

# Pharmacology Consult

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## Therapeutic and Recreational Marijuana

### *Safe Practice Within the Web of Politics, Science, Law, and Nursing*

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**C***annabis sativa*, or marijuana, is the most commonly used drug worldwide. Introduced in the western world during the 1800s, its popularity declined with the availability of aspirin and barbiturates.<sup>1</sup> Cannabis is a broad term to describe all the different chemicals that come from the *cannabis sativa* plant which includes marijuana and more than 100 different cannabinoids.<sup>2,3</sup> Cannabinoids become active by binding at cannabinoid receptors in the human brain, and primary chemicals include cannabitol, cannabidiol (CBD), and delta-9-tetrahydrocannabinol (THC), which has a half-life of 1 to 3 days. Cannabidiol and THC have opposing effects—CBD is an anxiolytic and THC provides anxiogenic effects.<sup>1</sup> About 22.2 million persons use marijuana each month in the United States.<sup>4,5</sup> On average, 1 in 10 persons will become addicted, with 1 in 6 if use begins before age 18 years.<sup>6</sup>

#### LEGAL CONSIDERATIONS

Cannabis was determined “illegal” in 1906.<sup>7</sup> However, physicians and pharmacists provided cannabis for a variety of therapeutic medical interventions. In 1937, the Federal Marijuana Tax Act was passed, which did not prohibit dispensing cannabis. However, the restrictions with prescribing were so oppressive that use of cannabis was all but stopped.<sup>8</sup> Laws promulgated in 1951 and 1956 further increased Federal controls.<sup>7</sup> Finally, the Federal Controlled Substance Act of 1970 defined cannabis as a “Schedule 1” substance with high risk of abuse and addiction, which made medical and recreational cannabis use illegal in the United States.<sup>8</sup> Federal law still categorizes

marijuana as a drug without accepted medical use with high potential for abuse and lack of proven benefits despite the evidence that synthetic cannabinoids have demonstrated significant therapeutic benefits.<sup>7</sup>

Since 2000, perception of risk associated with use of cannabis has declined with a concomitant rise in use by adults, particularly since 2015. As more states adopt specific medical marijuana laws and/or recreational marijuana laws, increased availability without penalty will likely increase the population of users and potentially cannabis related adverse health events. Certainly, more education is needed to minimize harms associated with fluid laws and weak evidence.<sup>8</sup>

#### CURRENT EVIDENCE

Public health concerns remain despite increasing acceptance and use of cannabis. Evidence supporting the benefits and harms of cannabis overall are weak. For the vulnerable, particularly pregnant women, adolescents, and infants, long-term effects and risks with exposure and use remain unknown. There is not enough evidence to guide *when*, *where*, and *how* to use cannabis safely for recreation and therapeutic interventions. The Table describes the strength of evidence supporting the use of cannabis for a select group of problems commonly encountered in practice.<sup>9</sup>

At this time, there is insufficient evidence to support or refute that cannabis or cannabinoids are an effective treatment for symptoms associated with the following: cancer and cancer-associated anorexia, irritable bowel syndrome, epilepsy, spasticity in spinal cord injury with paralysis, amyotrophic lateral sclerosis, Parkinson's disease, addiction, and schizophrenia. Although long-term smoking of cannabis is associated with more frequent episodes of chronic bronchitis, at this time, there is not statistical association between cannabis use and lung cancer.<sup>9</sup>

Finally, moderate evidence supports a relationship between cannabis use and the development of dependence and/or substance abuse disorders (alcohol, tobacco,

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**Table. Strength of Current Evidence Supporting Therapeutic Use of Cannabis or Cannabinoids<sup>9</sup>**

Use Type	Agent	Purpose/Effects	Level of Evidence Supporting Use
Therapeutic	Cannabis	Chronic pain in adults	Conclusive substantive
Therapeutic	Oral cannabinoids	Chemotherapy-induced nausea and vomiting	Conclusive substantive
Therapeutic	Oral cannabinoids	Reduction in patient-reported multiple sclerosis spasticity symptoms	Conclusive substantive
Therapeutic	Cannabis or cannabinoids	Improvement in short-term sleep outcomes in obstructive sleep apnea syndrome and fibromyalgia symptoms	Moderate
Therapeutic	Cannabis and oral cannabinoids	Increased appetite or decreased weight loss in HIV/AIDS	Limited
Therapeutic	Oral cannabinoids	Improvement in clinician-measured multiple sclerosis spasticity	Limited
Therapeutic	THC capsules	Improved symptoms for Tourette syndrome	Limited
Therapeutic	Nabilone (Cesamet)	Improved symptoms for posttraumatic stress disorder	Limited

and other illicit drugs), particularly in males, and substantial evidence links motor vehicle crashes with cannabis use.<sup>9</sup>

What about cannabis for chronic pain? Pain can be nociceptive (tissue injury) and/or neuropathic (nervous system source of pain), which may coexist with inflammatory pain. The California Compassionate Use Act in 1996 was the first state law legalizing use of cannabis as an option for analgesia and antiemesis for patients with AIDS. Cannabis can be helpful for neuropathic pain, with effects contingent on the amount of THC that is present; higher doses of THC are more effective in relieving pain. However, the higher the amount of THC, the greater the cognitive decline, making activities of daily living and work difficult or impossible. Efficacy in use for cancer pain is weak built on poorly designed small studies.<sup>9</sup>

Primary focus on THC effects has left CBD effects in the shadows, which is regrettable because this noneuphoriant cannabinoid appears to have a good safety profile with analgesia and anti-inflammatory activity. Furthermore CBD attenuates the euphoria resulting from THC and provides light anxiolysis. Finding cannabis with low THC and high CBD at this time is difficult related to plant design that has focused on maximizing THC content alone. At this time, evidence suggests that cannabis should not be considered yet as the best choice for pain management.<sup>10</sup>

What about teenager and child exposure to cannabis? Nearly 35% of 10th graders have reported use of cannabis. Even very low levels of previous cannabis use in teens are associated with alterations in gray matter volume in areas of the brain rich with cannabinoid receptors.<sup>11</sup> Long-term research is needed to determine if alterations in the brain and cannabis use are related or present before exposure.<sup>12</sup> For now, adolescent use is associated with cognitive impairment, lower educational attainment compared to peers who do not use, and increased risk of dependence with continued use.<sup>13</sup>

Marijuana is the most common illicit substance used during pregnancy, with a self-reported prevalence of 2% to 5%. Based on concerns for neurodevelopment impairment with exposure, women who are pregnant or contemplating pregnancy should be encouraged to stop marijuana use. Because there are insufficient data to evaluate the effects of marijuana use in infants during lactation and breastfeeding, marijuana use is also discouraged.<sup>14</sup> We do not know how cannabis metabolites accumulate in the infant, nor how the infant metabolizes and excretes cannabis. Theoretically, since THC is highly lipophilic, one can expect accumulation in fat-rich organs like the brain and cannabinoids—especially THC can interrupt axonal growth and development.<sup>15</sup> More research is needed for this at-risk group so that risks with use are not exaggerated or dismissed.<sup>16</sup>

## SCIENCE, POLITICS, AND NURSING

Classification of cannabis as a Schedule 1 substance continues to hamper needed clinical research. Difficult access to cannabis for researchers and lack of consistent research methodology make it difficult to improve knowledge regarding the risks and benefits associated with cannabis use. Shifting public acceptance, difficult conditions for research, and variable legislative agendas will not uncover the harms and benefits of cannabis. Knowledge of the pharmacokinetic and pharmacodynamic characteristics, as well as the dose-response relationships for cannabis, are very needed for safe practice.<sup>9</sup>

Even more understudied are the effects both positive and negative for edibles and topicals. Research needs to develop standardized testing for cannabis composition, related compounds, and a way to quantify rapidly and accurately exposure and impairment. Finally, strategies for surveillance for adverse events are needed.<sup>9</sup>

Much of the enthusiasm for cannabis rests on the belief that cannabis is “natural” and, therefore, “safe,” which has

attenuated a rigorous evaluation of the risks and benefits related to use. Consider also the belief that cannabis is not addictive, which was quickly debunked when users experience rebound hyperalgesia and craving with forced abrupt cessation.<sup>10</sup> These myths need to be erased by education.

The decriminalization, legislation, and medicalization of cannabis are increasing use among current users and adding new users, particularly in adolescents who will have greater cumulative negative effects of cannabis use compared to older users. How can this be? Advances in cultivation have produced more potent marijuana today compared to previous decades, creating hybrid plants with more THC. Unlike drugs with a single specific element, different strains of cannabis produce multiple active substances.<sup>1</sup>

The claim that cannabis could be a substitute for prescription drugs, alcohol, or other substances certainly needs further research. In a study of 473 persons using cannabis for therapeutic purposes, 87% substituted cannabis prescription drugs, alcohol, and illicit substances. Subjects reported fewer side effects and improved symptom management, particularly for pain. Medical use of cannabis may play a role in harm reduction with the use of these substances, and these findings may have implications for abstinence-based substance use treatment approaches. As the medical and recreational uses of cannabis continue to be normalized, further investigation is needed to maximize health benefits, particularly substitution practices for opiates, benzodiazepines, anti-inflammatories, as well as tobacco and caffeine.<sup>17</sup>

There is no established causal relationship between medical cannabis legalization and health outcomes. It may be a decade or more before there is enough evidence to decide whether legalization increased population use and/or increased heavy use among current users.<sup>13</sup> As long as cannabis remains a Schedule 1 drug, this needed research will remain difficult.<sup>10</sup>

## NOW AND THE FUTURE

For now, do we develop cannabis prescribing recommendations based on limited research evidence or wait for Food and Drug Administration evaluations of safety and efficacy? In the future, will prescribing rest on ideological and popular vote exempt from scientific evaluation? It seems unwise to assume that the effects of cannabis observed in persons who frequently use can be predictive for persons who use as necessary under the care of a prescriber who is charged to carefully dose for a therapeutic effect.<sup>18</sup>

Finally, patient education and counseling regarding operating a motor vehicle and using cannabis may be the most important information shared between the clinical nurse specialist and the patient. There is enough evidence to recommend abstinence from cannabis when driving or intending to drive and safe storage to protect children from

exposure. Colorado and Washington both demonstrated significant increases in motor vehicle accidents and traffic-related deaths with legalization of cannabis for recreational use. Additional consequences included increased hospital emergency department visits, particularly for child exposure related to poor child supervision and/or unsafe storage of cannabis, and higher rates of youth use compared with states where cannabis use is illegal.<sup>19</sup>

Cannabis may not be worse than alcohol and tobacco, which are responsible for thousands of deaths each year. However, while we wait for better evidence, remember that cannabis has significant effects on behavior, driving, and risky behaviors, as well as unsafe sex. Education is very much needed moving forward with less emphasis on policy and laws and more focus on health and risks.<sup>19</sup>

The removal of marijuana from the Schedule 1 list can protect the public from the harm associated with the understudied and/or unknown side effects of cannabis. Research will remain limited as long as marijuana is classified as a Schedule 1 drug. Reclassification to Schedule III or II would be helpful and would enhance public to access medical cannabis and evidence supporting its safe use as a therapeutic alternative.<sup>7</sup>

## References

1. Macdonald K, Pappas K. Why not pot?: a review of the brain-based risks of cannabis. *Innov Clin Neurosci*. 2016;13(3-4):13-22.
2. Grof CPL. Cannabis, from plant to pill. *Br J Clin Pharmacol*. 2018; 84(11):2463-2467.
3. Centers for Disease Control and Prevention: National Center for Chronic Disease Prevention and Health Promotion. Marijuana fast facts. <https://www.cdc.gov/marijuana/pdf/MJ-Overview-Fact-Sheet-H.pdf>. Accessed February 5, 2019.
4. Results from the 2015 National Survey on Drug Use and Health: detailed tables, SAMHSA, CBHSQ. <https://www.datafiles.samhsa.gov/study/national-survey-drug-use-and-health-nsduh-2015-nid16893>. Accessed February 6, 2019.
5. 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):120-130.
6. Hall W, Degenhardt L. Adverse health effects of non-medical cannabis use. *Lancet*. 2009;374(9698):1383-1391.
7. Krystal H. The misclassification of medical marijuana. *J Am Acad Psychiatry Law*. 2018;46(4):472-479.
8. Carliner H, Brown QL, Sarvet AL, Hasin DS. Cannabis use, attitudes, and legal status in the U.S.: a review. *Prev Med*. 2017;104:13-23.
9. National Academies of Sciences, Engineering, and Medicine 2017. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*. Washington, DC: The National Academies Press. <https://www.nap.edu/catalog/24625/the-health-effects-of-cannabis-and-cannabinoids-the-current-state>. Accessed February 6, 2019.
10. Carr D, Schatman M. Cannabis for chronic pain: not ready for prime time. *Am J Public Health*. 2019;109(1):50-51.
11. Orr C, Spechler P, Cao Z, et al. Grey matter volume differences associated with extremely low levels of cannabis use in adolescence. *J Neurosci*. 2019.
12. Meruelo AD, Castro N, Cota CI, Tapert SF. Cannabis and alcohol use, and the developing brain. *Behav Brain Res*. 2017;325(pt A):44-50.

13. Hall W, Weier M. Assessing the public health impacts of legalizing recreational cannabis use in the USA. *Clin Pharm Therap*. 2015;97(6):607–615.
14. Committee opinion no. 722. Marijuana use during pregnancy and lactation. *Obstet Gynecol*. 2017;130(4):e205–e209.
15. Ryan SA. A modern conundrum for the pediatrician: the safety of breast milk and the cannabis-using mother. *Pediatrics*. 2018;142(3):e20181921.
16. Mark K, Terplan M. Cannabis and pregnancy: maternal child health implications during a period of drug policy liberalization. *Prev Med*. 2017;104:46–49.
17. Lucas P, Walsh Z, Crosby K, et al. Substituting cannabis for prescription drugs, alcohol and other substances among medical cannabis patients: the impact of contextual factors. *Drug Alcohol Rev*. 2016;35(3):326–333.
18. Cohen PJ. Medical Marijuana: The conflict between scientific evidence and political ideology: part one of two. *J Pain Palliat Care Pharmacother*. 2009;23(1):4–25.
19. Donnelly J, Young M. The legalization of medical/recreational marijuana: implications for school health drug education programs. *J School Health*. 2018;88(9):693–698.

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