my legs vanished for the first time in months, as did the pain in my face. Though it did not stop the vertigo, it totally removed the nausea and 'sea sickness' which accompanies it. For the first time in months I slept like a baby, without

having to get up and empty my bladder every 2 hours. Though I would not go so far as to say that this was the beginning of my recovery, I would certainly say that it marked the end of my decline!

## **Anonymous**

I was diagnosed as having MS five years ago, when I was 45, and was informed that in my case it would probably just get steadily worse. The forecast proved correct. I had to give up work 2 years ago, and am now confined to a wheelchair. I suffer violent muscle spasms from the waist down, which lock my legs together like magnets, causing increasing pain and discomfort, and I feel as if I have flu permanently.

A year ago a friend showed me an article from the Daily Mail about an MS sufferer who obtained considerable relief from the most distressing symptoms using cannabis, and about her fight to become 'legal' by being prescribed Nabilone. Despite an in built aversion to banned substances, I bowed to family pressure, and have been using it ever since. I find the effects not exactly euphoric, but I can (with concentration) stretch my legs out straight, either sitting on the floor or lying in bed. I can watch TV for a couple of hours without frightening company by snapping myself into a knot while shrieking in pain. I can go on a car journey without fretting about my bladder. I can actually get 3 or 4 hours unbroken sleep sometimes, and more importantly so can my wife. Smoking cannabis is not a problem for me as I roll my own anyway. The main thing is, it works—as a muscle relaxant, a tranquilliser, whatever.

## **John E. Precup**

I was diagnosed with secondary-progressive multiple sclerosis in 1986, after waking up on the morning of April 5th with the worst case of the "bed spins" imaginable. I was unable to keep anything down, even water. On April 6th I was admitted to the hospital for a seven-day stay during which the 'spinning' continued for six days straight.

When I was sent home, the dizziness had subsided a little, but I still could not function well at all. My neurologist prescribed the drugs Compazine and Antivert. They had little affect on the nausea and no affect on the appetite, even after the dosage was doubled. After a couple of weeks of feeling sick and not eating, I had lost 15 pounds and no medication was helping. I was truly in fear for my life. It was then that I decided to try smoking Cannabis/Marijuana.

At first I felt worse, but after the effects of the smoke were gone I began to relax and get an appetite. I could finally eat again. Since that time, I have used cannabis to maintain a healthy body weight and a decent standard of living. For years I left my prescription drugs setting on the counter, as Cannabis was more effective. By November 1993, the disease had progressed to the point that I needed to use a cane and a wheelchair. The damage to the nerves that control the lower part of my body and legs caused my legs to be spastic and ache. Again, I saw a real benefit from using Cannabis, it allowed my muscles to relax. I was given a prescription for the drug Bacoflen in 1993 to help control muscle spasms. I experienced little benefit from the drug, it didn't alleviate the pain in my legs. However with cannabis I got relief and, without the spasms, I could get a good night's sleep.

I briefly discussed the benefits I had been getting from the cannabis with my neurologist, Dr. Vilnius S. Ciemins, upon my initial office visit with him in 1986. After learning of Ohio's medical marijuana defense law in December of 1996, I decided to talk him again about my use of the drug and the short-lived law. Dr. Ciemins, agreed that Cannabis is useful in the treatment of my condition. He provided me with a handwritten recommendation that states: "Told patient that marijuana may relive nausea, realizing that as yet the drug is still illegal." I feel the reason for the prohibition of cannabis is misinformation and the stigma that surrounds this medicine. So I have become active getting people informed and involved.

Today I weigh 155 lbs. and use a wheelchair most of the time. Cannabis has, no doubt, given me a better life than I would have had without it. I didn't ask for this. I would gladly give up using Cannabis and all the

other drugs that are prescribed for me if I were miraculously cured. I don't consider myself a criminal just for using the only thing I know that works to try to maintain what quality of life I have left.

## **Josie Chaplin**

I have had three major MS attacks. Each time I have deteriorated more. I had tried smoking pot over the years, but not on many occasions. Last Christmas, I was given a joint to smoke as a present. I had dragged myself, with help, out for Christmas dinner. After a lot of frustration, fretting and struggling, I was installed in my daughter's home. I smoked the joint after my dinner, and for a few hours, I got the old me back again, as I remember me! I have been smoking it on and off since, when things get impossible. It helps with spasticity, sleep, pain and bladder dysfunction. It just helps make life bearable for me. I gave up smoking, as I have Hodgkins, and thought I should do the right thing, then I started again because it helps my MS, so if they legalize cannabis or even better prescribe it in drug form, a lot of people would benefit from it.

How many of us have to convince the world that it helps, and it's not just a drug to get high on! We know what helps our condition, because the people that this is about, are the ones that are suffering. Try walking in my shoes if you can, because sometimes even I can't walk in them! I hope one day soon we will get what we want and not feel like criminals.

## **THE EXPERIENCE OF DOCTORS**

### **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 nor Lioresal are very effective spasm control drugs. Their marginal medical utility, high toxicity, and potential for serious adverse effects, make these drugs difficult to use in spasticity therapy.

As a result, many physicians routinely prescribe tranquilizers, muscle relaxants, mood elevators, and sedatives to patients experiencing spasticity. While these drugs do not directly reduce spasticity, they may weaken the patient's muscle tone, thus making the spasms less noticeable. Alternatively, they may induce sleep or so tranquilize the patient that normal mental and physical functions are impossible.

[Dr. Petro then related his experience with a twenty-seven year-old MS patient who reported he was smoking marijuana 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., former FDA Review Officer and principal investigator on spasticity and cannabis studies, in testimony submitted before the DEA In the Matter of Marijuana Rescheduling, October 18, 1987.