Cannabis (Marijuana) for Medical Use

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Contact hours: 5

Course price: $29

Course Summary

Reviews the medicinal use of cannabis, introduces the endocannabinoid system, addresses myths, outlines therapeutic indications, and spells out dosages and routes of administration. This course addresses public policy and legal issues as use of medicinal cannabis becomes legal in a growing number of states throughout the United States.

Course Objectives

When you finish this course, you will be able to:

1. Summarize 3 myths and 3 truths about cannabis as a medication.
2. Identify phytocannabinoids, and contrast Marinol with cannabis occurring in nature.
3. Explain the endocannabinoid system and its implications for the use of cannabis as medication.
4. Comment on 3 generally supposed health risks related to cannabis as medication.
5. State 3 therapeutic effects and indications for cannabis.
6. Discuss 4 common routes of administration of cannabis.
7. Describe 4 elements of patient and family education regarding cannabis.
8. Debate 3 public policy and legal issues associated with the medicinal use of cannabis.
9. Describe 3 special populations who may experience health risks related to cannabis.

Criteria for Successful Completion

80% or higher on the post test, a completed evaluation form, and payment where required. No partial credit will be awarded.

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Cannabis: A World of Controversy

> Penalties against possession of a drug should not be more damaging to an individual than the use of the drug itself—and where they are, they should be changed.
>
> Jimmy Carter
> Drug Abuse Message to Congress
> August 2, 1977

A world of controversy surrounds the medical use of cannabis. In the United States we have been taught about “marijuana” as a drug of abuse, and cannabis is currently a forbidden medication in Schedule I of the Controlled Substances Act. However, cannabis is an ancient medication with a wide margin of safety and it is useful in an array of medical conditions and ailments. A number of states have passed medical marijuana laws or are considering such laws despite the federal prohibition. Patients are using cannabis as medication, and it is imperative that healthcare professionals understand not only the risks and benefits of this herbal medication but also the legal issues involved in its use.

This course will review the current federal and state laws regarding cannabis and the history of its medicinal use throughout the world. It looks at the chemical components of the cannabis plant in light of the newly discovered cannabinoid system within the human body. It reviews the safety profile of cannabis and considers patient risks, then looks at the indications for use as well as dosage and administration. The course includes a section on patient and family education and concludes by addressing the legal and ethical challenges for healthcare professionals.

In the formal education of today’s healthcare professionals, marijuana has been seen exclusively as a drug of abuse. However, in the early twentieth century cannabis was presented as an effective analgesic and sleep medication in pharmacology classes (Blumgarten, 1919). At the time there were numerous preparations of cannabis and it was considered an essential medication (Aldrich, 1997).

What happened?

First, we will correct the common myths and misconceptions regarding marijuana/cannabis. A brief review of its use as an ancient medication will be followed by a historical reference to the reefer-madness era, which marked the beginning of marijuana prohibition and led eventually to its placement in Schedule I of the controlled substances.

Politics and prejudice are now coming head to head with science and compassion as we understand the plant and how it interacts with the human body. Patients are desperate for this medication and the public overwhelmingly supports legal access to it. State and federal laws are in conflict and healthcare professionals are caught in the middle. In this changing climate, it is important that healthcare workers understand the use of cannabis as a medication.

Myth Busters

Marijuana is not medication. **False.** Cannabis has been used as medication throughout recorded history (Abel, 1980; Aldrich, 1997). It was popular in the United States prior to the reefer-madness campaign that lied about its effects. As of July

2019, 34 states, the District of Columbia, Guam, Puerto Rico and the U.S. Virgin Islands, as well as the American Herbal Pharmacopoeia, have recognized marijuana/cannabis as a medicine.

Marijuana is a dangerous drug. **False.** Cannabis is "one of the safest therapeutic substances known to man" (Young, 1988). Acute and long-term use of cannabis has very low toxicity (Pertwee, 2014).

Cannabis is highly addictive. **False.** Compared to most drugs of abuse, cannabis is much less addictive (Hall et al., 1999; Grucza et al., 2016).

Marijuana is a "gateway" drug. **False.** The illegal status of marijuana exposes the user to the illicit drug trade. Cannabis use does not cause a person to try other, "harder" drugs (Joy et al., 1999).

Marijuana has more than four hundred constituents. **True.** Fruits, vegetables, and herbal medications contain hundreds of constituents, but that does not make them dangerous for consumption.

Marinol is legal marijuana in pill form. **False.** Marinol is synthetic tretrahydrocannabinol (THC) and lacks many of the other therapeutic constituents found in cannabis.

Marijuana kills brain cells. **False.** Cannabis has neuroprotective properties (Izzo et al., 2009, Pertwee, 2014).

Marijuana causes cancer. **False.** Longitudinal studies show no increase in cancers related to cannabis use (Freimuth et al., 2010; Hashibe et al., 2006). New research on the **endocannabinoid system (ECS),** as well as animal research, indicates that cannabis can kill cancer cells (Izzo et al., 2009; Velasco, et al., 2012).

Allowing the legal use of medical cannabis will send the message to kids that it is good for you. **False.** Medication should always be used cautiously. What is therapeutic for one person may be deadly for another. Children need to be taught to respect medications and their proper applications in their lives. Not allowing patients to use this medication sends a distorted message to our youth.

Marijuana causes schizophrenia. **False.** There is no evidence to show that cannabis causes schizophrenia (Macleod et al., 2006). In populations where there has been an increase in cannabis use, there has been no subsequent increase in the incidence of schizophrenia (Frisher et al., 2009). There does seem to be some consensus that the very high THC strains may precipitate a psychotic experience for some folks and should be taken as a warning sign for them with future use of cannabis (Pertwee, 2014).

Marijuana is more potent today. **Partly true.** Delta-9-tetrahydrocannabinol (THC) is the primary psychoactive cannabinoid found in cannabis, and many growers have developed strains with higher THC content. However, in its natural form, other cannabinoids found in cannabis—such as cannabidiol (CBD)—serve to dampen the psychoactive effects of THC.

History and Current Status

Cannabis has been used as medication since ancient times. As stated earlier, in the early twentieth century physicians routinely used various cannabis products with their patients. Many of the pharmaceutical companies (eg, Ely Lilly, Parke Davis, Merck) sold various cannabis tinctures, tablets, or topical preparations. By the 1930s, Prohibition had ended and the Director of the Bureau of Narcotics and Dangerous Drugs, Harry Anslinger, spearheaded a campaign to demonize cannabis. At that time cannabis was being used recreationally by jazz musicians in the South, who called it “reefer,” and by Mexican soldiers, who called it “marijuana.”

Anslinger began spreading stories about “a new drug menace called marijuana” that was causing users to commit violent crimes or go insane (Bonnie & Whitebread, 1974; Abel, 1980). His efforts led to the passage of the Marihuana Tax Act of 1937, which resulted in a prohibitive tax on the medication and ultimately led to its removal from the U.S. Pharmacopoeia by 1941. Since that time, cannabis has no longer been included as a medication in pharmacology texts, and healthcare professionals are taught only that marijuana is a drug of abuse.

In 1970 Congress passed the Controlled Substances Act (CSA), which created a system to regulate psychoactive drugs (CSA, 1970). Five levels (Schedules I to V) were established to categorize drugs according to their medical utility, abuse potential, and safety of use under medical supervision. Schedule V is the least restrictive category and Schedule I is the forbidden drug category.

To belong in Schedule I, a drug must meet three criteria:

- It has no currently accepted medical use in treatment in the United States.
- It is highly addictive.
- It is not safe for medical use.

Schedule I includes marijuana, heroin, LSD, and more.

Schedule II drugs are highly addictive, but have been determined to have medicinal value, and most of the drugs in this category are opioids such as morphine and dilaudid. Prescriptions for these medications are limited in the amount that can be prescribed and the prescription cannot be “called in.” Restrictions on prescriptions decrease as the schedule level decreases.

With the passage of the Controlled Substances Act, cannabis was wrongly placed in Schedule I. Responding to questions about the placement of marijuana in Schedule I, President Richard Nixon appointed experts to review the science and report back. This Commission on Marihuana and Drug Abuse, commonly referred to as the Shafer Commission (for its chairman), released its findings in a document, *Marijuana: A Signal of Misunderstanding*, which found that cannabis did not meet criteria for Schedule I (National Commission on Marihuana and Drug Abuse, 1972). However, Nixon ignored the commission’s findings, and cannabis remained forbidden.

Numerous challenges to the cannabis prohibition arose over the years. The National Organization for the Reform of Marijuana Laws (NORML) submitted a petition to reschedule marijuana to the Drug Enforcement Administration (DEA) in 1972 (Randall, 1988). Years later, the Alliance for Cannabis Therapeutics (ACT) joined the petition, and finally in 1988 the DEA's administrative law judge, Francis Young, ruled on the petition that marijuana should be moved to Schedule II (Young, 1988). However, the head of the DEA, John Lawn, ignored the judge's ruling and the prohibition of marijuana continued.

Back in the late 1970s, Robert Randall, a glaucoma patient, was arrested for growing marijuana on his back porch in Washington, DC. After a long federal court case he was found not guilty through a medical necessity defense (Randall and O'Leary, 1998). Randall was able to prove that cannabis was the only medication that could control his intraocular pressure and thus prevent blindness. Randall's law firm managed to get him into the Compassionate Investigational New Drug (IND) program. Randall would receive medical marijuana in rolled cigarette form from the federal government for free. The National Institute on Drug Abuse (NIDA) allows the University of Mississippi to grow marijuana for research on its dangers, and this marijuana farm was the source of Randall's medication.

Randall did not remain silent. He and his wife formed the Alliance for Cannabis Therapeutics (ACT) in 1981, with the goal of helping other patients gain legal access to cannabis (Randall & O'Leary, 1998). By 1992 the AIDS epidemic was universally acknowledged, and hundreds of applications for the IND program were being submitted for HIV-positive patients. Alarmed by the increased demand for cannabis, the Secretary of Health and Human Services closed access to it. At the time there were 15 patients in the program, and only they would be allowed to receive the medication. Today only 4 of those patients are still alive and only 2 remain in the program because the treating physician for the 2 Iowa patients relocated, leaving them with no physician willing to seek a Schedule I license from the DEA.

Patient awareness of the therapeutic potential of cannabis continued to grow, and desperate patients began helping each other. Cannabis buyers' clubs began to appear around the country. Patients would grow cannabis or find someone to grow it and then provide it to other patients in need. The buyers' clubs (now often referred to as compassion clubs or dispensaries) required patients to provide evidence that they had a medical need for cannabis, and in many cities (eg, San Francisco) law enforcement looked the other way. Finally in 1996 California voters passed Proposition 215, which permitted patients to grow and use cannabis as medication if they had a recommendation from a physician.

The Institute of Medicine (IOM) issued a report in 1999 that examined potential therapeutic uses for marijuana. The report found that

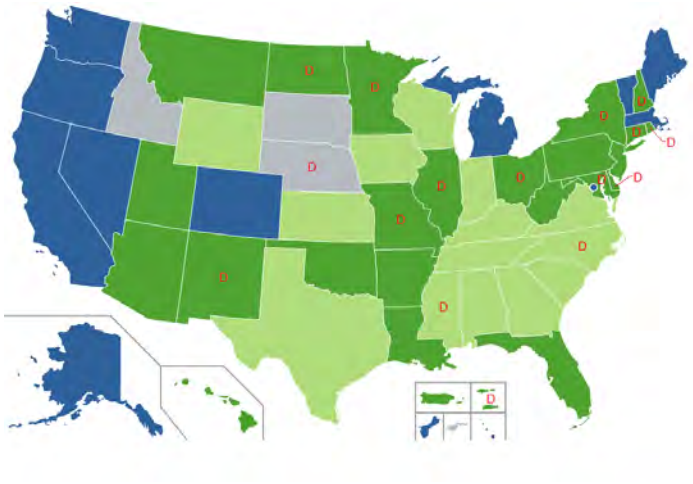
> Scientific data indicate the potential therapeutic value of cannabinoid drugs, primarily THC, for pain relief, control of nausea and vomiting, and appetite stimulation; smoked marijuana however, is a crude THC delivery system that also delivers harmful substances. The psychological effects of cannabinoids, such as anxiety reduction, sedation, and euphoria can influence their potential therapeutic value. Those effects are potentially undesirable for certain patients and situations and beneficial for others. In addition, psychological effects can complicate the interpretation of other aspects of the drug's effect. (Joy et al., 1999)

Further studies have found that marijuana is effective in relieving some of the symptoms of HIV/AIDS, cancer, glaucoma, and multiple sclerosis. In early 2017, the National Academies of Sciences, Engineering, and Medicine released a report based on the review of over 10,000 scientific abstracts from marijuana health research. They also made a hundred conclusions related to health and suggested ways to improve cannabis research.

By 2019, 33 states (Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Hawaii, Illinois, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Montana, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, Utah, Vermont, and Washington, West Virginia) plus Washington DC, Guam, and Puerto Rico have **medical marijuana**/cannabis laws.

Eleven states (Alaska, California, Colorado, Illinois, Maine, Massachusetts, Michigan, Nevada, Oregon, Vermont, Washington) and the District of Columbia, the Northern Mariana Islands, and Guam have legalized cannabis for **recreational use**; however, cannabis remained forbidden under federal law and patients are still at risk for federal prosecution. In addition, 14 other states have passed CBD-only cannabis laws due to its success with pediatric seizure disorders and pleas from desperate parents.

Legal Status of Cannabis in the United States



Legal | Legal for medical use | Legal for medical use, limited THC content | Prohibited for any use | D Decriminalized

Map showing legal status of medical cannabis in the United States.

Blue = No doctor's recommendation required

Dark green = Doctor's recommendation required

Light green = Limited THC content

Gray = Prohibited

Source: Courtesy of Wikimedia Commons.

States with Therapeutic Marijuana Use Laws and Date of Enactment (as of June 2019)	
State	**Date of enactment**
California	1996
Alaska	1998
Oregon	1998
Washington	1998
Colorado	2000
Hawaii	2000
Nevada	2000
Vermont	2004
New Mexico	2008
Michigan	2008
Rhode Island	2009
New Jersey	2009
Arizona	2010
Maine	2010
Delaware	2011
Montana	2011
Connecticut	2012
Maryland	2013
Massachusetts	2013
New Hampshire	2013
Illinois	2014
Minnesota	2014
New York	2014
Utah	2014
Louisiana	2015

Ohio	2016
Pennsylvania	2016
Arkansas	2016
North Dakota	2016
Florida	2017
Missouri	2018
Oklahoma	2018
West Virginia	2018

States That Have Legalized Recreational Use[1]	
State	**Date of Enactment**
Alaska	2015
Colorado	2014
Oregon	2015
Washington	2014
District of Columbia	2014
California	2016
Maine	2016
Massachusetts	2016
Nevada	2016
Michigan	2018
Illinois	2020[2]

[1] For persons at least 21 years old
[2] Bill goes into effect Jan 1, 2020, if the governor signs it as expected.

Because cannabis remains in Schedule I, physicians (and, in some states, nurse practitioners) cannot write a prescription for this medication even in states where it is lawful, but instead are allowed to “recommend” cannabis for certain conditions. Doctors with the Department of Veterans Affairs, even in states where medical cannabis is legal, cannot even discuss marijuana as an option with patients.

The Rohrabacher-Farr amendment prohibits the Justice Department from spending funds to interfere with the implementation of states’ medical cannabis laws. It passed after six attempts (beginning in 2001) and became law in 2014. It was the first time Congress voted to protect medical cannabis patients and was viewed as a historic victory at the federal level for cannabis reform advocates. The amendment must be renewed each fiscal year to remain in effect (Lopez, 2014).

In 2002 the Coalition to Reschedule Cannabis submitted another petition to the DEA to reschedule cannabis (see www.drugscience.org). It demanded that cannabis be removed from Schedule I because the current scientific evidence shows that it does have accepted medical value. After holding it for three years, the DEA finally passed the Petition on to the Department of Health and Human Services (DHHS) for their scientific review. The DHHS held onto the petition for years and finally in 2011 they denied any medical value with cannabis and thus, the DEA rejected the petition.

The Deputy Director for Regulatory Programs at the Federal Drug Administration (FDA) said at a June 2014 congressional hearing that the agency was analyzing whether marijuana should be downgraded, at the request of the DEA (Edney, 2014). In August 2016, the DEA reaffirmed its position and refused to remove Schedule I classification (Washington Post, 2017). DEA announced in 2016 that it would end restrictions on the supply of marijuana to researchers and drug companies that had previously only been available from the government's own facility at the University of Mississippi; however, the supply of research grade cannabis is limited to one approved source (W. Post, 2017; Californian, 2017).

The Democratic Party's 2016 platform called for removal of marijuana from Schedule I of the Controlled Substances Act:

Because of conflicting federal and state laws concerning marijuana, we encourage the federal government to remove marijuana from the list of "Schedule 1" federal controlled substances and to appropriately regulate it, providing a reasoned pathway for future legalization (Democratic Platform Committee, 2016).

Several House bills introduced in 2017 sought to reschedule cannabis to Schedule II or Schedule III, but were unsuccessful. In May 2017 the American Legion, a conservative veterans' group, petitioned the White House for a meeting to discuss rescheduling or descheduling cannabis and allowing it to be used medically, particularly to facilitate research into whether cannabis can help veterans experiencing post traumatic stress disorder (Bender, 2017).

In July 2017 a lawsuit was brought in U.S. District Court against the heads of the DEA and Justice Department on the grounds that Schedule I listing of cannabis is "so irrational that it violates the U.S. Constitution" (Pasquariello, 2017). The lawsuit was dismissed; however, in May 2019, a federal appeals court has reinstated the 2017 case against the federal government over the Schedule I status of cannabis. The plaintiffs argued that cannabis' Schedule I status represented a risk to patients' health and perpetuated economic iniquities in the United States.

Attorney Michael Hiller, who represents the plaintiffs, said the court has directed the DEA and federal government to act on the plaintiffs' de-scheduling petition "with all deliberate speed"(Hasse, 2019).

The 2018 United States farm bill descheduled some cannabis products from the Controlled Substances Act for the first time (Teaganne et al., 2018).

If cannabis is removed from Schedule I, other states will be able to allow the medical use of cannabis and patients will no longer be under threat of federal prosecution.

In addition, each state that has a medical cannabis law has the legal authority to challenge the federal government based on the understanding that state laws trump federal regulations regarding medical practice. The medical marijuana states have allowed the use of cannabis, therefore there is “accepted medical use in the United States” and that justifies the removal of cannabis from Schedule I. Unfortunately, no state government has made this challenge due to a lack of understanding of the law or fear of challenging the federal government (and possibly losing federal funds).

Healthcare professionals today are caught in a legal and ethical bind. Numerous state healthcare associations have passed resolutions that recognize the safety and efficacy of cannabis and support patient access to this medication.

In 2003 the American Nurses Associations (ANA) passed a similar resolution. They reaffirmed their position on medical cannabis in 2008 and in 2016, stating the ANA strongly supports:

- Scientific review of marijuana’s status as a federal Schedule I controlled substance and relisting marijuana as a federal Schedule II controlled substance for purposes of facilitating research.
- Development of prescribing standards that includes indications for use, specific dose, route, expected effect and possible side effects, as well as indications for stopping a medication.
- Establishing evidence-based standards for the use of marijuana and related cannabinoids.
- Protection from criminal or civil penalties for patients using therapeutic marijuana and related cannabinoids as permitted under state laws.
- Exemption from criminal prosecution, civil liability, or professional sanctioning, such as loss of licensure or credentialing, for health care practitioners who discuss treatment alternatives concerning marijuana or who prescribe, dispense or administer marijuana in accordance with professional standards and state laws. (ANA, 2016)

Because of its Schedule I placement, healthcare professionals cannot legally help their patients obtain cannabis and cannot themselves possess it.

In the meantime, patients are using cannabis and healthcare professionals have an obligation to provide education on its risks and benefits. This course presents evidence-based information about the safety and efficacy of cannabis and introduces the emerging science on the endogenous cannabinoid system. By understanding the science, healthcare professionals can be empowered to help end the prohibition of cannabis, which will not only allow legal access for the medicinal use but also permit quality control of this medication.

The Cannabis Plant

Cannabis has been grown and used for centuries as food, medication, fuel, fiber, shelter—as well as an intoxicant. When the plant is grown for its fiber and pulp it is called “hemp” and the crop is densely sown. When it is grown for its leaves and buds it is called “cannabis,” and the plants are sown more sparsely.

Unique to the cannabis plant is a group of chemicals called **cannabinoids** (or *phytocannabinoids*). Approximately one hundred different cannabinoids have been identified in cannabis. **Delta-9-tetrahydrocannabinol (THC) is** the primary psychoactive cannabinoid, and the THC content is often used to differentiate hemp from cannabis. Hemp plants generally have a THC content of <0.3%, while the medicinal cannabis plant has >1% THC content.

Cannabis is a fast-growing and sun-loving dioecious plant (meaning that the seeds will grow into male or female plants). When grown for its medical or psychoactive effects, the males are separated from the females and destroyed as soon as they can be identified, to avoid fertilization. Without fertilization, the female plant, referred to as **sinsemilla** (without seed), will focus its energy on producing flowers and resin. The primary source of the active cannabinoids is found in the leaves and flowers or, more specifically, in the glandular trichomes found on the vegetative material. These trichomes hold the sticky resin that is used to make hash oil. The cannabinoids are fat-soluble (lipophilic) rather than water-soluble (Martin et al., 2011).

Cannabis Plant Showing Trichomes

The trichomes are the primary source of the active cannabinoids. Source: Courtesy of Ethan Russo. Used by permission.

There have been several species of the genus Cannabis, but in general *Cannabis sativa* and *Cannabis indica* are the most widely recognized. The sativa plant generally is taller with longer branches and slender palmate leaves, while the indica is more compact with shorter branches and broader palmate leaves. The sativas generally produce a more psychoactive stimulating effect, while the indicas produce a more sedating or relaxing effect. Today’s growers have developed numerous strains combining genetics from indicas and sativas to produce new varieties.

Cannabis Sativa

Source: Wikipedia Commons. Originally from the U.S. Fish and Wildlife Service.

The Phytocannabinoids

While modern medicine and our pharmaceutical industry may continue to focus on specific chemicals in medical cannabis, others believe that the natural botanical with all of its constituents may be safer and more beneficial. When using the whole plant, these chemicals work together in a synergistic manner that provides more therapeutic benefits to the patient and usually fewer or milder side effects. In addition to the cannabinoids, cannabis also contains terpenoids and flavinoids that have therapeutic value (McPartland & Russo, 2001).

As stated earlier, delta-9-THC is the primary psychoactive cannabinoid found in the cannabis plant, but researchers have identified close to one hundred phytocannabinoids. The array of cannabinoids in the plant varies among its diverse strains. Most of the research on cannabis has been conducted on THC rather than the whole plant or its other cannabinoids. However, much has been learned about the pharmacologic actions of some of the other nonpsychoactive cannabinoids.

Cannabidiol (CBD) is a very promising cannabinoid that has a wide range of effects including anti-emetic, analgesic, anti-inflammatory, anxiolytic, neuroprotective, antipsychotic, anticancer, and bone stimulation. In addition, in Brazil, two research laboratories have been evaluating the use of CBD for anxiety, depression, bipolar disorder, psychosis, and post traumatic stress (Takahashi, 2010; Crippa, 2010).

Other cannabinoids of interest include cannabinol (CBN), cannabichromene (CBC), delta-8-THC, cannabigerol (CBG), and tetrahydocannabivarin (THCA) (Izzo et al., 2009). Cannabinol has sedative and antibiotic properties and, as a degradation product of THC, the amount of cannabinol increases as the plant material ages. Cannabichromene and CBG are noted for their anti-inflammatory, antibiotic, and antifungal properties. Delta-8-THC lacks the psychoactive properties of delta-9-THC but serves as an effective anti-emetic (Plasse, 2002).

In an Israeli study on eight pediatric oncology patients, delta-8-THC was uniformly effective in the management of chemotherapy-induced nausea and vomiting (Abrahamov et al., 1995). In fact, since October 2003 the U.S. government has held a patent (#6630507) on cannabinoids as anti-oxidants and neuroprotectants (Hampson et al., 2003).

Terpenoids are responsible for the distinctive smell of cannabis and are easily extracted as an essential oil. Although terpenoids are found in other plants, there are more than one hundred terpenoid compounds found in cannabis. Terpenoids also produce therapeutic effects including anti-inflammatory, antibiotic, antineoplastic, antimalarial, and antiviral. Approximately twenty flavinoids are found in cannabis and they provide additional therapeutic effects including anti-inflammatory, antiviral, and anxiolytic (McPartland & Russo, 2001).

Marinol vs. Cannabis

Marinol is synthetic THC in sesame oil and comes in capsules at doses of 2.5, 5, and 10 mg. In 1986 Marinol (dronabinol) was released as a new Schedule II medication and marketed as the pharmaceutical equivalent to cannabis. **Dronabinol,** developed by Roxanne Laboratories, was supposed to end the fight for medical marijuana because a "marijuana pill" was now available. It was initially allowed by prescription for chemotherapy-induced nausea and vomiting and later authorized as an appetite stimulant. After several years on the market and with no diversion problems, it was down-regulated* to Schedule III in 1999. In 2010 the patent expired for dronabinol and the DEA/FDA now allows both natural and synthetic forms of THC as legal medication in Schedule III.

*To date, **dronabinol** is the only drug ever down-regulated in the controlled substances scheduling classification. Many drugs have been rescheduled to a more restrictive category, but this was the first time a drug was moved to a less restrictive level.

Marinol Capsules Shown in Three Doses

Marinol is synthetic THC in sesame oil. Source: Courtesy of Ethan Russo. Used by permission.

The assignment of synthetic THC (Marinol) to Schedule III is not reasonable in light of cannabis's assignment to Schedule I. The DEA/FDA allows the use of the primary psychoactive substance in cannabis (the substance that produces the "high") in pill form, yet continues to prohibit the whole plant. The federal government complains that marijuana is much stronger today than decades ago; what they mean is that the THC content in the plant is higher. Strong strains of cannabis may be up to 20% THC, yet dronabinol is 100% synthetic THC in sesame oil.

As noted above, there are other nonpsychoactive cannabinoids found in whole cannabis. When CBD is present in cannabis, it dampens the psychoactive effects of THC; so, even if an individual used a strain with 20% THC, the CBD would interact with the THC to decrease the psychoactive effects. Patients report that cannabis works better for them than dronabinol. Many report dysphoria (feeling unwell or unhappy) with dronabinol (Holland, 2010).

FDA-Approved Forms

To date, FDA has approved one cannabis-derived and three cannabis-related drugs, which are only available with a prescription from a licensed healthcare provider. FDA has approved **Epidiolex**, which contains a purified form of CBD for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients 2 or older. FDA has concluded that Epidiolex is safe and effective for its intended use.

FDA also has approved **Marinol** and **Syndros** for therapeutic uses in the United States, including for the treatment of anorexia associated with weight loss in AIDS patients. Marinol and Syndros include the active ingredient dronabinol, a synthetic delta-9- tetrahydrocannabinol (THC) which is considered the psychoactive component of cannabis. Another FDA-approved drug, **Cesamet**, contains the active ingredient nabilone, which is chemically similar to THC and synthetically derived (FDA, 2019).

The Endocannabinoid System

An evolving body of science about our physiology was not available to us in school (and unfortunately this information is still absent in most nursing and medical schools). All animals except for insects have an **endogenous** (made within the body) cannabinoid system, or **endocannabinoid system (ECS**) (Richmond, 2010). It has been found that we make our own cannabinoids, and they are similar in structure to those of the cannabis plant; further, we have receptors for these molecules. This newly discovered molecular signaling system is essential for life and helps keep us in balance as we deal with daily stressors. Some researchers are suggesting that a weak or overstressed ECS may be the underlying cause of a variety of ailments, such as fibromyalgia or migraine headaches as well as auto-immune diseases. Russo has suggested naming such a problem a **clinical endocannabinoid deficiency, or CECD** (2004).

In 1988 American researcher Allyn Howlett and her graduate student William Devane discovered cannabinoid receptors in the brain and called them cannabinoid 1 receptors (CB1) (Devane et al., 1988). In 1992 researchers in Israel discovered an endogenous cannabinoid and called it N-arachidonoyl ethanolamine or *anandamide* ("ananda" means bliss in Sanskrit) (Devane et al., 1992). By 1993 another group of scientists found cannabinoid receptors in the immune system (CB2), followed by the discovery of a second endocannabinoid called 2-arachidonoyl glycerol or 2-AG (Munro et al., 1993).

The CB1 receptors are found mainly on neurons in the brain, spinal cord, and peripheral nervous system, but are also present in other organs and tissues including immune cells, the spleen, adrenal and pituitary glands, heart, lungs, and parts of the reproductive, urinary, and gastrointestinal tracts. The CB1 receptors are abundant in the cerebral cortex, basal ganglia (substantia nigra pars reticulata, globus pallidus, nucleus caudatus and putamen), cerebellum, hippocampus, peri-aqueductal grey, rostral ventromedial medulla, certain nuclei of the thalamus and amygdala, and dorsal primary afferent spinal cord regions, which helps explain the role of cannabinoids in motor control, memory processing, and pain modulation. The low number of CB1 receptors in the brain stem may help explain the absence of cannabis overdoses due to the depression of respirations. The CB2 receptors are primarily found in immune cells, among them leukocytes, the spleen, and tonsils. There are cannabinoid receptors throughout our bodies, and we have more receptors for cannabinoids than for any other substance (Grotenhermen, 2005).

The endocannabinoids bind with the cannabinoid receptors in a fashion similar to other neurotransmitters and can exert various effects depending upon the lock-and-key mechanisms. They can activate the receptors as full agonists or partial agonists, or they can dock in a receptor and act as a neutral antagonist, which does not activate the receptor, or as an inverse agonist, in which case it deactivates the receptor.

The endocannabinoids are not stored in the body, but are synthesized and released on demand. The activation of the endocannabinoid system (ECS) influences other chemical reactions, producing a cascade effect. The ECS helps in maintaining homeostasis and has the ability to move back and forth across the synapses between cells and may exert either an excitation or inhibition of activity (McPartland, 2008).

Robert Melemede calls the ECS the “oil of life” because it keeps numerous physiologic processes running smoothly (Melamede, 2006). Endocannabinoids serve as neurotransmitters or neuromodulators. Italian researcher Vincenzo DiMarzo noted that the ECS helps us eat, sleep, relax, protect, and forget (1998). The existence of this molecular system may explain why cannabis is helpful for such a wide array of conditions.

Cannabis as Medication

Cannabis seems unique in its wide array of indications for use. The newly discovered endocannabinoid system not only adds to our understanding of human physiology but also helps us understand how and why cannabis is safe and effective for so many indications. This section reviews the safety profile of cannabis and discusses its potential risks. Then it outlines the therapeutic effects and indications for use and presents information about dosage and administration. Cannabis seems to work synergistically with opioids, and most patients with chronic pain significantly reduce or eliminate their use of opioids; thus, cannabis can be viewed as an opiate-sparing medication (Abrams, 2010; Nielsen et al., 2017). Finally, the section ends with some case examples of patients using medicinal cannabis.

Safety Profile

> In its natural form, marijuana is one of the safest substances known to man. . . . It would be unreasonable, arbitrary, and capricious for the DEA to continue to stand between those sufferers and the benefits of this substance in light of the evidence in this record.
>
> Francis Young, 1988 DEA Administrative Law Judge

That statement was made after reviewing more than 5000 pages of evidence during the hearings to reschedule marijuana in 1988. Note that he drew these conclusions in 1988, even before researchers discovered the endocannabinoid system.

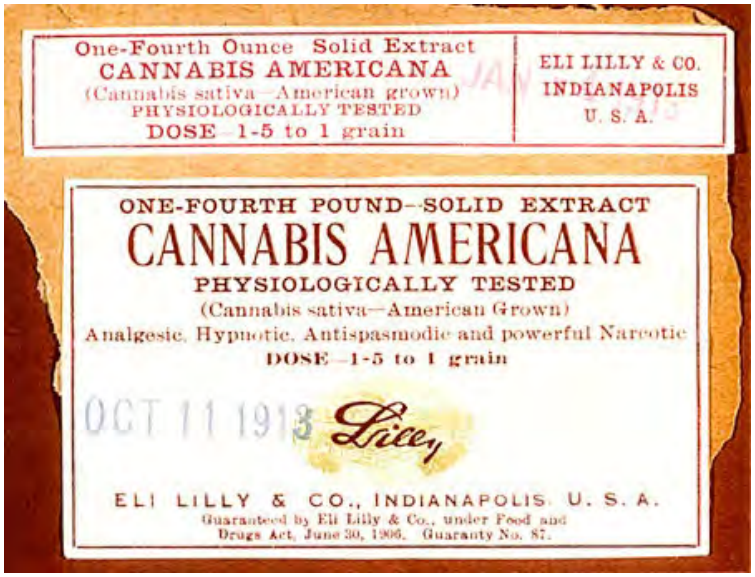
By trial and error over centuries of use, humans have learned how to use many herbal plants as medication. With more modern research, physicians have moved from using botanicals to specific chemicals within those plants or synthetic versions of those chemicals. In research studies it is much easier to focus on a particular chemical; however, although these specific chemicals may have stronger and more direct effects, they can come with stronger and sometimes-toxic side effects.

Today clinicians are taught to rely on the scientific method, and double-blind placebo-controlled studies are the gold standard. To safeguard the public, the FDA allows new drugs on the market only after they have met basic safety studies and have been shown to have therapeutic value in clinical trials. This research takes years to come to fruition and, even then, some drugs have been allowed on the market and found to have dangerous side effects or adverse reactions when consumed by a larger population.

This course is about the medicinal use of a plant called cannabis. What's so different about cannabis?

Cannabis is an ancient drug that has been used by countless individuals over the centuries. It is not a new drug. As noted earlier, cannabis was a very popular medication in early American history. Included on numerous bottles of medicinal cannabis would be the claim that it was "guaranteed under the Pure Food and Drugs Act of June 30, 1906" (see below). This was the forerunner of our FDA process today. Many of our early medications (eg, aspirin) had been found to be safe for medical use based on their historical record, and so they were grandfathered in to the list of FDA-approved drugs. Had it not been for the politically driven reefer-madness campaign of the 1930s, cannabis would have also been grandfathered in as an approved medication based on its safety record and efficacy.

Package Label from Eli Lilly, 1913



Note that this preparation was “guaranteed” under the Food and Drugs Act of 1906. Source: Courtesy of Patients Out of Time. Used by permission.

Throughout centuries of use there has never been a recorded human death as a result of cannabis consumption. It has a remarkably wide margin of safety. The median lethal dose or LD-50 (dose at which 50% of rats using a drug will die from overdose) of oral THC was 800 to 1900 mg/kg for rats, depending on sex and strain. No cases of death due to toxicity followed a maximum THC dose in dogs (up to 3000 mg/kg) and monkeys (up to 9000 mg/kg) (Grotenhermen, 2007). Stated another way, **humans would have to consume 1500 pounds in 15 minutes to induce death**. In other words, it is nearly impossible to overdose on this herbal plant. Compare that record to the fact that approximately 120 persons die each year from the use of aspirin or that high doses of acetaminophen can lead to liver damage and death.

Thousands of studies have been funded by the National Institute on Drug Abuse (NIDA) to determine the harmful effects of marijuana. In fact, for many years, researchers could not get federal funding or approval for a study through NIDA if the purpose is to determine its safety or efficacy as a medication (Holland, 2010). Numerous claims have been made, such as marijuana causes cancer, it destroys the immune system, it’s the gateway drug that leads to heroin, it kills brain cells, during pregnancy it will result in fetal abnormalities, and on and on.

Upon taking a closer look, many of these studies have been exposed for their flawed methodology, or the dosage was dramatically increased in an attempt to create a negative outcome. For example, there were early claims of marijuana use causing brain damage based on a study of monkeys that were exposed to cannabis smoke. However, it was discovered that the monkeys were forced to breathe only cannabis smoke for a period of time, and the damage was more likely caused by asphyxiation than cannabis smoke. No subsequent study showed such damage. Another early published study on THC and the immune system managed to show negative results but the dosage used on the rats were extremely high (Zimmer & Morgan, 1997).

In 1974, at Virginia Commonwealth University, research was conducted on rats under the theory that cannabis was carcinogenic. Rather than causing cancer, it was discovered that cannabis was effective in killing the lung-cancer cells. The funding was discontinued and the study was never published in the literature (Munson et al., 1975; Cushing, 2001). Early studies by pulmonologist Donald Tashkin of UCLA found that one cannabis cigarette had the same amount of carcinogenic material in its smoke as four tobacco cigarettes (Wu et al., 1988). The federal government held fast to this claim, but neglected to keep up with Tashkin's work. Admittedly surprised, Tashkin completed a longitudinal study on thousands of subjects and found no pulmonary disease (Tashkin, 2008).

In 1999 the Institute of Medication (IOM) completed an 18-month study on the medical value of cannabis and found that cannabis is not highly addictive, is not a gateway drug, and is safe for medical use. Specifically the IOM stated that "except for the harms associated with smoking, the adverse effects of marijuana use are within the range of effects tolerated for other medications." At that time, the study panel maintained some concern regarding administration of cannabis by smoking, yet they clearly noted that for patients suffering from cancer or AIDS the pulmonary risks were inconsequential compared to the disease being treated. For all other patients, the IOM panel found cannabis to be safe enough to allow physicians to conduct "n of 1" (individual case) studies. For example, if a glaucoma patient's intraocular pressure could not be controlled by standard pharmaceuticals, the physician should be allowed to use cannabis as an individual case study with that patient (Joy et al., 1999).

Since August 2016, National Institutes of Health (NIH) has been working with Office of National Drug Control Policy (ONDCP), the DEA, and the FDA to explore ways to streamline and facilitate research on cannabis. Barriers to research still exist:

- Registration process creates administrative burdens that act as disincentives to researchers. NIDA and DEA have been working to decrease the time for researcher to get Schedule I registration.

- Evaluation of consitutent compounds is hindered by the fact that although CBD does not appear to have abuse potential, all compounds in cannabis are Schedule I. In 2016, DEA began accepting applications from researchers currently registered to conduct clinical research with materials containing 99% CBD for a waiver of some regulatory requirements.

- Single source of marijuana for research. University of Mississippi, through a contract with NIDA, cultivates and distributes research grade cannabis for the United States. The NIDA supply of cannabis has diversified to include different strains, but it is costly and time consuming to grow. (NIDA, 2016)

In 2017 the NIH supported 330 projects totaling almost $140 million on cannabinoid research. Within this investment, 70 projects ($36 million) examined therapeutic properties of cannabinoids, and 26 projects ($15 million) focused on CBD (NIH, 2018).

Health Risks Related to Cannabis

No drug is without risks, and no drug works for everyone. However, given the long recorded history of cannabis used as medication and the inability to find clear evidence of harmful effects despite decades devoted to that goal, unadulterated cannabis can be said to present low risk as a medication.

The following sections discuss risks related to cannabis use, including risks related to its federally illegal status as a Schedule I drug, risks related to smoking cannabis, risks of mental health disorders, risks of impaired driving, and the potential for abuse and addiction. Additionally, certain population groups experience specific health risks related to cannabis use.

Related to Cannabis Prohibition

Over the past several decades Congress and state legislatures have passed numerous laws in the name of the war on drugs, including mandatory minimum prison sentences and asset forfeiture. In addition, a felony conviction of cannabis "manufacturing" or possession can lead to collateral damage, including revocation of professional licenses, loss of employment, loss of federal grant funding for colleges and universities, loss of child custody, and bars on voting, adoption, receiving food stamps, and living in public housing. For some patients, just admitting cannabis use to their healthcare provider or testing positive for THC in a urine drug screen may result in denial of healthcare services.

Despite the fact that cannabis is an illegal drug placed in Schedule I (forbidden medication) so that healthcare providers cannot legally prescribe it, patients throughout the country willingly take the legal risks because of the beneficial effects on their health.

Although cannabis is easy to grow, it requires knowledge and experience to grow medicinal-grade cannabis. If a patient grows it outdoors, the plants must be kept out of sight of prying eyes. If a patient grows it indoors, the plants require extra equipment and a dedicated room that must be protected from visitors. Most patients don't have this knowledge or, due to their illness, are not able to properly tend to the plant, so they depend on an outside source. Often family members will grow it for the patient or procure it from an outside source, putting themselves in legal jeopardy as well.

When patients must obtain cannabis from an outside source they have no guarantee of the quality of their medication (eg, contamination with pesticides, heavy metals, mold). This is one of the problems of using a Schedule I drug and the cost can be extreme with no insurance coverage. And, of course, as an illegal substance, patients who use cannabis as medication do not receive the basic education about safe administration from healthcare professionals that they do with other medications.

Related to Smoking Cannabis

How many times have you heard someone justify the cannabis prohibition by declaring "We cannot approve of patients smoking their medication"? Actually, before the cannabis prohibition there were several "cigarette" preparations of cannabis developed to treat patients with asthma. We now know that there are cannabinoid receptors in the bronchi and that cannabinoids help to dilate the airways.

Inhaled cannabis smoke has effects on the lung that are similar to tobacco smoke, including increased cough, sputum production, hyperinflation, and upper lobe emphysematous changes. It does not appear that marijuana smoke contributes to the development of chronic obstructive pulmonary disease (Owen et al., 2014). One 1993 study found that cannabis smokers had more outpatient visits than people who do not smoke (NIDA, 2018).

Cannabis smoke does contain tar and other carcinogenic materials and, from a health perspective, it makes sense to avoid this route of administration (NIDA, 2018):

> Marijuana smoke contains carcinogenic combustion products, including 50% more benzoprene and 75% more benzanthracene (and more phenols, vinyl chlorides, nitrosamines, reactive oxygen species) than cigarette smoke.

NIDA says that because marijuana smoke is typically inhaled deeper and held for longer, smoking marijuana may lead to four times more tar deposition than cigarette smoking (NIDA, 2018).

Donald Tashkin is the leading U.S. researcher on the clinical effects of smoking cannabis. In his extensive longitudinal study, Tashkin followed thousands of patients for years and evaluated their pulmonary status. He looked at three groups of individuals: cannabis-only smokers, cannabis-and-tobacco smokers, and tobacco-only smokers. To his surprise, the tobacco-only and cannabis-and-tobacco smokers had higher incidences of COPD or lung cancer, but the cannabis-only smokers did not. Tashkin concluded that, although the smoke itself may contain carcinogens, the cannabinoids counter the harmful effects of the smoke (Tashkin, 2008, 2013).

The well-established health risks of secondhand cigarette smoke raise reasonable questions about whether secondhand exposure to cannabis smoke poses similar risks, particularly among vulnerable populations such as children and people with asthma. At this time, little research on this question has been conducted. A 2015 study showed that THC can be measured in the blood of people who do not smoke cannabis and had spent 3 hours in a well-ventilated space with people casually smoking marijuana. Further, nonsmoking people in a confined space with people smoking high-THC marijuana reported mild effects of the drug, including a “contact high,” and had minor motor impairments (NIDA, 2018; Cone et al., 2015). Impairment of lung function equal to that caused by secondhand tobacco smoke has been found in rats exposed to secondhand marijuana smoke, and the effects lasted longer (NIDA, 2018).

A large epidemiologic study of a Los Angeles population looked at 1,212 cancer cases and 1,040 cancer-free controls; they found no positive relationship between smoking cannabis and the investigated cancer types, which included mouth, larynx, lung, and pharynx (Hashibe et al., 2006).

In 2001 Ethan Russo led a team that conducted a thorough study of the longitudinal effects of cannabis on the health of four patients in the Compassionate IND program (referred to as *the Missoula Study*). These four patients had been receiving cannabis from a known source from 11 to 27 years and, although they were theoretically in a research program, no one had been tracking their health status over the years. It is important to note that these patients had been using the government-issued cannabis that was grown on the farm at the University of Mississippi, then shipped to North Carolina for rolling into cigarettes and packaging them in labeled canisters that held approximately 300 cigarettes. The label identified the THC level of the cannabis and the date of processing.

The patients received low-grade medicinal cannabis containing from 2% to 4% THC and some of their shipments were up to 13 years old. The quality was poor and even included stems and seeds. At the time, Irv Rosenfeld received and consumed up to 13 ounces over a 3-week period. A complete set of pulmonary function tests was conducted on each of these patients and no long-term pulmonary damage or disease was noted except for mild bronchitis (Russo et al., 2002).

Risks Related to Mental Health

Several studies have linked marijuana use to increased risk for psychiatric disorders, including psychosis (schizophrenia), depression, anxiety, and substance use disorders. It is not clear whether the cannabis use causes or triggers these conditions.

While cannabis is often used as an anti-anxiolytic medication, one of the most common adverse effects is an acute panic reaction, which usually occurs with novice or inexperienced users or with high doses of THC (as in dronabinol or a high-THC strain of cannabis). This rarely requires any pharmacologic intervention and treatment includes a quiet, relaxing environment with reassurance that the patient is fine and the effects will soon wear off.

Research using longitudinal data from the National Epidemiological Survey on Alcohol and Related Conditions examined associations between marijuana use, mood and anxiety disorders, and substance use disorders. After adjusting for various confounding factors, Blanco and colleagues found no association between marijuana use and mood and anxiety disorders. The only significant associations were increased risk of alcohol use disorders, nicotine dependence, marijuana use disorder, and other drug use disorders (Blanco et al., 2016).

Psychotic symptoms have been described following acute cannabis consumption and claims have been made that cannabis may cause schizophrenia. Some research finds that cannabis did not “cause” schizophrenia, but its use was associated with earlier onset of symptoms and more severe psychosis, especially paranoia. Yet some schizophrenic patients report a reduction in their symptoms with the use of cannabis. Although an association has been noted, no causal relationship has been determined (Macleod et al., 2006).

In 2014, Radhakrishnan and colleagues found:

> In individuals with an established psychotic disorder, cannabinoids can exacerbate symptoms, trigger relapse, and have negative consequences on the course of the illness. Several factors appear to moderate these associations, including family history, genetic factors, history of childhood abuse, and the age at onset of cannabis use. Exposure to cannabinoids in adolescence confers a higher risk for psychosis outcomes in later life and the risk is dose-related.
>
> People with preexisting genetic vulnerability may be at increased risk for psychotic disorders when exposed to cannabinoids, as are individuals with a family history of psychotic disorders or a history of childhood trauma. The relationship between cannabis and schizophrenia fulfills many but not all of the standard criteria for causality, including temporality, biologic gradient, biologic plausibility, experimental evidence, consistency, and coherence. At the present time, the evidence indicates that cannabis may be a component cause in the emergence of psychosis, and this warrants serious consideration from the point of view of public health policy.

As cannabis use has increased in some populations, there has been no corresponding increase in the incidence of schizophrenia, which would be expected if cannabis was a causal factor. It is of interest to note that, independent of cannabis use, there are more cannabinoid receptors in the brains of patients with schizophrenia that in normal individuals.

In Brazil researchers at two separate laboratories have been conducting research with CBD as an antipsychotic medication (Crippa, 2010; Takahashi, 2010). Remember that CBD is non-psychoactive and when taken with THC it will dampen the psychoactive effects of THC. Some posit that the use of high-THC-content cannabis by patients prone to schizophrenia may trigger the onset of schizophrenia, while high-CBD content cannabis may help manage the symptoms? More research is needed in this area and, until then, patients with a family history of schizophrenia may be cautioned against the use of medicinal cannabis.

Risks Related to Impaired Driving

THC can impair perception and psychomotor performance, which means that patients may be at increased risk for accidents if operating equipment (eg, driving a vehicle). Research has shown that driving under the influence of cannabis can result in an increase in lane weaving, poor reaction time, and altered attention to the road. Marijuana affects psychomotor skills and cognitive functions critical to driving, including vigilance, drowsiness, time and distance perception, reaction time, divided attention, lane tracking, coordination, and balance. Cannabis used in combination with alcohol makes drivers even more impaired (NIDA, 2019).

Other studies have not shown impairment on these psychomotor tasks and cognitive and executive functions. It is not clear why this is the case. It may stem from different THC doses, time between doses and testing or driving, differences in the tasks used to assess the effects, tolerance developed through frequent use, and other differences (Compton, 2017).

Currently, there is no impairment standard for drivers under the influence of marijuana. There is no chemical test for marijuana impairment, like a BAC or BrAC test for alcohol that quantifies the amount of alcohol in their body, indicates the degree of impairment, and the risk of crash involvement that results from the use of alcohol. THC does not correlate well with impairment. Although very high levels of THC indicate recent consumption (for example, by smoking marijuana), it is unlikely a police officer would encounter a suspect and obtain a sample of blood or oral fluid within a short enough time for high THC levels to be detected. As was mentioned earlier, impairment is observed for 2 to 3 hours after smoking; whereas by an hour after smoking peak THC levels have declined 80% to 90% (Compton, 2017).

There are currently no evidence-based methods to detect marijuana-impaired driving. Testing of blood or urine specimens for THC is problematic because it is impractical, and while tests can confirm the presence of THC, they cannot determine degree of a driver's impairment. Oral fluid drug screening devices are now available on a limited scale; however, the accuracy and reliability of such devices have not been clearly established (Compton, 2017).

All states have laws prohibiting driving while impaired (under the influence or intoxicated) by alcohol and other drugs, including cannabis. Some states have zero-tolerance statutes. In 2017, 12.8 million people aged 16 or older drove under the influence of illicit drugs in the past year (NIDA, 2019).

After alcohol, cannabis is the drug most often found in the blood of drivers involved in crashes. Several studies have shown that drivers with THC in their blood were roughly twice as likely to be responsible for a deadly crash or be killed than drivers who had not used drugs or alcohol. However, a large National Highway Traffic Safety Administration (NHTSA) study found no significant increased crash risk traceable to marijuana after controlling for drivers' age, gender, race, and presence of alcohol (NIDA, 2019).

It is difficult to determine how many automobile crashes are caused by drugged driving because:

- A good roadside test for drug levels in the body does not yet exist.
- Some drugs, such as cannabis, stay in the body for days or weeks after use, making it difficult to determine if the use impaired driving.
- If alcohol is detected to be at illegal levels, police don't test for the presence of drugs because the alcohol is sufficient for a DUI charge.
- Many drivers involved in car crashes are found to have both alcohol and drugs in their system, so it's hard to know which substance had the greater effect. (NIDA, 2019)

With chronic use, many patients develop tolerance to the effects that may contribute to impaired driving, though research is lacking on impairment in frequent cannabis users. For users who use less than weekly, 10 mg or more of THC is likely to impair the ability to safely drive, bike, or perform other safety-sensitive activities. Colorado's Department of Public Health recommends that less-than-weekly users should wait at least 6 hours after smoking or 8 hours after eating or drinking marijuana to allow time for impairment to resolve (Colorado Department of Public Health and Environment, 2018).

Risks Related to Cancer

Researchers have investigated the role cannabis may play in the development of certain kinds of cancers. Gurney and colleagues (2015) conducted a systematic review and meta-analysis on the association between cannabis use and testicular germ cell tumors. They found a statistically significant association between current, frequent, or chronic cannabis use and the incidence of non-seminoma-type testicular germ cell tumors. By comparison, cannabis use was not associated with a statistically significant risk of developing seminoma-type testicular germ cell tumors. Lacking further evidence, an extrapolation of this association to other types of testicular cancer is unwarranted. Gurney and colleagues (2015) found an association between the incidence of testicular cancer (without further specification) and frequent or long-term cannabis use. “There is limited evidence of a statistical association between current, frequent, or chronic cannabis smoking and non-seminoma-type testicular germ cell tumors” (National Academies, 2017).

The National Academies 2017 review of evidence concluded that smoking cannabis does not increase the risk for certain cancers (i.e., lung, head and neck) in adults. Furthermore, there is insufficient evidence to support or refute a statistical association between cannabis smoking and the incidence of esophageal cancer, prostate cancer, cervical cancer, malignant gliomas, non-Hodgkin lymphoma, penile cancer, anal cancer, Kaposi’s sarcoma, or bladder cancer (National Academies, 2017).

Risks Related to Medicinal Cannabis

Healthcare professionals are well aware of the possibility of health risks related to medications even when used under medical supervision. When using any medication, the goal is for the benefit (reason for use) to outweigh the risks (side effects and/or adverse reactions). The usual side effects that accompany the use of cannabis include a mild tachycardia, injected conjunctivae (red eye), dry mouth, short-term memory loss, relaxation, sedation, euphoria (sense of well-being), dizziness, and an increased appetite (“the munchies”). Cannabis is not a hallucinogen, but users may experience an alteration of time perception and/or an increased sensory perception.

A side effect for one patient may be a desired effect for another patient. A cancer patient may use cannabis to control the nausea and increase the appetite (for the benefit or desired effect), yet may also experience the side effects of euphoria (not generally a negative effect) and sedation. Dry mouth may be an undesired side effect for many patients, but a desired effect for ALS patients who have difficulty managing their oral secretions. The tachycardia is usually of little concern to most patients, but could be a risk to persons with cardiac disease. Many pain patients have reported that they never experience the euphoria or “high” that is sought by recreational users.

The low risk of any serious adverse event occurring with initial use of cannabis makes it an ideal first trial medication (if it were legal) for many patients. No medication works for everyone, and if cannabis is not helpful to an individual patient there is essentially no harm done in trying it. If cannabis is an effective medication, then the clinician and patient need to know the potential risks related to chronic use of this herbal medication.

The primary purpose of the Missoula Study was to determine what, if any, were the negative effects of chronic use of smoking cannabis. In addition to the pulmonary function tests, this study of the four long-term federally supplied cannabis patients included exams such as a complete physical exam, chest x-ray, MRI of the brain, neuropsychological testing, hormone and immunological assays, and an EEG. The overall conclusions were that cannabis provided these patients with symptomatic relief from pain, muscle spasms, and intraocular pressure, helped reduce their use of other prescription medications, produced no long-term sequelae, and improved their quality of life. Obviously these four patients are a small sample size, but each of these patients is convinced that cannabis is an essential medication for them (Russo et al., 2004).

Long-term use of cannabis has not been associated with increased mortality in animals or humans. In an animal study, rats were administered 50 mg/kg of THC for a period of 2 years and at the end of the observation the survival rate was higher among the treated rats than in the controls (a higher incidence of cancer was noted in the control rats) (Chan et al., 1996). A longitudinal study of 65,171 Kaiser Permanente Medical Care Program enrollees found no relationship between cannabis use and mortality (Sidney et al., 1997).

Some studies have shown a reduction in sperm count with chronic cannabis use, but it is reversible if cannabis is discontinued. A surprising 2019 study, however, found that men who had smoked marijuana had higher sperm concentration and count and lower serum FSH concentrations than men who had never smoked marijuana (Nassan et al., 2019). Studies are inconclusive regarding the effects of cannabis on male and female sterility.

Much research has been conducted on the effects of THC or cannabis on the immune system:

> A large body of data from in vitro studies and animal models indicates that THC and CB_2 agonists can lead to decreased resistance to infectious agents, a comparable linkage in humans has yet to be demonstrated. (Cabral et al., 2015)

The negative effects seem to be dose-related, with negative findings associated with excessive dosage.

In clinical studies of HIV-infected men, the use of cannabis was not associated with the onset of AIDS, and no negative drug interactions were found with the use of cannabis in HIV-positive adults taking protease inhibitors (Abrams et al., 2003). There has been some evidence that cannabis use is a risk factor for the progression of fibrosis in chronic hepatitis C patients (Herzode et al., 2005); however, cannabis use improved retention and virologic outcomes in patients treated for hepatitis C with interferon and ribavirin (Sylvestor et al., 2006).

Numerous case reports suggesting that cannabis use is associated with the occurrence of heart attack. A recent study warned of a possible risk of heart attack with acute cannabis intoxication. Cannabinoids affect the cardiovascular system by raising resting heart rate, dilating blood vessels, making the heart pump harder (Harvard Health Publishing, 2019). Smoking cannabis may put individuals, particularly those at high risk for cardiovascular disease, at increased risk for heart attack (National Academies, 2017).

And yet chronic cannabis use has not been associated with cardiovascular risk factors such as blood triglyceride levels and blood pressure in the longitudinal CARDIA study, which began in 1986 (Grotenhermen, 2007). There is no evidence to support or refute a statistical association between chronic effects of cannabis use and the risk of heart attack (National Academies, 2017).

Smoking cannabis may have other cardiovascular effects as well. Numerous reports and studies describe vascular changes that may be associated with stroke, suggesting that smoking increases the risk of stroke. Wolff and colleagues (2013) found that several reports have indicated a close temporal relationship between cannabis smoking and stroke. In a 2015 study, Wolff and colleagues describe the effects that may lead to stroke: orthostatic hypotension with secondary impairment of the auto-regulation of cerebral blood flow, altered cerebral vasomotor function, supine hypertension and swings in blood pressure, cardioembolism with atrial fibrillation, other arrhythmias, vasculopathy, vasospasm, reversible cerebral vasoconstriction syndrome, and multifocal intracranial stenosis (Wolff et al. 2013). Wolff and colleagues (2013) concluded “cannabis has to be considered as harmful, and the cerebrovascular risk when cannabis is consumed is probably underestimated.” Among younger adults (25–34), recreational marijuana use is independently associated with 17% increased likelihood of acute ischemic stroke hospitalization (Rumalla et al., 2016). There is limited evidence of a statistical association between cannabis use and ischemic stroke or subarachnoid hemorrhage (National Academies, 2017).

There is strong evidence that people who use cannabis daily or near daily are more likely to have impaired memory lasting more than a week after quitting (Colorado Department of Public Health and Environment, 2018).

Long-term, daily, or near-daily cannabis use is associated with cyclic vomiting, and is known as cannabinoid hyperemesis syndrome. People who stop using cannabis may find the cyclic vomiting resolves.

Risks for Specific Populations

Pregnant Women

Cannabis is the illicit drug most commonly used during pregnancy. Self-reported prevalence of use during pregnancy ranges from 2% to 28% in some studies (ACOG, 2017). Some research shows that marijuana use during pregnancy is associated with risks such as preterm labor, low birth weight, neonatal intensive care admissions, and stillbirth (CDC, 2018a; Hyatbakhsh, 2013). THC readily crosses the placenta, but it appears unlikely that cannabis causes fetal abnormalities. When socioeconomic variables have been accounted for, there appear to be no significant fetal problems

related to cannabis use by the mother (Dreher, 1997).

The American College of Obstetricians and Gynecologists (ACOG) published a Committee Opinion in 2017 on marijuana (*Cannabis sativa*) use during pregnancy and lactation. ACOG recommends the following:

- Before pregnancy and in early pregnancy, all women should be asked about their use of tobacco, alcohol, and other drugs, including marijuana and other medications used for nonmedical reasons.
- Women reporting marijuana use should be counseled about concerns regarding potential adverse health consequences of continued use during pregnancy.
- Women who are pregnant or contemplating pregnancy should be encouraged to discontinue marijuana use.
- Pregnant women or women who are contemplating pregnancy should be encouraged to discontinue use of marijuana for medicinal purposes in favor or alternative therapy for which there are better pregnancy-specific safety data.
- There are insufficient data to evaluate the effects of marijuana use on infants during lactation and breastfeeding, and in the absence of such data, marijuana use is discouraged. (ACOG, 2017)

Did You Know. . .

One in twenty, or 5%, of women use marijuana while pregnant. (CDC, 2018a)

The research on the subject of cannabis use during pregnancy is mixed, however. A study by Conner and colleagues (2016) shows that although low birth weight and preterm delivery were associated with cannabis use during pregnancy, when researchers isolated the results from tobacco use, there was no statistically significant increase in low birth weight of infants whose mothers used cannabis. The authors concluded that maternal marijuana use during pregnancy is not an independent risk factor for adverse neonatal outcomes after adjusting for confounding factors. The association between maternal marijuana use and adverse outcomes appears attributable to associated tobacco use and other confounding factors (Conner, 2016).

Lactating Mothers and Babies

Marijuana can be passed to babies in their mother's breastmilk. THC is stored in fat and is slowly released over time, which may mean that even if a woman stops using cannabis, her baby may still be exposed (CDC, 2018a).

THC is present in human milk up to 8 times that of maternal plasma levels, and metabolites are found in infant feces, indicating that THC is absorbed and metabolized by the infant (Reece-Stremtan et al., 2015). It is rapidly distributed to the brain and adipose tissue and stored in fat tissues for weeks to months. It has a long half-life (25–57 hours) and stays positive in the urine for 2 to 3 weeks. Evidence regarding the effects of THC exposure on infant development via breastfeeding alone is sparse and conflicting, and there are no data evaluating neurodevelopmental outcomes beyond the age of 1 year in infants who are only exposed after birth (Reece-Stremtan et al., 2015).

Researchers noted that the potency of marijuana has been steadily increasing, from about 3% in the 1980s to 12% in 2012, so data from previous studies may no longer even be relevant. Furthermore, concern over cannabis use during lactation stems from possible infant sedation and the mother's potential inability to safely care for her infant while under its influence (Reece-Stremtan et al., 2015).

According to the Academy of Breastfeeding Medicine (ABM), evidence regarding long-term effects of marijuana use by the breastfeeding mother on the infant remains insufficient to recommend complete abstention from starting or continuing breastfeeding. However, they extrapolate in utero exposure and the limited data available to make the following recommendations to health care providers in ABM Clinical Protocol #21:

- Counsel mothers who admit to occasional or rare use to avoid further use or reduce their use as much as possible while breastfeeding, advise them as to its possible long-term neurobehavioral effects, and instruct them to avoid direct exposure of the infant to marijuana and its smoke.
- Strongly advise mothers found with a positive urine screen for THC to discontinue exposure while breastfeeding and counsel them as to its possible long-term neurobehavioral effects.
- When advising mothers on the medicinal use of marijuana during lactation, one must take into careful consideration and counsel on the potential risks of exposure of marijuana and benefits of breastfeeding to the infant.
- The lack of long-term followup data on infants exposed to varying amounts of marijuana via human milk, coupled with concerns over negative neurodevelopmental outcomes in children with in utero exposure, should prompt extremely careful consideration of the risks versus benefits of breastfeeding in the setting of moderate or chronic marijuana use. A recommendation of abstaining from any marijuana use is warranted.
- At this time, although the data are not strong enough to recommend not breastfeeding with any marijuana use, ABM urges caution. (Reece-Stremtan et al., 2015)

Children and Teens

In Colorado, medical cannabis has been legal since 2000 and recreational cannabis was legalized in 2012. When Colorado became one of the first two states in the nation to legalize retail marijuana, the Colorado Legislature mandated that the Colorado Department of Public Health and Environment (CDPHE) study the potential public health effect of cannabis use. The 2018 *Monitoring Health Concerns Related to Marijuana in Colorado* report tracks information about cannabis use among children and teens in this state. In 2017 Healthy Kids Colorado Survey estimated 19.4% of Colorado high school students and 5.2% of middle school students reported using marijuana in the past 30 days. Past-30-day use has remained stable among high school students since 2005 and among middle school students since 2011. Use among high school students in Colorado is not statistically different than national estimates of past-30-day use. Prevalence of use increases with grade level. Frequency of use has declined or remained stable among adolescents. Use of cannabis is higher than smoking cigarettes, but less than alcohol use and nicotine vaping among high school students (MHMRP, 2018).

In 2017 the Child Health Survey estimated 11.2% of homes with children reported cannabis being present in or around the home, which is up from 6.9% in 2014. Survey respondents reported storing marijuana safely by keeping it in child-resistant packaging, out of reach, or in a locked location. Also in 2017 it was estimated that 23,009 homes in Colorado with children aged 1 to 14 years had marijuana in the home and potentially stored unsafely (MHMRP, 2018).

In Colorado homes with children cannabis is smoked, vaporized, or dabbed (83.1%), and 33% reported marijuana edibles being used in the home. It is estimated that approximately 32,800 homes with children aged 1 to 14 had possible second-hand marijuana smoke or vapor exposures (MHMRP, 2018).

The Colorado Retail Marijuana Public Health Advisory Committee reviewed unintentional marijuana exposure relative to marijuana legalization and child-resistant packaging. They found strong evidence that more unintentional marijuana exposures of children occur in states with increased legal access to marijuana, and that exposures can lead to significant clinical effects requiring hospitalization. Evidence shows that child-resistant packaging prevents exposure to children from potentially harmful substances, such as THC (MHMRP, 2018).

Accidental ingestion/exposure in homes with cannabis products, especially edibles, is on an upward trend in Colorado. Data from the Rocky Mountain Poison and Drug Center show that in 2017 edible marijuana products comprised 65.6% of all exposures in children ages 0 to 8 years, followed by smokable products (23.4%) and other marijuana products (10.9%) (MHMRP, 2018).

Children's Hospital Colorado recommends the following precautions if marijuana products are in the home where children live or visit:

- Keep marijuana up and away and out of the sight of children. Pick a place your children cannot reach.
- Put marijuana away every time, even products you use every day.
- Consider purchasing a medication lock box for safe, convenient storage of marijuana products.

- Talk to your children about marijuana, and teach your children about medicine safety.
- Ask houseguests and visitors to keep purses, bags, or coats that have marijuana products in them away and out of sight when they are in your home.
- If you use a babysitter, choose those who are mature, trained and responsible, and are recommended by someone you trust.
- Ask other parents if they have marijuana products in their home before sending your child to play at their house. Ask that they make sure all products are stored up and away and out of children's sight.
- Be prepared in case of an emergency; program the poison control number into your phone. (Children's Hospital Colorado, 2019)

Did You Know. . .

38% of high school students report having used marijuana in their life (CDC, 2018b).

Decline in School Performance

According to the CDC, use of cannabis in adolescence or early adulthood can have a serious impact on a teen's life. Some research shows that cannabis can have permanent effects on the developing brain when use begins in adolescence, particularly in regular and heavy use (CDC, 2018b). Students who smoke marijuana may get lower grades and may more likely to drop out of high school than their peers who do not use (CDC, 2018b, citing a 2016 systematic review by Broyd et al. of research published between January 2004 and February 2015 on acute and chronic effects of cannabis and cannabinoids and on persistence or recovery after abstinence).

Some studies suggest regular marijuana use in adolescence is associated with altered connectivity and reduced volume of specific brain regions that are involved in a range of executive functions such as memory, learning, and impulse control compared to people who do not use. Other studies have not found significant structural differences between the brains of people who do and do not use the drug (NIDA, 2018). Some studies suggest that marijuana use can cause functional impairment in cognitive abilities but that the degree and duration of the impairment depends on the age at which cannabis use began and how much and how long the person used cannabis (NIDA, 2018).

A longitudinal New Zealand study found that persistent marijuana use disorder with frequent use starting in adolescence was associated with a loss of 6 to 8 IQ points measured in mid-adulthood. In that study, those who used marijuana heavily as teenagers and quit using as adults did not recover the lost IQ points. People who only began using marijuana heavily in adulthood did not lose IQ points. These results suggest that marijuana has its strongest long-term impact on young people whose brains are still busy building new connections and maturing in other ways (NIDA, 2018).

At the 2016 Neuroscience Research Summit on Marijuana and Cannabinoids, Susan Tapert presented on adolescent marijuana use and its influence on learning,

memory, and brain changes. She noted that it is presently unclear how the use of marijuana affects the major brain development processes that occur during adolescence, and made five points about what we know about marijuana use and cognition:

- Marijuana adversely influences learning.
- Memory and attention also can show long-term effects.
- These outcomes improved with days to weeks of abstinence.
- The effect of marijuana on cognition appears worse with earlier age of onset.
- Some neuroimaging data support these effects of marijuana. (NIH, 2016)

There is moderate evidence of a statistical association between acute cannabis use and impairment in the cognitive domains of learning, memory, and attention. There is limited evidence of a statistical association between sustained abstinence from cannabis use and impairments in the cognitive domains of learning, memory, and attention (National Academies, 2017).

Dating Violence Among Adolescents and Young Adults

A number of studies have linked cannabis use to intimate partner violence. Among young adults, all analyzed patterns of marijuana use during adolescence and early adulthood were associated with a 1.2 to 2.4 times increased risk of intimate partner violence perpetration and victimization (Reingle et al., 2012). Researchers found that **any use of marijuana during adolescence and young adulthood increases the risk of intimate partner violence**. Consistent users were at greatest risk of perpetration and victimization, independent of alcohol use and other risk factors. Unexpectedly, results indicated that males were more likely to be victims and less likely to be perpetrators of intimate partner violence compared with females (Reingle et al., 2012). A recent review and meta-analysis of literature published between 2003 and 2015 by Johnson and colleagues found that among people ages 11 to 21, adolescent girls who use marijuana may be more likely to commit physical violence against their dating partners, and adolescent boys who use marijuana may be more likely to be victims of physical dating violence (Johnson et al., 2017; MHMRP, 2018). Findings suggest that marijuana use is associated with a 54% increase in the odds of physical dating violence victimization, and a 45% increase in the odds of perpetration (Johnson et al., 2017).

Risks Related to Abuse and Addiction

Since marijuana is commonly referred to as a drug of abuse, the risk of tolerance, dependence, and addiction should be addressed. **Tolerance** is defined as the need to increase the dose with chronic use to in order to get the same effects. Healthcare professionals commonly see this with the use of opioids for chronic pain; over time patients develop a tolerance and require higher doses to manage their pain. When used medicinally on a regular basis over a period of time, patients who use cannabis often develop a tolerance to the cognitive and psychomotor impairment as well as the psychological “high,” yet they do not develop a tolerance to its medicinal benefits.

The first patient admitted into the Compassionate IND program, Robert Randall, consumed 10 cannabis cigarettes per day for years to control his intraocular pressure. One month, he seemed to be going through his supply faster than usual. Upon further investigation he discovered that his federal prescription had been changed without his or his physician's knowledge. Each of his cannabis cigarettes contained 0.8 grams of cannabis rather than the usual 1 gram. Not realizing this decrease in dosage, he simply smoked more cigarettes to continue with his daily requirements. Once discovered, his physician complained and the correct dosage was provided in his next cannabis shipment (Randall and O'Leary, 1998). On the other hand, patients *have* noticed a tolerance to the therapeutic effects with the use of dronabinol (synthetic THC).

Dependence is a term often misused as a synonym for addiction, but the two terms are not synonymous. Dependence (also referred to as physical dependence) is the result of continued regular use of a drug that produces a physiologic change in the central nervous system to the extent that abrupt cessation of the drug causes withdrawal symptoms.

The seriousness of the withdrawal symptoms depends upon the drug being used and the extent of its use (risks increase with higher doses over long periods of time). For those drugs that do produce physical dependence, there is an expected physiologic response that would occur in anyone who used the drug on a regular basis, but this is not by itself indicative of addiction. For some drugs, such as alcohol or benzodiazepines, withdrawal symptoms can be serious and life-threatening. Opioids can cause withdrawal symptoms similar to a severe case of the flu. However withdrawal from cannabis is generally mild in comparison. Cannabis withdrawal symptoms may include irritability, restlessness, difficulty sleeping, decreased appetite, anxiety, anger, and strange dreams. Less common symptoms include headaches, sweating, chills, stomach pain, and general discomfort.

Most of the cannabis withdrawal symptoms begin within 24 hours following abrupt cessation, are most severe 2 to 4 days later, and last 1 to 2 weeks. Withdrawal from cannabis is generally uncomfortable but not dangerous and does not require medical management. Not all persons complain of withdrawal when discontinuing use. A large survey in Australia found approximately 30% of current marijuana users reported withdrawal symptoms when they stopped using cannabis (Teesson et al., 2002).

It seems important to note that some patients begin using cannabis to manage what some researchers consider withdrawal symptoms. Patients have used cannabis as a sleep aid, appetite stimulant, relaxant, and calming agent. If they stop using cannabis, are their initial reasons for use simply reemerging or are they experiencing true withdrawal symptoms?

Cannabis abuse is a very ambiguous and value-laden term, and therefore its use is questionable. “Drug abuse” has often been defined as use of a drug without a prescription or use of an illegal drug. Those notions are not very helpful. Some persons or cultures may not accept the paternalistic notion that only a physician can decide whether a person should use a drug, when to use it, or how often to use it. And the idea that drugs are legal or illegal leads many people to believe that the legal drugs are good and the illegal drugs are bad. Drugs are not inherently good or bad but, as Andrew Weil noted years ago, it is their manner of use that is either bad or good (Weil & Rosen, 1993).

Addiction (sometimes referred to as *psychological dependence*) is defined as a pattern of drug abuse characterized by an overwhelming preoccupation with the compulsive use of a drug and securing its supply, and a high tendency to relapse if the drug is taken away. Tolerance and dependence are common results of addiction, but are not necessary components of addiction. The new edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) of the American Psychiatric Association (APA) has been developed with the input of thousands of expert psychiatrists over several decades to classify and characterize human mental health disorders, including substance-use disorders. To provide some continuity in the concept/diagnosis of cannabis addiction, clinicians can use the criteria set up in the DSM-5 (as reported in the DSMV, 2013):

According to the DSM-5, **substance use disorders** has replaced the terms *abuse* or *addiction* and they are identified by drug type, so here we use the term *cannabis use disorder,* and depending upon the number of positive criteria, the person is diagnosed with a mild, moderate or severe cannabis use disorder. Below is a list of the 11 criteria of which at least 2 must be met within a 12-month period:

1. Cannabis is often taken in larger amounts or over a longer period than was intended.

2. There is a persistent desire or unsuccessful efforts to cut down or control cannabis use.

3. A great deal of time is spent in activities necessary to obtain cannabis, use cannabis, or recover from its effects.

4. Craving, or a strong desire or urge to use cannabis.

5. Recurrent cannabis use resulting in a failure to fulfill major role obligations at work, school, or home.

6. Continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of cannabis.

7. Important social, occupational, or recreational activities are given up or reduced because of cannabis use.

8. Recurrent cannabis use in situations in which it is physically hazardous.

9. Cannabis use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by cannabis.

10. Tolerance, as defined by either of the following: (a) a need for markedly increased amounts of cannabis to achieve intoxication or desired effect or (b) markedly diminished effect with continued use of the same amount of cannabis.

11. Withdrawal, as manifested by either of the following: (a) The characteristic withdrawal syndrome for cannabis (the following symptoms develop within a week of cessation of cannabis: irritability, anger or aggression; nervousness or anxiety; sleep difficulty; decreased appetite or weight loss; restlessness; depressed mood; and at least one of the following physical symptoms: abdominal pain, shakiness/tremors, sweating, fever, chills, or headache. (b) Cannabis (or a closely related substance) is taken to relieve or avoid withdrawal symptoms.

Addiction to cannabis rarely occurs because, in general, persons who have problems with drug addiction usually prefer more potent psychoactive drugs and caution should be used in making a cannabis use disorder diagnosis to ensure that the problems come from the *use* of cannabis rather than from the *prohibition* of cannabis. When dronabinol was initially approved as a medication it was placed in Schedule II of the CSA. After several years on the market, it was down-regulated to Schedule III because of the lack of diversion and little evidence of addiction. Initially, animal studies are used to evaluate the abuse potential of drugs, with the understanding that these do not necessarily reflect similar outcomes in humans. It is important to note that numerous studies have concluded that while cannabis may produce a feeling of euphoria in humans, in general animals will not self-administer THC (DSM-V, 2013).

In 1994 Jack E. Henningfield, of the National Institute on Drug Abuse (NIDA), and Neal L. Benowitz, of the University of California at San Francisco (UCSF), ranked six commonly used drugs by five criteria: withdrawal symptoms (dependence), reinforcement (craving), tolerance, dependence (addiction) potential, and intoxication. They ranked the six drugs from 1 as the most serious to 6 as the least serious. Cannabis (marijuana) was ranked lowest for withdrawal symptoms, tolerance, and dependence (addiction) potential; it ranked close to caffeine in the degree of reinforcement and higher than caffeine and nicotine only in the degree of intoxication (Henningfield & Benowitz, 1994).

Ranking of Six Commonly Used Drugs										
	Withdrawal		Reinforcement		Tolerance		Dependence		Intoxication	
	NIDA	UCSF	NIDA	UCSF	NIDA	UCSF	NIDA	UCSF	NIDA	UCSF
Nicotine	3	3	4	4	2	4	1	1	5	6
Heroin	2	2	2	2	1	2	2	2	2	2
Cocaine	4	3	1	1	4	1	3	3	3	3
Alcohol	1	1	3	3	3	4	4	4	1	1
Caffeine	5	4	6	5	5	3	5	5	6	5
Marijuana	6	5	5	6	6	5	6	6	4	4

Ranking scale: 1= Most serious 6 = Least serious
Explanation of terms:
Withdrawal (physical dependence). Presence and severity of characteristic withdrawal symptoms.
Reinforcement. Substance's ability, in human and animal tests, to get users to take it repeatedly, and instead of other substances.
Tolerance. Amount of substance needed to satisfy increasing cravings and level of plateau that is eventually reached.
Dependence (addiction). Difficulty in ending use of substance, relapse rate, percentage of people who become addicted, addicts self-reporting of degree of need for substance, and continue use in face of evidence that it causes harm.
Intoxication. Level of intoxication associated with addition, personal, and social damage that substance causes.
Source: Henningfield & Benowitz, 1994.

Also in 1994, the U.S. National Comorbidity Study found that 9% of lifetime cannabis users met the DSM-R-III criteria for dependence at some time in their life, compared to 32% of tobacco users, 23% of opiate users, 17% of cocaine users, and 15% of alcohol users (Anthony, et al., 1994). It does appear that early onset of first use of cannabis is associated with an increased risk of later developing addiction. According to the National Survey on Drug Use and Health, in 2015, about 4.0 million people in the United States met the diagnostic criteria for a marijuana use disorder; 138,000 voluntarily sought treatment for their marijuana use.

Research Gaps

The National Academies of Sciences, Engineering, and Medicine (National Academies) Committee on the Health Effects of Marijuana published a report entitled *An Evidence Review and Research Agenda* (National Academies, 2017). The Committee on the Health Effects of Marijuana consisted of 16 experts in the areas of marijuana, addiction, oncology, cardiology, neurodevelopment, respiratory disease, pediatric and adolescent health, immunology, toxicology, preclinical research, epidemiology, systematic review, and public health. The committee reviewed the current evidence base for the potential efficacy of cannabis or cannabinoids on prioritized health conditions, including chronic pain, cancer, chemotherapy-induced nausea and vomiting, anorexia and weight loss associated with HIV, irritable bowel syndrome, epilepsy, spasticity, Tourette syndrome, amyotrophic lateral sclerosis, Huntington's disease, Parkinson's disease, dystonia, dementia, glaucoma, traumatic brain injury, addiction, anxiety, depression, sleep disorders, posttraumatic stress disorder, and schizophrenia and other psychoses.

The committee has identified that research gaps exist concerning the effectiveness of cannabidiol or cannabidiol-enriched cannabis in treating the following conditions:

- Cancer in general
- Chemotherapy-induced nausea and vomiting
- Symptoms of irritable bowel syndrome
- Epilepsy
- Spasticity due to paraplegia from spinal cord injury
- Symptoms associated with amyotrophic lateral sclerosis (ALS)
- Motor function and cognitive performance associated with huntington's disease
- Motor system symptoms associated with parkinson's disease or levodopa-induced dyskinesia
- Achieving abstinence or reduction in the use of addictive substances, including cannabis itself
- Sleep outcomes in individuals with primary chronic insomnia
- Post traumatic stress disorder symptoms
- Mental health outcomes in individuals with schizophrenia or schizophreniform psychosis
- Cannabidiol short-term relief from anxiety symptoms (National Academies, 2017)

NIH believes that FDA's drug review and approval process is the best way to ensure that new medicines, including those derived from marijuana, are appropriately evaluated for safety and effectiveness. To date, the FDA has approved three medications, Marinol (dronabinol), Cesamet (nabilone), and Syndros (oral drabinol solution), for severe nausea and wasting in patients with HIV and cancer. These medications contain synthetically-derived cannabinoids. Dronabinol is identical in chemical structure to delta-9-tetrahydrocannabinol (THC), the main active ingredient found in the marijuana plant; nabilone is similar in structure to THC. With Americans across the country consuming marijuana for health related conditions, there is a pressing need for more research in this area (NIDA, 2016).

Therapeutic Effects and Indications for Cannabis Use

Cannabis is not only remarkable in its wide margin of safety as a medication but also for the wide array of conditions, symptoms, or illnesses for which it is used. This may be a stumbling block for many clinicians, who find it hard to believe that a medication can be effective for so many indications. Although just in its infancy, the growing understanding of our ECS helps explain how and why cannabis is so versatile. As stated earlier, the ECS is involved in numerous physiologic processes that affect how we eat, sleep, relax, protect, and forget (Di Marzo, 1998).

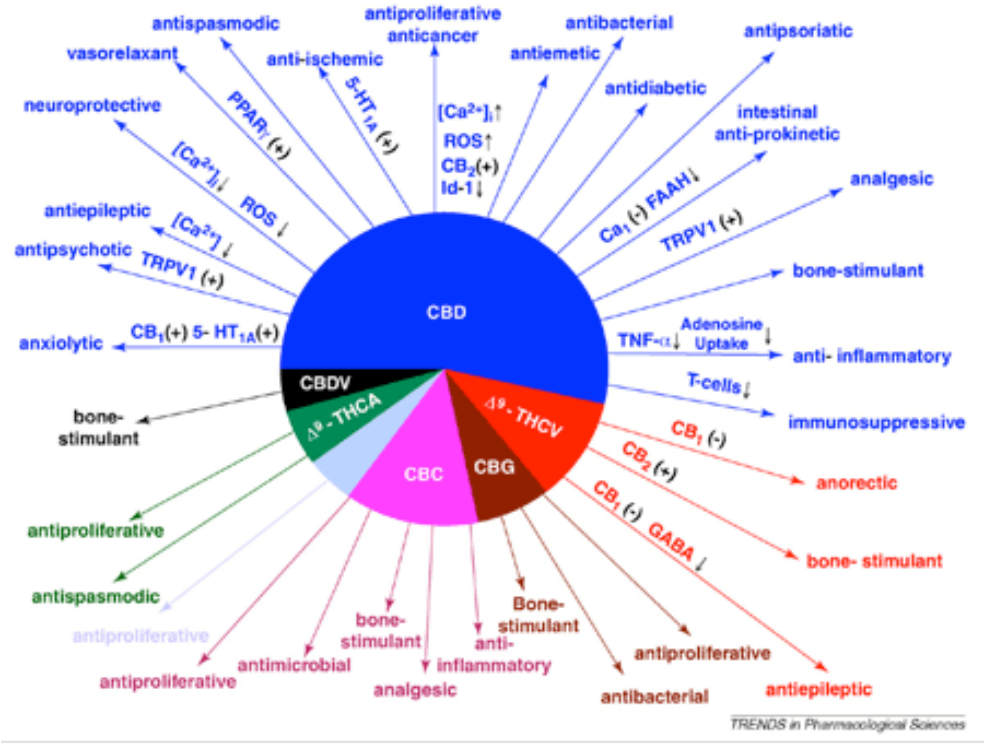
Cannabis Matches Our Own Human Receptors

Cannabis is the only plant that contains cannabinoids similar to the endocannabinoids found in humans. Delta-9-THC is the primary psychoactive cannabinoid and the most studied, but researchers are finding therapeutic potential in some of the other plant-based cannabinoids as well.

The therapeutic properties of cannabinoids include anti-inflammatory, neuroprotective, analgesic, antispasmodic, anti-oxidant, antibiotic, anticonvulsive, antiviral, antifungal, bone stimulant, anxiolytic, antipsychotic, vasorelaxant, antidiabetic, antiproliferative, and anti-tumor. The following figure shows some of the actions of some of the non-psychoactive cannabinoids, to give you an idea of their therapeutic potential (Izzo et al., 2009).

Kogan and Mechoulam (2007) wrote that the therapeutic value of cannabinoids is too great to ignore and identified numerous diseases that are being treated by or have the potential to be treated by the cannabinoids in cannabis: anorexia, emesis, pain, inflammation, multiple sclerosis, neurodegenerative disorders (Parkinson's disease, Huntington's disease, Tourette's syndrome, Alzheimer's disease), epilepsy, glaucoma, osteoporosis, schizophrenia, cardiovascular disorders, cancer, obesity, and metabolic syndrome-related disorders, to name just a few.” NIDA (2016) acknowledges a growing body of evidence that cannabinoids have therapeutic value in numerous health conditions including pain, nausea, epilepsy, obesity, wasting disease, addiction, autoimmune disorders, and other conditions.

Pharmacologic Actions of Non-psychotropic Cannabinoids



Abbreviations: CBN, cannabinol; CBD, cannabidiol; D9-THCV, D9-tetrahydrocannabivarin; CBC, cannabichromene; CBG, cannabigerol; D9-THCA, D9-tetrahydrocannabinolic acid; TRPV1, transient receptor potential vanilloid type 1; PPARg, peroxisome proliferator-activated receptor g; ROS, reactive oxygen species; 5-HT1A, 5-hydroxytryptamine receptor subtype 1A; FAAH, fatty acid amide hydrolase. (+), direct or indirect activation; ↑, increase; ↓, decrease. Source: Izzo et al., 2009. View full-size graphic here.

Indications for Use

While the use of cannabis for chemotherapy-induced nausea and vomiting may be the best-known and accepted use of cannabis by healthcare professionals, pain management is the most common reason for use among the medical marijuana states that keep records (although New Jersey does not accept chronic pain as an acceptable use). Listed below are recent statistics from the Colorado, Oregon, Rhode Island, and New Mexico medical cannabis programs. Note that the state laws vary in the conditions allowed for cannabis recommendations. For example, Arizona does not allow physicians to recommend cannabis for post traumatic stress, yet Colorado and New Mexico do. Oregon passed a law in 2013 allowing PTSD as a qualifying condition.

As of May 2019 there were 87,879 registered medicinal cannabis patients in Colorado. The following table shows their medical conditions. For all patient groups age 11 and older, severe pain was the top reported condition.

Colorado Medical Marijuana Registry Frequency of Conditions (as of May 2019)	
Reported condition	Number of patients
Cachexia	1,130
Cancer	4,436
Glaucoma	1,131
HIV/AIDS	0
Muscle spasms	30,090
Seizures 2,971	
Severe nausea	14,414
Severe pain	78,129
Post traumatic stress disorder (PTSD)	9,021
Autism spectrum disorder	62

Source: Colorado Department of Public Health and Environment, 2019.

As of November 2016, there were 25,697 registered medicinal cannabis patients in New Mexico. The following table shows their qualifying conditions.

New Mexico Medical Cannabis Program (active status as of 11/2016)	
Qualifying condition	Count
Amyotrophic lateral sclerosis	21
Cancer	1,932
Crohn's disease	126
Damage to the nervous tissue of the spinal cord	133
Epilepsy	443
Glaucoma	183
Hepatitis C infection	55
HIV/AIDS	387

Hospice care	52
Huntington's disease	5
Inclusion body myositis	1
Inflammatory autoimmune-mediated arthritis	488
Intractable nausea/vomiting	307
Multiple sclerosis	351
Painful peripheral neuropathy	856
Parkinson's disease	108
Post traumatic stress disorder (PTSD)	12,854
Severe Anorexia/Cachexia	151
Severe chronic pain	8968
Spasmodic torticollis (cervical dystonia)	29
Ulcerative colitis	65
TOTAL	25,697

Source: New Mexico Department of Health (2016).

As of April, 2019, there were 28,177 registered medicinal cannabis patients in Oregon. The following table shows their qualifying medical conditions. Medical marijuana patients in Oregon now have the option to apply or renew using a secure online system: ommpsystem.oregon.gov.

In 2019 we found dramatically different statistics about qualifying conditions than were found by the writer of the previous edition (2015). The table below shows 2019 data.

Qualifying Conditions* for Medicinal Use of Cannabis (Oregon, 2019)	
Qualifying condition	No. of patients
A degenerative or pervasive neurologic condition	1,422
Cachexia	449
Cancer	1,953
Glaucoma	460
HIV/AIDS	300
Severe nausea	2,960
Post traumatic stress disorder	3,486
Severe pain	24,749
Seizures, including but not limited to epilepsy	875
Persistent muscle spasms, including spasms caused by multiple sclerosis	5,867

*A patient may have more than one diagnosed qualifying medical condition.
Source: Oregon Health Authority, 2019.

As of June 30, 2017 there were 18,050 cannabis patients registered in the state of Rhode Island. For the fiscal year July 1, 2016, to June 30, 2017, Rhode Island's DOH approved and issued 6,313 registrations for patients, caregivers, and/or authorized purchasers. In the table below, which shows statistics from 2017, note that many patients have more than one diagnosis code; thus, the count of diagnosis codes used will always be higher than the number of patients.

Medical Marijuana Program Patients by Diagnosis in Rhode Island, 2017	
Diagnosis	No. of patients
Cancer or treatment	476
Severe or persistent muscle spasms	389
Agitation related to Alzheimer's disease	3
Glaucoma or treatment	71
Positive status for HIV or treatment	25
AIDS or treatment	11
Hepatitis C or treatment	77
Cachexia or wasting syndrome	104
Severe, debilitating chronic pain	4,558
Severe nausea	922
Seizures, including epilepsy	149

Source: Rhode Island Department of Health, 2017.

As you can see, the indications for use of cannabis as medication are numerous and cover all specialty areas of practice. From a nursing perspective, cannabis can be effective for many common patient problems: nausea and vomiting, lack of appetite, inability to sleep, pain, depression, and anxiety. One way of categorizing the indications for cannabis is to use the descriptive properties of the ECS noted by DiMarzo:

- Eat
- Sleep
- Relax
- Protect
- Forget (DiMarzo, 1998)

Eat

Studies have clearly shown that THC and cannabis are effective anti-emetics. As an anti-emetic, cannabis may be used to combat the nausea and vomiting from chemotherapy (cancer, HIV/AIDS, hepatitis treatment), post operative nausea and vomiting related to anesthesia or intra-operative medications, motion sickness, morning sickness, and hyperemesis gravidarum. Cannabis is effective as an appetite stimulant for cancer patients or HIV/AIDS patients with cachexia or wasting syndrome (Abrams, 2002; Schnelle & Strasser, 2002; Plasse, 2002). There have been cases of hospitalized patients on tube feedings using cannabis to start eating again.

Sleep

Cannabis helps induce sleep and, unlike many pharmaceuticals used as sleep aids, cannabis does not leave a person feeling drugged in the morning (Russo, et al., 2007).

Relax

As a muscle relaxant, cannabis helps decrease the muscle spasms experienced by chronic pain patients; it can ease the spasticity in patients with multiple sclerosis or spinal cord injuries, and it can ease menstrual cramps. Cannabis can relax blood vessels and prevent migraines. Although the mechanism of action is not completely understood with glaucoma patients, cannabis can reduce the intra-ocular pressure that leads to blindness. Cannabis can relax the bowels for persons suffering from irritable bowel syndrome or Crohn's disease. Cannabinoids help induce bronchial dilation, which is helpful for asthmatic patients. It can relax the anxious person, help reduce stuttering, and help decreases obsessive behavior with OCD patients. Cannabis has also been helpful in eliminating or reducing the frequency of seizures (Mathre, 1997; Russo & Grotenhermen, 2002).

Protect

This covers a broad array of conditions because the cannabinoids have anti-inflammatory, neuroprotective, antibacterial, antifungal, antiviral, anti-tumor, and antiproliferative properties. Cannabis may be helpful after acute injuries such as traumatic brain injury (TBI), in part through its anti-inflammatory effects. One of the cannabinoids has been found to kill MRSA in the laboratory; clearly we need further study on this action (Appendino et al., 2008). Cannabis has been helpful with phantom limb pain and other neuropathic pain conditions. It is now believed that certain auto-immune diseases may be the result of an overactive immune system and cannabis can help put it back in balance. Research on the ECS indicates that cannabinoids may prevent Alzheimer's disease. As a bone stimulator, cannabinoids can help hasten the healing process of bone fractures and prevent osteoarthritis (Mechoulam, 2010a).

Cancer patients have used cannabis to combat chemotherapy-induced nausea and vomiting and to help manage cancer pain. Animal research is showing that cannabinoids can kill cancer cells, and there are a growing number of case studies of cancer patients who have used concentrated cannabis oils or tinctures in treating their cancer. Research on the ECS shows that one of its functions is to identify cancer cells and induce *apoptosis* (cell suicide), prevent *angiogenesis* (the formation of blood vessels that feed a tumor), and prevent the spread of cancer to other areas (Holland, 2010). This leads researchers to explore the use of cannabis as a perfect cancer chemotherapy agent—one that can actually differentiate and destroy cancer cells rather than healthy cells. Studies have shown that cannabis/cannabinoids may be helpful in cancer treatment of *glioma* (aggressive brain cancer), lung, pancreatic, cervical, breast, colon, prostate, thyroid, and skin cancer, as well as leukemia and lymphomas (Pacher et al., 2006).

Forget

Many jokes have been made about short-term memory loss with persons who smoke cannabis recreationally. However, research on the endocannabinoid system shows that it is involved in the process of helping us forget painful experiences, such as traumatic experiences or the pain of childbirth. Many of our combat veterans, as well as rape and incest victims, have used cannabis to help them manage their post traumatic stress symptoms. Based on research findings, Israel and Czechoslovakia now allow the use of cannabis for their veterans who suffer from post traumatic stress (Mechoulam, 2010b).

Addressing the substance abuse issue: During the reefer-madness campaign, marijuana was portrayed not only as dangerous and addictive but also as a “gateway” drug. Prohibitionists claim that marijuana use will cause the user to try hard drugs such as cocaine or heroin. The IOM report noted that “it was not the substance itself but the illegal status of cannabis that served as a gateway to stronger drugs.” To purchase cannabis, a user had to interact with illicit drug dealers. If the drug dealer did not have cannabis, he would encourage the potential buyer to try whatever else was available (Joy et al., 1999).

Historically, cannabis pharmaceuticals were used to “combat habits of morphine and chloral hydrate” and to “manage delirium tremens from alcohol withdrawal.” Today, in many of the bigger compassion clubs and cannabis dispensaries, staff are noting that many patients report that cannabis has helped them get off of a drug of abuse. Philippe Lucas, of the Vancouver Island Compassion Society (VICS) in Canada, coined a new term to describe cannabis; he called it an *exit drug* (Lucas, 2004).

Rather than causing persons to use stronger drugs, patients are finding that cannabis helps them get off and stay off of drugs such as alcohol, nicotine, cocaine, methamphetamine, benzodiazepines, prescription opioids, and heroin. Some report that cannabis helped manage their withdrawal symptoms when they quit using their problem drug. Others found that if they used cannabis they could resist using their previous drug of choice and their lives became more manageable (Reiman, 2008).

How Medical Is Marijuana?

For a July 20, 2015 *New York Times* article by Aaron E. Carroll about the scant number of studies done on the medical use of cannabis, go to this link.

Opiate Sparing

Severe chronic pain is commonly treated with opioids (eg, morphine, oxycodone, methadone). Unfortunately, opioids cause physical dependence with regular use and patients readily develop a tolerance to their analgesic effects, requiring increased dosage over time. Some of the opioids are in combination drugs (eg, Percoset, Vicodin) that also contain acetaminophen (Tylenol). Opioids carry the risk of overdose by respiratory depression, and acetaminophen carries a substantial risk of fatal liver damage with excess dosage. We currently have an epidemic of opioid overdoses.

Opioids present other problems as well. Many patients complain of feeling “drugged” and unable to think clearly when using opioids. Care has to be taken to avoid severe constipation as an expected side effect of opioids; some patients experience nausea and some suffer from depression (which may in part be due to the depressive effects of opioids as well as the result of living with chronic pain).

Many pain patients have found that they can significantly reduce or eliminate their use of opioids when they begin using cannabis. In addition, cannabis is not constipating, prevents nausea, and can act as an anti-depressant. Thus patients report effective pain relief and no longer require additional medications to counter the side effects of opioids (Mathre, 1997; Holland, 2010). A 2014 study found a 24.8% lower mean annual opioid overdose death rate in states with medical cannabis laws (Bachhuber, et al., 2014).

A review and meta-analysis of the opioid sparing effects of cannabis by Nielsen and colleagues (2017) concluded that pre-clinical studies support the opioid-sparing effect of delta-9-THC, but that the findings from clinical trials are inconsistent, with some studies having important limitations. An opioid-sparing effect of cannabinoids in chronic pain patients was observed in one “very-low-quality clinical study.” Nielsen and colleagues found that the topic warrants exploration. “It remains to be seen if these promising pre-clinical and observational findings can be replicated in large, well-designed clinical studies” (Nielsen et al., 2017).

Dosage and Administration of Medical Cannabis

Given that the cultivation of cannabis currently remains a criminal offense under federal law, growers have focused their horticultural skills on developing stronger strains (higher THC content) with the intention of raising the price and increasing their profits. Unfortunately, these overzealous growers have developed some strains that are high in THC but almost devoid of CBD and other cannabinoids. Based on the therapeutic value of the non-psychoactive cannabinoids, these high-THC content plants are not as beneficial to patients. They are too psychoactive for novice patients, especially elders, and are not as effective therapeutically.

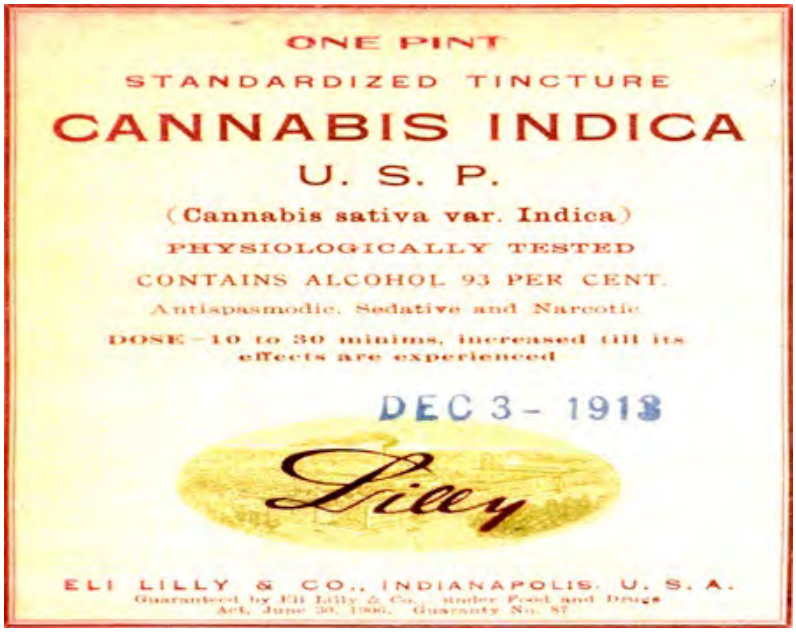
Project CBD was created to correct this situation by reaching out to growers of medicinal-grade cannabis and educating them about the need to develop strains rich in CBD and other cannabinoids. Project CBD also reaches out to educate patients and clinicians so that they will create a demand for CBD-rich cannabis (www.projectcbd.com).

The research on the various phytocannabinoids will eventually lead to pharmaceutical products targeted specifically to various illnesses or conditions. However, the whole natural plant may continue to be preferred by many patients. In the states that currently allow the medical use of cannabis, cannabis growers and dispensaries are keeping records on patient preferences for various conditions. They are finding trends that suggest certain strains, with their specific cannabinoid makeup, work best for particular indications.

A seed from a particular strain may develop into a plant with a different chemical profile when grown in a different region under different conditions. What this means is that much more research is needed to match specific strains with various indications. Once a strain is found effective for a particular ailment, clones can be taken from the mother plant to produce new plants with the same genetic makeup. In the meantime, this section will focus on general dosing guidelines for use of whole cannabis, and medical professionals should understand that individual patients will prefer some cannabis strains or hybrids over others.

Cannabis has a remarkably wide margin of safety; thus, there is virtually no risk of death by overdose. Clinicians who have experience in the use of cannabis have found that the dosage will vary greatly among patients, even when treating the same condition. The basic principal for dosing is to start low and go slow. Prior to the marijuana prohibition, many of the pharmaceutical tinctures were highly concentrated, and the dosage was in “minums.” The top of the container was a dropper to administer the medication. The label of an Ely Lily tincture of cannabis included dosage instructions that said: “DOSE 10–30 minums, increased till its effects are experienced.”

Label from Eli Lilly Cannabis Preparation, 1913



The label instructions read: "DOSE 10 to 30 minums, increased till its effects are experienced." Source: Courtesy of Patients Out of Time. Used by permission.

Although the federal government—and more recently the American Society of Addiction Medication (ASAM)—continue to denigrate the medicinal use of cannabis by focusing on "smoked marijuana," the truth is that cannabis can be formulated in a variety of preparations, and healthcare professionals need to separate the false propaganda from the facts.

Medicinal-Grade Cannabis

The term *medicinal-grade cannabis* means that care has been taken in growing the plant in a clean environment without the use of dangerous pesticides or nonorganic fertilizers. Once the cannabis is ready for harvest it needs to be properly cured or dried to prevent mold (eg, aspergillus fungus). To keep the raw material from decomposing and losing its effectiveness it should be kept in a dry, air-tight container and out of sunlight. Freezing cannabis will also help maintain freshness. The stems and any seeds should be removed.

In the more sophisticated dispensaries, owners are responding to the patient need for quality control, and some are beginning to only use cannabis that has been tested for contaminants and cannabinoid content. Without clear regulations, this lack of quality control can be a serious problem for patients.

Inhalation

Many Americans think of smoking as the primary delivery method for cannabis; this limited view arose because of the marijuana prohibition that put an end to its medicinal use back in 1937, when pharmaceutical companies and physicians stopped making the medicinal formulations. In truth, cigarette forms of medicinal cannabis had been used earlier to treat asthma, since the effect of inhaling cannabis was to open the airway. Inhalation has the primary advantage of allowing a patient to titrate the dosage easily for maximum benefit because the onset of action is almost immediate. The medication is taken into the lungs and quickly absorbed through the capillaries into the bloodstream. The effects of inhaled cannabis will last approximately four hours.

Smoking

Patients can smoke raw cannabis in several forms. The “joint” or cigarette form (hand-rolled or machine-rolled) is the most common among recreational users, but cannabis can be smoked using a pipe or bong (water pipe) as well. Smoking by joint is the least efficient because much of the medication goes up in smoke as the cigarette burns. Smoking small amounts using a pipe is more efficient, and the use of a bong can cool the smoke so that it is less irritating to the airway.

Vaporization

Rather than burning the plant material and creating smoke, cannabis can be heated to a temperature that will release the medication in vapors that can be inhaled, much like the nebulizer treatment common in hospitals. The original vaporizers were somewhat clumsy and the heat source was not well-regulated. Today there are numerous vaporizers on the market ranging in cost, size, shape, and effectiveness. There are home models and smaller portable models that patients can use when traveling. The better models have digital temperature controls that allow the patient precise control with heating, since the individual cannabinoids vaporize at different temperatures.

Sublingual Delivery

The sublingual (under the tongue) or oromucosal (in the oral cavity) delivery method of an oil or tincture provides another rapid onset of action as the medication is readily absorbed into the blood system. Tinctures are usually prepared in a base of alcohol, oil, or glycerol. Many concentrated tinctures are taken by dropper under the tongue, and within a few minutes the patient will feel the effects. Other tinctures may be in a spray container and sprayed in the mouth to be absorbed in the oral cavity and thence into the bloodstream. Many patients who never smoked cigarettes are more comfortable with this delivery method.

Oral Ingestion

Taking cannabis by mouth in pill form or swallowed as a liquid has both benefits and drawbacks. Since the cannabinoids are fat-soluble, their absorption through the gut is slower and less predictable, being dependent upon the individual’s metabolism as well as the contents of the stomach. The onset of action may take as long as 30 minutes to an hour, making it more difficult to determine an effective dose, especially for the novice patient. In addition, when taken orally, the medication gets metabolized through the liver before getting into the bloodstream.

The liver converts the THC to another chemical called 11-hydroxy-THC, which is more psychoactive than THC, and so the effects will be different than if inhaled or taken sublingually. The advantage of the oral route is that it will last much longer, so a patient does not have to medicate as frequently. This can be helpful for glaucoma patients who are trying to maintain a lower intraocular pressure.

In addition to pills, many dispensaries offer *medibles*, or edible cannabis products, as in tea, brownies, cookies, and even ice cream. An easy and versatile preparation is cannabis butter; since the cannabinoids are fat-soluble they mix well with butter and this can be used in cooking or put on toast or crackers. An advantage is that the butter can be made from the leaves that are often waste products for growers who only want the bud. The disadvantage is that patients can easily overdose on medibles, causing dizziness and/or couch lock, and extreme nausea and vomiting because the onset of action may not occur for 30 minutes or longer and the peak may not occur until 2 hours after ingestion. These symptoms will subside in a few hours, but patients need to be instructed on safe dosing.

Topical Application

Cannabis can be applied externally as a topical ointment, lotion, or poultice, and may be used in the treatment of skin inflammations, arthritis, or muscle pains. The goal is for the medication to be absorbed at the specific location being treated. Although it is unclear how well the cannabinoids are absorbed through the skin, the more soluble terpenoids and flavinoids also have anti-inflammatory properties that can be effective.

Pharmaceuticals

In Jamaica, physicians have developed cannabis-based eye drops for glaucoma patients. Canasol and Canalol (cannabis and Timolol) are available by prescription in Jamaica (West, 1997). In England, GW Pharmaceuticals has developed an oromucosal cannabis extract spray (Sativex) for use with multiple sclerosis, as well as neuropathic and cancer pain. It has taken years of research to get approval in the European countries, but Canada approved its use in 2005. Clinical trials using Sativex for severe pain in cancer patients have taken place in the United States, and the company is working to get FDA approval (www.gwpharm.com).

Single cannabinoid products are also on the market. We have already discussed Marinol as a capsule containing synthetic THC in sesame oil. It comes in 2.5, 5, and 10 mg capsules that resemble fish eggs. Originally approved for use as an anti-emetic and appetite stimulant, it can now be prescribed for off-label uses as well. It has been proven to be effective for some patients, but most find it less effective than whole cannabis. Nabilone is a synthetic cannabinoid similar to THC that is available in the United Kingdom, Australia, Canada, and some European nations. Other synthetic cannabinoids—Levonantradol made by Pfizer, Ajulemic acid (CT3) developed in Massachusetts, and HU-308 made in Israel—are emerging as new medications. Research has also been done to develop a dermal patch (Grotenhermen & Russo, 2002).

Rimonabant, or SR141716, is a cannabinoid antagonist that was developed for use as an appetite suppressant for treatment of obesity. The initial idea was that, since cannabis and the endocannabinoids are known to increase the appetite, blocking the cannabinoids could result in a decreased appetite and subsequent weight loss. However, once this medication was used by a larger population, reports of serious depression and potential suicide caused it to be withdrawn (http://news.bbc.co.uk/2/hi/health/7687311.stm). As we learn more about the endogenous cannabinoid system, it makes sense that blocking the normal action of the endocannabinoids could lead to serious health problems.

Drug Interactions

A drug interaction should always be considered when taking more than one medication. A problem with patients using cannabis is that they may not report their use of it to their healthcare provider because of its illegality, and this prevents the healthcare provider from monitoring for possible interactions. Experts agree that more research in this area is needed.

Cannabis and THC have been shown to alter the absorption and elimination of other drugs. Because of possible additive or synergistic action, cannabis should not be used in combination with alcohol, sedatives, anti-anxiety drugs (benzodiazepines like valium, Xanax, or Klonapin), or sleeping pills; increased sedation is one potential outcome. CBD can slow the body's metabolization of cholesterol medications (eg. Lipitor). For patients using theophylline, cannabis will increase the metabolic processing of that drug. Because cannabis seems to work synergistically with opioids, patients may be able to decrease or cease their use of an opioid because they find they no longer need it.

Case Examples of Cannabis Use

Case 1

Jamie, a 40-year-old female with MS, had progressively lost her ability to walk due to leg spasms that required a cane or wheelchair. She had lost vision to the degree that she had to give up her drivers' license. She had lost control of her bladder, especially at night. Another MS patient suggested that she try cannabis. Jamie found that smoking the cannabis almost immediately relaxed her spasms. Since she had never used cannabis before, she started slowly by smoking part of a cannabis cigarette. When she felt a spasm starting, she would smoke some more. Over time she came to smoke about 10 low-grade (2%–3% THC) cannabis cigarettes throughout the day. She still doesn't drive, but her vision has improved. On good days she walks without her cane and she no longer requires diapers for incontinence. She no longer needs the prescription Valium and her anti-depressant.

Case 2

Eileen is a 72-year-old female who was born with congenital cataracts. After multiple surgeries on both eyes, she developed glaucoma that could not be controlled with standard medications. Complications with the last surgery on her right eye caused her to lose all her vision. In her late thirties she began smoking and eating cannabis. She initially used the cannabis to help her quit smoking. Eileen found that she could keep her eye pressures within safe limits by eating homemade cookies throughout the day and that the oral route lasted longer. A few years later, she learned to make cannabis butter and ate a teaspoon of it on a cracker throughout the day and at bedtime. Eileen had a history of insomnia and initially could sleep only around 4 hours. As a bonus, she found that with the cannabis she could get 6 to 7 hours of sleep a night.

Case 3

Casey was a 19-year-old male when he was diagnosed with Crohn's disease. He suffered from extreme abdominal pain and was losing >10 pounds/week, which resulted in his dropping out of college. His team of doctors tried everything, fearing Casey was going to die if he couldn't maintain his weight. Casey tried cannabis at the urging of friends, and he began gaining weight. He told his medical team about his use and they quietly supported him. He no longer needed a strong opioid for pain management, but his consulting physician for pain did give him a prescription for Marinol; in case he was tested for drugs, this would justify a positive THC finding. Casey lives in a state that has no medical cannabis law and his main concern is getting quality medicine at an affordable price. His parents had always thought marijuana was a drug of abuse, but now support him, since they too believe it saved his life. He cannot afford a vaporizer, but has been advised to smoke a pipe rather than cannabis cigarettes, to inhale and limit his breath-holding to <3 seconds, and to clean the pipe daily to avoid tar build-up.

Case 4

Brian is a 45-year-old male who was diagnosed with AIDS more than ten years ago. Following the advice of his support group, he started using cannabis when his medical treatment for AIDS began. To avoid any risk related to inhaling contaminated cannabis, he bought a cannabis tincture. Brian found that he only needed a quarter to a half of a dropper of the tincture at a time. He would start with a quarter of a dropper and take an additional quarter if needed after waiting for 10 minutes.

Case 5

As a baby, Jeffrey was not eating or sleeping well and was always restless. As a toddler he was soon known as the out-of-control problem child who had temper tantrums and aggressive behavior. By age 7 he had been diagnosed with ADHD, impulse disorder, OCD, Tourette syndrome, intermittent explosive disorder, conduct disorder, oppositional defiance disorder, PTSD, and bipolar disorder. Over the years he had been prescribed 15 medications—Ritalin, Mellaril, Dexidrine, Imiprimine, Adderall, Clonidine, Depakote, Tenex, risperdal, Tegretol, Seroquel, Neurontin, Klonopin, Zoloft and Zyprexa—many of which are not approved for children.

Jeffrey's desperate mother heard about cannabis and, through the Internet, located a compassion center in their state of California that could supply an edible form of cannabis and a physician who would write the recommendation. She was instructed on how to dose Jeffrey (now age 7½). About a half-hour after eating part of a medicated muffin, while being driven to his special school, Jeffrey relaxed his grip on his mother's hand and began smiling. He said "Mommy, I'm not mad. I'm happy, and my head doesn't feel noisy." His teachers noticed his calmer demeanor and over time his outbursts decreased. Within 6 months of using cannabis Jeffrey was learning how to have fun and was able to benefit from counseling. (For the full story see: Debbie and LaRayne Jeffries, *Jeffrey's Journey: Healing a Child's Violent Rages*, 2005, Oakland, CA: Quick American.)

Patient and Family Education About Medicinal Cannabis

When conducting an initial intake on all patients, always ask about their use of cannabis. They may not be willing to volunteer the information, but most patients will admit to use if asked directly (Mathre, 1985). If they admit to use, continue to assess their use patterns and reasons for use. This will help you understand if they are using it recreationally or medicinally. Either way, patients still need to understand the potential risks and benefits and be taught how to use cannabis safely.

Until cannabis is removed from Schedule I, begin by reminding the patient or family members that cannabis is illegal under federal law and that they are subject to legal consequences if arrested for possessing or growing the plant. For example, you could say “You understand that cannabis is illegal, so I cannot help you obtain it and you could get arrested if your use is known by law enforcement.” This is simply stating the fact and also letting the patient know that you are not going to report their use.

It is important to ask the patient if they want their use noted in their record. Some patients will not, due to fear of their use being known by others, yet the record can be useful if they are arrested for cannabis possession and need to prove medical necessity. In the legal medical-cannabis states, patients need to understand that they are still in danger of federal prosecution.

The healthcare professional needs to know the conditions under which cannabis can be recommended for medicinal use because they vary among states. Another area of concern is reciprocity between states; patients need to understand that even though they have a legal recommendation for cannabis in one state, it does not mean they can take their medication into another state and use it.

Here are some other points to help patients use cannabis safely and responsibly:

1. **Vocabulary.** Teach patients to call it “cannabis.” This allows the patient to understand that there is a long history that supports cannabis as medication.
2. **Legality.** Know the laws of the state regarding how much a patient can grow or possess and under what conditions/diagnoses medicinal cannabis may be recommended.
3. **Storage.** Dark glass or metal tins are preferred over plastic. Use an opaque container or store in a cool, dark area. Freeze for long-term storage.
4. **Inhaling cannabis:**
    - Use a pipe rather than a cigarette to be more efficient.
    - Clean the pipe daily because the tar will build up after each use. Glass pipes are easy to clean. Purple Power is a biodegradable cleaner that is effective and can be found in automotive supply stores.
    - Do not hold your breath for more than 3 seconds after inhaling. Holding it for longer periods of time will only allow more smoke to be absorbed into the pulmonary tissue.
    - Never use cannabis with mold on it. If you are in doubt, it can be baked at 350°F for 15 minutes. This will kill any aspergillus, which can be dangerous, especially to patients with a compromised immune system.
    - Encourage the use of a vaporizer to eliminate any potential harm from smoking.
    - Always begin with one inhalation when using a new supply and wait several minutes to determine if you need more.
5. **Taking Cannabis sublingually.** Start with a few drops, wait 10 minutes, and take more only if needed. Store in dark glass container.
6. **Using medibles.** Keep them clearly marked and out of reach of children or others who could ingest the food without realizing it is medication. Take a small dose and wait at least 30 minutes to determine its effects.
7. **If obtaining medication from a dispensary.** Ask about quality control testing. Ask for strains that are rich in CBD (this will encourage growers to develop and grow these strains). Expect the dispensary to clearly label the contents of their products, including the cannabinoid and terpenoid content.

Public Policy and Legal Issues Regarding Cannabis

Drug Testing

THC is included in most urine drug screens that are used in the workplace for pre-employment, random, and for-cause testing. In the hospital setting, urine drug screens have been used as a diagnostic tool in the emergency department, on newborn babies if drug use is suspected, and in pain clinics when opioids are prescribed. Healthcare professionals should understand that drug screens are not diagnostic of drug abuse—they only help confirm recent drug use.

Cannabis is different from the other drugs included in the screening in that it can be detected in the urine for as long as a month after the last use (Gieringer, Rosenthal, and Carter, 2008). This is important to understand, because a positive urine drug screen for THC does not confirm impairment by cannabis.

Some clinicians believe they must confirm that the patient is not using cannabis before they can prescribe an opioid because it is illegal to provide an opioid to a narcotic addict. Cannabis is not a narcotic, but because it is an “illicit” drug many clinicians blindly include it in the testing. If the patient tests positive for THC, some clinics counsel the patient to quit and others either deny further treatment or simply stop prescribing any opioids.

With an understanding of the safety and efficacy of cannabis for management of chronic pain, one could question the value of including THC in the drug panel that is used to screen patients. One could further question the therapeutic value with pain patients of a urine drug screen for THC. If patients experience better pain management and require lower doses of opioids when using cannabis for pain management, how does it make sense for the healthcare provider to demand that the patient stop using the cannabis? If the only answer is that cannabis is illegal, one can wonder if the healthcare provider is practicing law rather than medicine. Due to the epidemic of opioid overdoses, the Centers for Disease Control (CDC) just recently issued guidelines on prescribing opioids for chronic pain. In them, the authors question the need to include THC in the random drug screens since it poses no clinical risk to a patient on opioids (Dowell et al., 2016).

Research Monopoly

As stated previously, NIDA allows the University of Mississippi to grow cannabis for research purposes, but until recently, NIDA was only interested in studies on the abuse potential or negative effects of cannabis and did not allow the cannabis to be used in studies regarding its medicinal value. Although clinicians and legislators demand more research to validate the medical value of cannabis, but it is very difficult to conduct clinical research on cannabis in the United States because of all of the legal restrictions.

There has been a legal challenge to allow for another research facility to grow medicinal-grade cannabis for research studies. Lyle Craker, of the University of Massachusetts, applied for such a license and won his case before a DEA administrative judge. However, the ruling has been ignored, and to date cannabis can only be legally grown at the University of Mississippi farm (Craker, 2010). A U.S. Court of Appeals for the 1st Circuit ruled against him in 2013.

The DEA announced in August 2016 that it would grant additional cultivation licenses. As of July 2017, 25 applications had been submitted to the DEA and none had been approved, with no timeline given by the DEA for the approval of any licenses (Edwards Staggs, 2017).

Veterans

Over the years, numerous combat veterans have found cannabis helpful in managing symptoms of post traumatic stress as well as chronic pain related to wounds or injuries. In July 2010, the Undersecretary of Health for the Department of Veterans Affairs issued a directive to the healthcare providers of the Veterans Administration that provided some access to some veterans (VHA Directive 2010-035). Because cannabis remains illegal under federal law, the VA physicians still cannot recommend it to their patients, but this directive states that if a veteran lives in a medical marijuana state and has a recommendation for cannabis from a civilian physician, then the VA will treat that as medication and will continue to treat the veteran. However, this creates another problem—in effect, this directive allows veterans access to cannabis based on their geographic location and thus creates unequal treatment for veterans.

Nursing Implications

As a healthcare professional, it is important that you use the proper name of the plant, **cannabis**, rather than the derogatory term, *marijuana*. Using the term *cannabis* lets others know that you are aware of its long history as a medication and allows you to educate others on its medicinal value. Using the correct term can also help change the negative image associated with marijuana.

Learn more. Since 2000, Patients Out of Time has co-sponsored an accredited biennial series of national clinical conferences on cannabis therapeutics that feature international cannabis researchers, clinicians, and cannabis patients. All of the proceedings have been filmed and are available as DVD sets. In addition, much information is available on the website: www.medicalcannabis.com or www.patientsoutoftime.org. Based on the discovery of the endocannabinoid system and the value of cannabis as medication, a new specialty nursing organization has been created: the American Cannabis Nurses Association (www.cannabisnurse.org). Although in its infancy, this organization can be a resource to healthcare professionals who need or are interested in learning more about cannabis and the ECS.

Based on science, history, and compassion, there is no justification for the placement of cannabis in Schedule I. Because cannabis is still a Schedule I drug, patients are denied safe and legal access to a medication that can relieve suffering and improve quality of life. Nursing leaders agree that healthcare professionals should be more involved in public policies, especially when they are health-related. We now have a variety of state laws that are meant to help patients gain access to this medication, but as long as it remains in Schedule I on the federal level, patients remain under threat of legal consequences for growing or possessing cannabis and healthcare providers are hesitant to recommend its use when there is no assurance of quality control. Healthcare professionals need to help correct this situation by being more proactive:

Educate your legislator.

- Get your state association or professional specialty organization to pass a formal resolution supporting patient access to cannabis.
- Break the silence and discuss the medicinal use of cannabis with your co-workers.
- Encourage patients who use cannabis to use a vaporizer or other delivery forms rather than smoking it.
- In states that allow medicinal cannabis, work to create policies in healthcare facilities (hospitals, assisted-living facilities, clinics) to allow patient use of their medication.
- Request the medicinal use of cannabis as a topic at your professional conferences.

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Post Test

1. The Controlled Substances Act lists cannabis (marijuana) as a:

a. Schedule IV substance.

b. Schedule III substance.

c. Schedule I substance.

d. Cannabis is no longer a controlled substance.

2. Marijuana was dropped as a medication by the U.S. Pharmacopoeia when:

a. The National Prohibition Act became law in 1919.

b. Prohibition was repealed in 1933.

c. A few years after “Marihuana” was taxed prohibitively in 1937.

d. The U.S. Congress made marijuana illegal in 1941.

3. President Nixon appointed the Shafer Commission to determine whether cannabis met the criteria for Schedule I. The Commission reported that:

a. Cannabis should be treated similarly to heroin and cocaine.

b. They were unable to come to an agreement on the matter.

c. Cannabis met the criteria for Schedule III.

d. Cannabis did not meet the criteria for its assignment to Schedule I.

4. The Alliance for Cannabis Therapeutics (ACT) assisted patients and their doctors in completing the IND application to help them gain legal access to cannabis. The result was:

a. Virtually no one applied because they still feared legal retribution.

b. It was a panacea for HIV-positive patients and thousands took advantage of it.

c. The government became alarmed by the increased demand for cannabis and closed access to the program.

d. The federal government took away Robert Randall's IND access to cannabis.

5. By July 2019, 33 states had medical marijuana laws, but:

a. Only states with laws that regulate legalized marijuana are exempt from federal prosecution.

b. Patients in all states are still at risk for federal prosecution.

c. Only state attorneys general have the discretion to legalize use in their states.

d. State governors have the power to legalize cannabis within their own states.

6. In states that have legalized medical cannabis:

a. The physician and patient must together attend a hearing and get a permit before the prescription for cannabis can be honored.

b. Only "recommendations," not prescriptions, are allowed by physicians.

c. Only a limited number of medical cannabis prescriptions can be written in the state each year.

d. Patients must be eligible for hospice before cannabis is legally available to them.

7. The American Nurses Association strongly supports relisting marijuana as a Schedule II controlled substance for the purposes of facilitating research.

a. True

b. False

8. Cannabis has been grown and used for centuries. When the plant is grown for fiber and pulp it is called "hemp."

a. True

b. False

9. Cannabis is a dioecious plant, meaning that the seeds will grow into male or female plants. The female plant, without fertilization, is referred to as:

a. Sativa.

b. Indica.

c. Sinsemilla.

d. Cannabia.

10. Close to one hundred cannabinoids have been found in cannabis, and all of them are psychoactive.

a. True

b. False

11. Delta-9-tetrahyrocannabinol (THC) is the primary psychoactive cannabinoid found in cannabis, and Marinol is:

a. Illegal in all forms under federal law.

b. An unregulated form of THC.

c. Available as “injectable THC.”

d. Synthetic THC available in capsule form.

12. The endocannabinoid system (ECS) is:

a. A name for the body’s response to cannabis.

b. A system created by the federal government to regulate the desire for marijuana.

c. A molecular signaling system in the human body that produces natural cannabinoids and has receptors for them.

d. A mechanism found only in humans.

13. A 1999 Institute of Medicine study on the medical value of cannabis found that:

a. More study was needed before meaningful results could be reported.

b. The conditions of cancer and AIDS patients were negatively impacted by exposure to cannabis smoke.

c. Except for the harms associated with smoking, any adverse effects of marijuana use are within the range tolerated for other medications.

d. The intraocular pressure of glaucoma patients was unaffected by cannabis.

14. Risks arising from the prohibition of cannabis can include all but one of the following:

a. Loss of grant funding for colleges and universities.

b. Revocation of professional license or loss of employment.

c. Loss of food stamps and right to live in public housing.

d. Revocation of life insurance coverage.

15. Cannabis smoke does contain tar and other carcinogenic materials and, from a health perspective, it makes sense to avoid this route of administration.

a. True

b. False

16. When cannabis is used as an anti-anxiolytic medication, some novice users experience an acute panic reaction. Treatment includes:

a. Countering with another anti-anxiolytic medication.

b. Providing a quiet, relaxing environment and reassurance that the patient is fine and the effects will soon wear off.

c. Feeding snacks to divert the patient's attention to "the munchies."

d. Explaining that cannabis is not a gateway drug and is not harmful.

17. The amount of THC found in the bloodstream is directly correlated to the level of a driver's impairment.

a. True

b. False

18. Tolerance is defined as:

a. Seeing no perceptible change in drug response over time.

b. The need to increase the dose with chronic use in order to get the same effects.

c. Being free of side effects.

d. Accepting medicinal use of cannabis in the face of federal prohibitions.

19. Dependence is defined as:

a. A drug-related physiologic change in the central nervous system so that abrupt cessation causes withdrawal symptoms.

b. Wanting to take the next dose before it is scheduled.

c. Thinking about the medication between doses.

d. Checking to see if there are still remaining refills on your prescription.

20. Abrupt cessation of medical cannabis can cause withdrawal symptoms that:

a. Begin within minutes and last as long as 3 days.

b. Affect virtually all of the patients who have taken medical cannabis.

c. Include rashes and hives.

d. Are generally uncomfortable but not dangerous and do not require medical management.

21. Addiction is defined as:

a. The need to sever relationships in preference to living on the streets.

b. An overwhelming preoccupation with the compulsive use of a drug and securing its supply coupled with a high tendency to relapse if the drug is taken away.

c. Abnormal fear of withdrawal symptoms.

d. A tendency to choose illegal activities in all realms of life.

22. Which of the following common patient problems is not an indication for the use of cannabis?

a. Depression and anxiety.

b. Nausea and vomiting.

c. Lack of appetite.

d. Cardiac arrhythmia.

23. The term medicinal-grade means the cannabis:

a. Has been carefully stored in a sunny, well-aired environment.

b. Has been grown in a clean environment with no pesticides or nonorganic fertilizers.

c. Contains aspergillus, which enhances its therapeutic properties.

d. Has maintained freshness through retaining stems and seeds.

24. Nonsmokers have no alternate inhalation route for therapeutic cannabis.

a. True

b. False

25. A difficulty of taking cannabis by mouth is:

a. It is irritating to the oral mucosa.

b. Onset of action is too fast, with resulting anxiety for some patients.

c. Absorption through the gut is slower and less predictable.

d. The patient may have to medicate more often because effects don't last as long.

26. Until cannabis is removed from Schedule I, you should begin by telling the patient and family:

a. Everyone knows that cannabis is against the law, but it's OK to use it medicinally.

b. There are ways to obtain cannabis, and you can give them some leads.

c. Law enforcement tends to look the other way when cannabis is used for medication.

d. Cannabis is illegal and you can't help them obtain it, plus they could be arrested if use is known to law enforcement.

27. If you were legally prescribed cannabis in your own state, you can take your cannabis from state to state with no repercussions.

a. True

b. False

28. When taking cannabis sublingually (under the tongue), start with:

a. A few drops.

b. A half-teaspoon.

c. A teaspoon.

d. One ounce.

29. Urine drug screens for THC used in the workplace:

a. Do not confirm impairment by cannabis at the time of the test.

b. Indicates possible ongoing drug abuse.

c. Confirm that the employee is a drug addict.

d. Can pick up on use of THC as much as a year earlier.

30. The only place under federal law where cannabis can be legally grown in the United States is the University of Mississippi.

a. True

b. False

31. Combat Veterans have found cannabis helpful in managing symptoms of PTSD and chronic pain. The legal situation is:

a. The federal Department of Veterans Affairs has exempted Veterans from laws against use of cannabis.

b. VAs in the states can prescribe cannabis if their state is a medical marijuana state.

c. A Rhode Island VA will treat cannabis as a medication if the Vet is from RI and has a “recommendation” from a civilian physician.

d. The ACLU has sued on the basis that differences among the states is unequal treatment for veterans.

32. To support corrective legislation legalizing the medical use of cannabis:

a. Request the medicinal use of cannabis as a topic at your professional conferences.

b. Meet with colleagues in private to create advocacy groups.

c. Publicly accuse your congresspersons of purposely withholding legalization due to outdated fears of addiction.

d. Encourage patients to smoke cannabis openly in defiance of current laws.

Answer Sheet

Name (Please print) _____

Date _____

Passing score is 80%

1. _____	18. _____
2. _____	19. _____
3. _____	20. _____
4. _____	21. _____
5. _____	22. _____
6. _____	23. _____
7. _____	24. _____
8. _____	25. _____
9. _____	26. _____
10. _____	27. _____
11. _____	28. _____
12. _____	29. _____
13. _____	30. _____
14. _____	31. _____
15. _____	32. _____
16. _____	
17. _____	

Course Evaluation

Please use this scale for your course evaluation. Items with asterisks * are required.

5 = Strongly agree 4 = Agree 3 = Neutral 2 = Disagree 1 = Strongly disagree

*Upon completion of the course, I was able to:

1. Summarize 3 myths and 3 truths about cannabis as a medication.	5 4 3 2 1
2. Contrast Marinol with cannabis occurring in nature.	5 4 3 2 1
3. Explain the endocannabinoid system and its implications for the use of cannabis as medication.	5 4 3 2 1
4. Comment on 3 supposed health risks related to cannabis as medication.	5 4 3 2 1
5. State 3 therapeutic indications for cannabis.	5 4 3 2 1
6. Discuss 4 common routes of administration of cannabis.	5 4 3 2 1
7. Describe 4 elements of patient and family education regarding cannabis.	5 4 3 2 1
8. Debate 3 legal issues associated with the medicinal use of cannabis.	5 4 3 2 1
9. Describe 3 populations who may experience health risks from cannabis.	5 4 3 2 1

*The author(s) are knowledgeable about the subject matter.	5 4 3 2 1
*The author(s) cited evidence that supported the material presented.	5 4 3 2 1
*Did this course contain discriminatory or prejudicial language?	Yes No
*Was this course free of commercial bias and product promotion?	Yes No
*As a result of what you have learned, will make any changes in your practice?	Yes No

If you answered Yes above, what changes do you intend to make? If you answered No, please explain why.

*Do you intend to return to ATrain for your ongoing CE needs?

_____Yes, within the next 30 days. _____Yes, during my next renewal cycle.

_____Maybe, not sure. _____No, I only needed this one course.

*Would you recommend ATrain Education to a friend, co-worker, or colleague?

_____Yes, definitely. _____Possibly. _____No, not at this time.

*What is your overall satisfaction with this learning activity? 5 4 3 2 1

*Navigating the ATrain Education website was:

_____Easy. _____Somewhat easy. _____Not at all easy.

*How long did it take you to complete this course, posttest, and course evaluation?

_____60 min (or more) per contact hour _____59 min per contact hour

_____40-49 min per contact hour _____30-39 min per contact hour

_____Less than 30 min per contact hour

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_____Government or Department of Health website. _____State board or professional association.

_____Searching the Internet. _____A friend.

_____An advertisement. _____I am a returning customer.

_____My employer. _____Social Media

_____Other _____

Please let us know your age group to help us meet your professional needs.

_____18 to 30 _____31 to 45 _____46+

I completed this course on:

_____My own or a friend's computer. _____A computer at work.

_____A library computer. _____A tablet.

_____A cellphone. _____A paper copy of the course.

Please enter your comments or suggestions here:

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*Zip: _____

*Card type: Visa Master Card American Express Discover

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