

## INTRODUCTION

## Medical Marijuana: Myth or Magic?

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**M**arijuana use in the United States is a controversial subject that polarizes health care providers and patients alike and has garnered immense attention recently for many reasons—legalization, decriminalization, medical uses, and abuse as a “gateway” drug. Irrespective of personal opinions, it remains a mystery to many primary care physicians and should be addressed with scientific evidence (as well as subjective experience). In this themed edition of *SGIM Forum*, we have convened a group of pioneers and experts to discuss current medical and societal aspects of marijuana.

Marijuana, a mixture of the dried leaves and flowers from the plant *Cannabis sativa*, is the most common illegal recreational drug in the world. It can be smoked, eaten, brewed as tea, or administered in tablet or liquid form. Globally, 3.5% of the population has used marijuana at least once. It has conventionally been labeled as a schedule 1 drug in the United States, indicating that it is a drug of addiction with no known medicinal value, on par with heroin and cocaine. In the last couple of decades, however, attention has shifted to its medicinal properties. Proponents of medical marijuana claim that the premise of labeling it as an addictive drug is based on *insufficient* evidence regarding its pharmacological properties, that the prevalence of addiction to marijuana is less than 10%, and that—as opposed to alcohol, cocaine, or heroin—neither intoxication nor withdrawal is life threatening.<sup>1</sup>

Of all the different cannabis compounds, tetrahydrocannabinol (THC) is the psychoactive ingredient that causes altered mood; impairment in movement, thinking, and problem solving; and hallucinations and para-

noia. Cannabidiol (CBD) is believed to have medicinal properties. These include neuroprotective, anxiolytic, anti-convulsant, anti-inflammatory, and sedative effects. It has been suggested that a form of cannabis with a higher proportion of CBD and low amounts of THC can be beneficial in several debilitating conditions for which traditional medications prove ineffective, although many find it challenging to promote a drug that traditionally has had only recreational uses. The current medical literature regarding the potential medicinal applications for this drug is inadequate and scientifically weak. However, case reports and case series have been described that are compelling.

Acknowledging that research on marijuana has been difficult due to regulatory limitations, here are a few conditions for which medical marijuana may be of benefit when traditional treatments have been ineffective:

1. *Multiple sclerosis (MS)*. There is definite evidence that marijuana reduces spasticity in multiple sclerosis and spasm-related pain (attributed to its anti-inflammatory properties) as shown in 12 trials with 1,600 patients.<sup>2</sup> Urinary bladder symptoms, depression, constipation, insomnia, fecal incontinence, and defecation urgency have also been relieved. The American National MS Society supports patients who are interested in exploring this option. Marijuana does not reduce tremors, neuropathic pain, or disease progression and may elevate the risk for cognitive impairment. An oral spray (Sativex) is available for prescription use.
2. *Chronic pain syndromes*. This is

the most common use of medical marijuana. Evidence from six small clinical trials (325 patients)<sup>2</sup> suggests that it can be used with negligible side effects or addiction in labor pain, migraines, arthritis, cancer pain, pain from spasticity, endometriosis, and fibromyalgia. After robust review of existing literature, the Institute of Medicine (IOM) has deemed that marijuana in any form can cause mild to moderate pain relief on par with codeine.

3. *Cachexia/wasting syndrome*. This is usually seen in patients with AIDS, cancer, or advanced dementia whose poor appetite results in weight loss and failure to thrive. Several small clinical trials have demonstrated that marijuana in inhaled or oral form stimulates appetite, arrests weight loss, causes weight gain, and reduces nausea more than placebo in patients with AIDS, cancer, or advanced dementia.<sup>3</sup> These effects were found to be long term. It is usually well tolerated and has few side effects. Based on this moderate evidence for marijuana, the Food and Drug Administration (FDA) has approved the use of dronabinol (i.e. a synthetic form of cannabis, trade name Marinol) for use in AIDS patients with weight loss.
4. *Severe nausea and vomiting*. Dronabinol and nabilone are synthetic forms of cannabis used for treatment of intractable chemotherapy-related nausea and vomiting.<sup>3</sup> Dronabinol is FDA approved for this indication. According to the American Society of Clinical Oncology, however, it should not be a first-line treatment.

continued on page 2

## INTRODUCTION

continued from page 1

5. *Amyotrophic lateral sclerosis (ALS)*. Cannabis can relieve muscle spasm and pain, improve breathing through relaxation of bronchial muscles, reduce drooling by inhibiting saliva, stimulate appetite and sleep, and reduce depression.<sup>4</sup> It improves speech, swallowing, and sexual dysfunction. Cannabis may slow the progression of ALS but can aggravate the already-compromised respiratory system and cause death by respiratory failure. It is legally available for use in ALS in six states. The ALS Association supports further research related to the use of cannabis for ALS but also issues a cautious approach to the use of marijuana as a drug of choice based on current evidence.
6. *Crohn's disease (CD)*. Due to its anti-inflammatory properties, patients with Crohn's disease report a reduction in symptoms with marijuana as proven in one clinical trial.<sup>5</sup> Crohn's disease is one of the few diseases for which a human clinical trial has been conducted with cannabis. In this study, subjects were given inhaled marijuana twice daily for eight weeks. The trial concluded that cannabis can resolve symptoms of pain and nausea, improve appetite and sleep, have minimal side effects, and be steroid sparing. Unfortunately, the effects are short term, with all symptoms returning after two weeks.
7. *Seizure disorder*. Twenty percent of adult patients with epilepsy in the United States smoke marijuana and report reduction in seizures. Childhood intractable seizure syndromes like Dravet syndrome may respond to marijuana dramatically.<sup>6</sup> Large clinical trials are needed to conclusively demonstrate its anti-

convulsant efficacy, and several are ongoing. Anecdotal reports, as seen in the Cable News Network "Weed" documentaries by Dr. Sanjay Gupta, are impressive. The well-known product Charlotte's Web has a waiting list of almost 10,000.

8. *Glaucoma*. Smoking marijuana reduces pressure within the eyes, but this effect is of short duration, and no clinical trials have been conducted. Side effects include sedation, dry mouth, dizziness, depression, confusion, and weight gain. The American Glaucoma Society position statement on the use of marijuana for glaucoma is that "although marijuana can lower the IOP, its side effects and short duration of action, coupled with a lack of evidence that its use alters the course of glaucoma, preclude recommending this drug in any form for the treatment of glaucoma at the present time."
9. *Post-traumatic stress disorder (PTSD)*. Many patients with PTSD smoke marijuana to improve their sleep, appetite, and depression. A single study showed reduction in nightmares in PTSD patients. Reconsolidation is a process in which latent memories persist by being repeatedly reawakened. If reconsolidation is blocked, then there is a weakening of the original memory. Research suggests that one of the cannabinoid chemicals may block negative memories or fear associated with psychological trauma, a process called reconsolidation blockage.
10. *Movement disorders and dementia*. Marijuana may ameliorate a few symptoms in Parkinson's, Huntington's, and Alzheimer's disease patients. No large clinical trials have been reported, though several are

currently ongoing with Sativex spray.

Regardless of one's personal beliefs, it is clear that the safety as well as the medical applications for marijuana will continue to be a hot topic for years to come. It is therefore critical that health care providers enhance their knowledge about marijuana with an open mind.

### References

1. Lopez-Quintero C, Pérez de los Cobos J, Hasin DS, et al. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). *Drug Alcohol Depend* 2011; 115(1-2):120-30.
2. Hill KP. Medical marijuana for treatment of chronic pain and other medical and psychiatric problems: a clinical review. *JAMA* 2015; 313(24):2474-83.
3. Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for medical use: a systematic review and meta-analysis. *JAMA* 2015; 313(24):2456-73.
4. Amtmann D, Weydt P, Johnson KL, et al. Survey of cannabis use in patients with amyotrophic lateral sclerosis. *Am J Hosp Palliat Care* 2004; 21(2):95-104.
5. Naftali T, Bar-Lev Schleider L, et al. Cannabis induces a clinical response in patients with Crohn's disease: a prospective placebo-controlled study. *Clin Gastroenterol Hepatol* 2013; 11(10):1276-80.
6. Devinsky O, Cilio MR, Cross H, et al. Cannabidiol: pharmacology and potential therapeutic role in epilepsy and other neuropsychiatric disorders. *Epilepsia* 2014; 55(6):791-802.

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