

Legalizing Mary Jane: past, present, and future use of cannabis in medicine

Emma Avery, MSc*

Max Rady College of Medicine, University of Manitoba
727 McDermot Avenue, Winnipeg, R3E 3P5

Abstract

Recreational marijuana (or cannabis) is scheduled to be legalized by the Federal Government of Canada on October 17th, 2018 with passing of the Cannabis Act, ending a 95 year prohibition. Before the drug ban, cannabis was used throughout the western hemisphere for both recreational and medicinal purposes. Notwithstanding prohibition, in recent decades, the medical field has become interested in the therapeutic benefits of cannabis. Physicians currently prescribe cannabis for a number of conditions, including cancer pain and chemotherapy-induced nausea and vomiting, as well as multiple sclerosis-related spasticity, amongst others. Despite the medical benefits of cannabis, there are important considerations of safety to be made, as cannabis has (1) been shown to have neurotoxic effects in the developing brain, (2) may potentiate psychiatric illness in some individuals, and (3) when smoked, can lead to harmful disease sequelae. These deleterious side effects are relevant to both recreational and medical cannabis use. This article provides a very brief history of medical marijuana and outlines some of the key events leading to the prohibition and subsequent legalization of cannabis. It also touches on some of the physician considerations surrounding medical and recreational cannabis use.

Keywords: Cannabis, cannabinoids, marijuana, cannabis act, medicine

Cannabis was introduced to Western medicine in the 1830s by Irish physician Dr. William O'Shaughnessy, who recognized that cannabis appeared to have both analgesic and anticonvulsant effects.¹ This discovery led to the eventual popularization of medicinal cannabis throughout Europe and the United States.¹ Interestingly, despite widespread use in North America, cannabis would not gain popularity in Canada (medicinally or otherwise) until after the country's drug ban. The total prohibition on drugs in Canada began in 1912 when the International Convention Relating to Dangerous Drugs made recommendations to restrict the international exportation of opium and cocaine.² The convention would later expand its scope to include the prohibition of cannabis cultivation; and in 1923, the Canadian parliament criminalized both medicinal and recreational cannabis use.^{2,3} However, similar to other illegal substances, prohibition did not prevent the use of cannabis, which was beginning to gain popularity in 1960s.⁴ It was around this time that the medical field regained an interest in cannabis as cancer patients were reporting symptom relief from chemotherapy-induced nausea and vomiting and cachexia.⁵ In response to the reported benefits, countries began to decriminalize the use of cannabis, and in 2001 Canada established the Marijuana for Medical Purposes Regulations (MMPR),

allowing physicians to prescribe cannabis to patients who fit a prescribed eligibility criteria.⁶ Since then, increasingly more countries have recognized the economic and social burden of criminalizing the personal use of cannabis, and have begun to decriminalize and/or legalize cannabis, and later this year it is anticipated that Canada will join the list of countries to legalize the cannabis.

On April 4th, 2017, the Canadian Minister of Health announced the government's plan to legalize recreational cannabis by passing Bill C-45, (referred to as the Cannabis Act), which will also serve to amend the current Controlled Drugs and Substances Act.⁷ While initially anticipated that the Cannabis Act would be passed on July 1st of 2018, signing has since been delayed to October 17th, 2018. The passing of Bill C-45 will allow individuals 18 years and older to purchase cannabis for recreational use.⁷

Many physicians believe that the proposed minimum age for legal marijuana use is inappropriate, as cannabis has been shown to have deleterious effects on neurologic development, which is incomplete until the mid-twenties.⁸ For this reason, under the current MMPR system, some physicians will not prescribe cannabis to patients under 25. Nonetheless,

*correspondence to: averye@myumanitoba.ca

recreational use of cannabis is not uncommon amongst adolescents, as certain components of the cannabis plant (when ingested or inhaled) can elicit psychoactive effects.⁹ These psychoactive effects are caused by terpenophenolic compounds, or phytocannabinoids, of which over one hundred have been isolated from the cannabis plant.⁹ The most notable of these compounds is delta-9-tetrahydrocannabinol (THC), which is responsible for the inebriated effect that is often desired by recreational users.⁹ THC acts directly on the endocannabinoid system (ECS) through partial agonist activity of cannabinoid receptors type 1 and 2 (CB1 and CB2).¹⁰ CB1 receptors are ubiquitous throughout the central and peripheral nervous systems (CNS and PNS), and are found in high concentrations in neurons and non-neuronal cells of the brain.¹¹ CB1 stimulation can lead to release of norepinephrine (NE) and serotonin (5-HT); this is the likely basis of the psychogenic and emotional effects of cannabis.¹⁰ Conversely, CB2 receptors are found primarily in peripheral tissues of the immune system, the gastrointestinal tract, and to a lesser extent, in the CNS and PNS.¹⁰

While many cannabinoids, including THC, alter perception and behaviour, there are some, such as cannabidiol (CBD), that have zero psychomimetic effects.¹² In fact, CBD, which constitutes approximately 40% of the plant's extract, and has been shown to mitigate some of the cognitive impairment and anxiety associated with psychoactive cannabinoids, particularly THC, via a mechanism of action which is unclear at this time, but is likely polypharmacological.^{13;14}

Due to the widespread biological distribution of cannabinoid receptors and their many neuromodulating effects, it is not surprising that cannabis use and targeted activation or repression of the ECS has gained medical interest, and certain uses of cannabis have been demonstrated to have medical benefit. For example, access to medical cannabis has been associated with reduced opioid requirements in patients with chronic pain, and significantly lower rates of opioid overdoses.^{15;16;17} Beyond pain control, cannabis may confer improved seizure control in patients with epilepsy.¹⁸ However, cannabis is not currently a recommended anti-epileptic medication, especially in the pediatric population, due to the undesired psychoactive and neurotoxic effects of THC.⁸ However, animal models have demonstrated that CBD, the non-psychoactive component of cannabis, has a better anticonvulsant profile than THC and does not elicit negative neurological side effects, suggesting that there may be a future therapeutic role for purified cannabis-derived products such as CBD.¹⁴ Interest in CBD as a pharmacological agent has led to altered cannabis breeding practices aiming to increase the ratio of CBD to THC in plants, and companies are beginning to develop synthetic cannabis products for medicinal use.¹⁹

Although the use of medical marijuana in Canada

has nearly a two-decade history, and the creation of a commercial market for cannabis has been anticipated for several years, some physicians remain uncomfortable prescribing cannabis to patients. One basis for this hesitation lies in a lack of knowledge and education on effective dosing.²⁰ For example, the maximum blood concentration of THC (and other psychoactive cannabinoids) with which it is safe to operate vehicles and heavy machinery is unknown; nonetheless, physicians must make decisions on how much cannabis is safe to prescribe for regular, daily use. Additionally, the mode of delivery (i.e., inhalation versus ingestion) is yet another factor that complicates precise dosing.¹⁴ There is also significant apprehension surrounding the detrimental effects of prescribing cannabis to certain populations, primarily pregnant women and persons under 25, due to neurotoxic effects in the developing fetal and adolescent brain, respectively.^{8;21} Beyond this, some physicians are apprehensive in prescribing marijuana in general, as studies have shown that cannabis use is associated with an increased incidence of psychiatric illness.²² To assist consumers in making positive and informed choice about their cannabis use, it has been suggested that the government should regulate the amount of the psychoactive cannabinoids, particularly THC, in recreational cannabis, or at least mandate that THC levels in any given cannabis product be clearly advertised such that consumers are aware of the amount of THC to which they are exposed. Such mandatory reporting of THC concentrations is reasonable, as (1) provincial governments already enforce similar laws for ethanol content in alcoholic beverages, and (2) as with alcohol, there will be ramifications if consumers are unaware the amount of THC that they are ingesting.²³ There is also concern pertaining to the negative health effects of smoking dried cannabis. Legalizing marijuana may raise the number of individuals engaging in this activity, thus increasing the burden of lung disease and the funds needed to treat inhalation-related disease sequelae.

Notwithstanding the wide array of opinions on recreational cannabis use and marijuana as a treatment modality, it is evident that recreational and medical marijuana are here to stay. As such, physicians and healthcare practitioners must become familiar with best practices regarding cannabis in order to meet the needs of their patients. Agencies such as *Patients Out of Time* and *The Medical Cannabis Institute* provide continuing medical education (CME) focusing on clinical cannabis, and provide CME credits for course completion.^{24;25}

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