

**Going to Pot:
Weeding Out Potential Benefits and Dangers of Marijuana Use**

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Presenter Disclosures Betsy Reynolds, RDH, MS

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Agenda:

- Introduction
- History of Cannabis
- How Marijuana 'Works'
- Methods of Administration
- Oral and Systemic Ramifications of Cannabis Use
- Cannabis Headliners

Headliners: Prevalence of Marijuana Use Among U.S. Adults Doubles Over Past Decade; Source: National Institute on Alcohol Abuse and Alcoholism (NIAAA); division of the National Institutes of Health; posted 21 OCT 2015; accessed on 30 OCT 2017 at: <https://www.nih.gov/news-events/news-releases/prevalence-marijuana-use-among-us-adults-doubles-over-past-decade>

The percentage of Americans who reported past-year use of marijuana more than DOUBLED between 2001-2002 and 2012-2013—the increase in marijuana use disorder during that time was nearly as large. Past year marijuana use rose from 4.1% to 9.5% of the U.S. adult population—the prevalence of marijuana use disorder rose from 1.5% to 2.9%

'Based on the results of our surveys, marijuana use in the United States has risen rapidly over the past decade, with about 3 in 10 people who use marijuana meeting the criteria for addiction. Given these increases, it is important that the scientific community convey information to the public about the potential harms.'--Source: George Koob, Ph.D., director of NIAAA

'These findings highlight the changing cultural norms related to marijuana use, which could bring additional public health challenges related to addiction, drugged driving and access to effective treatment. NIDA will continue to work with our partners at NIAAA and across the federal government to educate the public and policymakers on these and other issues related to the use of psychoactive drugs.'--Source: Nora D. Volkow, M.D.; director; National Institute on Drug Abuse (NIDA)

When examined by age, young adults (ages 18–29) were found to be at highest risk for marijuana use and marijuana use disorder—use increased from 10.5% to 21.2% and disorder increasing from 4.4% to 7.5% over the past decade

Something to consider:

- As marijuana and alcohol are frequently used together, more research is also needed to understand the effects of combined use—studies have suggested that using marijuana and alcohol together impaired driving more than either substance alone and that alcohol use may increase the absorption of THC (the psychoactive chemical found in marijuana)

In June 2015, NIAAA published a study based on NESARC data showing that alcohol use disorder (AUD) was on the rise in the U.S. over the last decade—the results showed that nearly one-third of adults in the United States have an AUD at some time in their lives, but only about 20% seek AUD treatment

Headliners: What is the scope of marijuana use in the United States?; Source: National Institute on Alcohol Abuse and Alcoholism (NIAAA); division of the National Institutes of Health; posted AUG 2017: accessed on 30 OCT 2017 at: <https://www.drugabuse.gov/publications/research-reports/marijuana/what-scope-marijuana-use-in-united-states>

In 2016, 9.4% of 8th graders reported marijuana use in the past year and 5.4% in the past month ('current use')

Among 10th graders, 23.9% had used marijuana in the past year and 14.0% in the past month

Rates of use among 12th graders were higher—35.6% had used marijuana during the year prior to the survey and 22.5% used in the past month

Additionally, 6.0% of 12th graders reported they used marijuana daily or near-daily

Headliners: Key Substance Use and Mental Health Indicators in the United States: Results from the 2016 National Survey on Drug Use and Health; Rebecca Ahrnsbrak et al; The Substance Abuse and Mental Health Services Administration; September 2017; accessed 24 OCT 2017 at: <https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2016/NSDUH-FFR1-2016.htm#illicit2>

An estimated 24.0 million Americans aged 12 or older in 2016 were current users of marijuana—this number of past month marijuana users corresponds to 8.9% of the population aged 12 or older

The percentage of people aged 12 or older who were current marijuana users in 2016 was higher than the percentages from 2002 to 2015—this increase in marijuana use among people aged 12 or older reflects the increase in marijuana use by adults aged 26 or older and, to a lesser extent, the increase in marijuana use among young adults aged 18 to 25

2016 Stats:

Aged 12 to 17

- In 2016, 6.5% of adolescents aged 12 to 17 were current users of marijuana—meaning that approximately 1.6 million adolescents used marijuana in the past month
- The percentage of adolescents in 2016 who were current marijuana users was lower than the percentages in most years from 2009 to 2014 (but it was similar to the percentage in 2015)

Aged 18 to 25

- In 2016, about 1 in 5 young adults aged 18 to 25 (20.8%) were current users of marijuana—meaning that 7.2 million young adults used marijuana in the past month
- The percentage of young adults who were current marijuana users in 2016 was higher than the percentages between 2002 and 2013 (but it was similar to the percentages in 2014 and 2015)

Aged 26 or Older

- In 2016, 7.2% of adults aged 26 or older were current users of marijuana—representing about 15.2 million adults in this age group
- The percentage of adults aged 26 or older who were current marijuana users in 2016 was higher than the percentages in 2002 to 2015

History Lesson

Around 2,700 B.C., the first documented consumption of cannabis was attributed to the Chinese herbalist Emperor Shen Nung

In cannabis, the Emperor found a remedy for gout, rheumatism, malaria and absentmindedness

Indian culture also named cannabis one of the five sacred plants in The Vedas—sacred Hindu texts dating back to 1,400 B.C.

In India cannabis was smoked and also mixed with milk, ghee and spices, in the concoction of an intoxicating beverage called **bhang**

History of Marijuana in the U.S.

March 25, 1584

- Queen Elizabeth granted a charter to Sir Walter Raleigh to explore and establish colonies in the 'New World'
- Soon after, a colony was established in Roanoke, North Carolina where Thomas Harriot (a pal of Walter's) wrote in his journal that he witnessed hemp growing wild in the nearby North American region that would soon be called Virginia

August 2-4, 1619

- The Virginia colony enacts legislation making hemp a mandatory crop for ALL farmers
- In 1553, Henry VIII passed a similar act in Britain that forced farmers with 60+ acres to devote a quarter-acre to hemp cultivation

April 30, 1789

- George Washington—whose Virginia farm was partially dedicated to growing hemp—is inaugurated at the first president of the United States
- Thomas Jefferson was also growing hemp at his Virginia farm and actually developed a device for processing hemp in 1815

September 11, 1836

- Fitz Hugh Ludlow is born in New York City—his 1857 story 'The Hasheesh Eater' is one of the first cultural representations of recreational marijuana use

April 29, 1911

- Massachusetts becomes the first U.S. state to ban cannabis

July 2, 1911

- Henry J. Finger urges the first international opium conference to take up the question of marijuana—Finger is especially concerned with California's influx of 'Hindoos' and their 'demand for cannabis indica'
- By 1913, California was among states which had outlawed cannabis

February 19, 1925

- The League of Nations signed a multilayer treaty restricting 'Indian hemp' to scientific and medical uses only

October 29, 1929

- The stock market crashes and with the beginning of the Great Depression came the appointment of **Harry Anslinger** as America's first drug czar
- Anslingers' quotes resonated with newspaper magnate, Willian Randolph Hearst—not a big fan of cannabis or industrial hemp because he had vast investments in the timber industry (which provided the newsprint he printed his papers on)
- Hearst made sure Mr. Anslinger and his rants also drew front-page ink—the duo brought the word 'marihuana' into the English lexicon as it related to shady Mexican immigrants
- About this same time, the Dupont company was introducing its new manmade fiber—nylon—which would also have direct competition from cannabis' super fibers
- Andrew Mellon of Mellon Bank was one of Dupont's financial backers—as well the Treasury Secretary of the United States which made him Harry Anslinger's boss
- Additionally, Harry Anslinger was married to Mellon's favorite niece

- During the decade of the 1920's various states started passing laws regulating marijuana as a poison—Iowa, Nevada, Oregon, Washington, Arkansas, Nebraska, Louisiana and Colorado all passed legislation placing marijuana under the same restrictions as other poisons
- In all, thirty states had marijuana restriction laws on the books by the time Prohibition was repealed in 1933

March 3, 1930

- The Production Code Administration—known as the 'Hays Office'—began regulating American cinematic releases—all depictions of narcotics use was banned (although the code itself was not widely enforced until 1934)

March 9, 1931

- Louis Armstrong is charged in California for possession of marijuana while on tour
- Armstrong was a lifelong advocate for cannabis use and even tried to convince Dwight D. Eisenhower to legalize it in the 1950's

November 24, 1936

- A Hearst Metrotone Newsreel decrying the dangers of marijuana premieres in U.S. cinemas
- Additionally, films like 'Marijuana' and 'Reefer Madness (Tell Your Children)' are released—they remain cultural touchstones in the cannabis legalization debate

August 2, 1937

- President Franklin D. Roosevelt signed the Marijuana Tax Act which banned cannabis use, production and sales—including industrial hemp products

September 13, 1938

- New York mayor Fiorello La Guardia expressed concern to the NY Academy of Medicine about the need for impartial research into the 'marijuana problem'
- La Guardia convened the 'La Guardia Committee' which sought to determine the effects of the drug and the validity of the federal government's case for prohibition
- The committee found that marijuana use did not lead to violence, addiction or use of other narcotics—and recommended decriminalization and regulation in their 1944 report

December 7, 1941

- The U.S. entered WWII—and hemp restrictions were loosened
- By 1942, a newsreel was produced entitled Hemp for Victory—which encouraged farmers to grow hemp to help boost wartime production

February 25, 1949

- Actor Robert Mitchum was released from prison after serving two months for marijuana possession

August 16, 1964

- A San Franciscan named Lowell Eggemeier marches into the city's Hall of Justice and lights a joint in the presence of the police inspector
- 'I am starting a campaign to legalize marijuana smoking. I wish to be arrested.'--Source: Eggemeier

January 10, 1965

- Beat poet Allen Ginsberg leads a march for legalization of marijuana outside the New York Women's House of Detention in lower Manhattan

March 22, 1972

- A federal commission report ordered by President Richard Nixon recommended decriminalizing marijuana—Congress does not act on the legislation

September 15, 1978

- Cheech and Chong's 'Up in Smoke' premiered—the film represented the beginning of a new era of marijuana in popular culture

October 14, 1982

- Nancy Reagan made an appearance at Longfellow Elementary School in Oakland, CA and was asked by a student what to do if someone offered her drugs
- Her response became a hallmark of the 1980's war on drugs

September 6, 1988

- Drug Enforcement Administration (DEA) Chief Administrative Law Judge Francis Young issued the ruling 'In the Matter of Marijuana Rescheduling'
- **Judge Francis Young's Quote:**
'Marijuana, in its natural form, is one of the safest therapeutically active substances known to man. By any measure of rational analysis, marijuana can be safely used within a supervised routine of medical care. It would be unreasonable, arbitrary and capricious for DEA to continue to stand between those sufferers and the benefits of this substance in light of the evidence in this record. The administrative law judge recommends that the Administrator conclude that the marijuana plant considered as a whole has a currently accepted medical use in treatment in the United States, that there is no lack of accepted safety for use of it under medical supervision and that it may lawfully be transferred from Schedule I to Schedule II [of the federal Controlled Substances Act].'
- The government ignored the judge's suggestion for rescheduling and marijuana maintained its status as a Schedule 1 narcotic

November 5, 1996

- Californians adopt Proposition 215 which legalized the use of medical marijuana in the state

November 3, 1998

- Alaska, Oregon, Washington and Arizona passed medical cannabis laws and patent protections

November 7, 2000

- Nevada, Hawaii and Colorado voters approved medical cannabis initiatives

November 2, 2004

- Montana and Vermont voters approved medical marijuana initiatives and legislation

June 6, 2005

- The Supreme Court upheld the power of Congress to prohibit and prosecute medical marijuana even in the eleven states that permitted it

November 3, 2010

- California rejected a proposition that would have legalized and taxed marijuana for recreational use

November 6, 2012

- Washington and Colorado became the first states to legalize recreational marijuana use as referendums appeared on ballots in several states

November 4, 2014

- Legalization of recreational marijuana use is passed in Washington, DC, Oregon and Alaska

How does marijuana work?

In order to understand how cannabis works in the body, it is necessary to examine the body's **endocannabinoid system**

The endocannabinoid (EC) system—named after the marijuana plant *Cannabis sativa* and its active ingredient delta-9-tetrahydrocannabinol (THC)—is a unique communications system in the brain and body that affects many important functions

In 1964, researchers in Israel discovered the therapeutically active substances in cannabis that have come to be called **cannabinoids**—more than 20 years later, in 1988, researchers identified the human body's endocannabinoid system

Further research endeavors led to the discovery and identification of specialized receptors in the body associated with the endocannabinoid system

Cannabinoid receptors are present throughout the body and are embedded in cell membranes—they are believed to be more numerous than any other receptor system in the body

Knowledge of these receptors—CB1 and CB2—has greatly enhanced the overall knowledge of how cannabinoids synergistically interact with other cannabinoids and endocannabinoids to produce sometimes profound systemic effects

CB1 Receptors

- CB1 receptors are located throughout the brain and central nervous system predominately but are also found in the kidneys, liver, lungs, digestive tract, and even the eyes
- Cannabinoid CB1 receptors influence brain functions—including pleasure, appetite, concentration, perception of time and memory, pain tolerance, and other psychological and physiological functions
- In the brain, the CB1 receptors are abundant in the cerebellum, basal ganglia, hippocampus and dorsal primary afferent spinal cord regions—which is why cannabinoids influence functions such as memory processing, pain regulation and motor control
- In the brain stem, the concentration of cannabinoids is low because these receptors are not present in the basal regions of the brain that are responsible for vital functions (such as heart and respiratory function)—explaining why sudden death overdoses due solely to cannabis use simply do not occur

CB2 Receptors

- CB2 receptors are primarily found in the peripheral organs—especially particular tissues associated with the immune system (including the tonsils, thymus, spleen, and bone marrow)
- During situations of injury or inflammation, the CB2 receptors can also be created and up-regulated in other tissues where they are not normally found
- The endocannabinoid system is not only responsible for **immune function** but it regulates and affects proliferation of the integumentary system (responsible for skin and hair)—in the near future, researchers are hoping to find ways to keep the endocannabinoid system in balance to control skin conditions (psoriasis, eczema, acne, dermatitis, systemic sclerosis, etc)

Endocannabinoids are molecules made in the body to interact with cannabinoid receptors

The two most well understood of these molecules are called **2-arachidonoylglycerol (2-AG)** and **anandamide**

The endocannabinoids are synthesized on-demand from cell membrane **arachidonic acid derivatives**, have a local effect and short half-life before being degraded by the enzymes fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL)

Recently, endocannabinoid hydrolytic enzymes such as **fatty acid amide hydrolase (FAAH)** and **monoacylglycerol lipase (MAGL)** have become **new therapeutic targets in the treatment of major depressive disorder**

Several FAAH or MAGL inhibitors are reported to have no cannabimimetic side effects and could provide potential therapeutic options for patients with MDD who are resistant to first-line antidepressants (selective serotonin and serotonin-norepinephrine reuptake inhibitors)--Source: Ogawa S and Kunugi H: Inhibitors of Fatty Acid Amide Hydrolase and Monoacylglycerol Lipase: New Targets for Future Antidepressants *Curr Neuropharmacol*. 2015; 13(6):760-75. Accessed on 26 OCT 2017 at: <https://www.ncbi.nlm.nih.gov/pubmed/26630956>

Headliners: U.S. Antidepressant Use Jumps 65% in 15 Years; Laura Pratt; lead investigator; CDC's National Center for Health Statistics (NCHS); results released 15 AUG 2017; as reported by HealthDay News; 15 AUG 2017; accessed on 23 OCT 2017 at: <http://klinikkok.com/uncategorized/u-s-antidepressant-use-jumps-65-percent-in-15-years/>

According to the CDC, the number of Americans who say they have taken an antidepressant over the past month rose by 65% between 1999 and 2014

The 2017 report is based on replies by more than 14,000 Americans—aged 12 and older—to a federal government health survey conducted between 2011 and 2014 (results were compared to those from prior surveys stretching back to 1999)

By 2014, about one in every eight Americans over the age of 12 reported recent antidepressant use. Women are nearly TWICE as likely as men to be taking the medications—with antidepressants used by 16.5% of females compared to just under 9% of males

“Despite our society being progressive, there are still ongoing gender stigma related to seeking treatment for depression. It is more ‘OK’ for a woman to be depressed and seek out treatment for this, whereas men are supposed to be tough, suck it up and move on. One other possible confounder is that males, in my experience, are more upset by the sexual side effects associated with antidepressants—such as erectile dysfunction and delayed ejaculation—and could make them more reluctant to take these medications.”--Source: Dr. Seth Mandel; director of psychiatry; Northwell Health's Huntington Hospital (Huntington, NY)

The researchers noted that ‘one-fourth of all people [surveyed] who took antidepressants over the past month reported having taken them for 10 years or more’

Why the steep rise in antidepressant use?

One explanation:

- ‘People have become increasingly stressed and depressed in our society. Social media continues to paradoxically cause people to be more isolated and out of touch with their feelings. In addition, direct-to-consumer advertising, coupled with an evolving societal mindset to just take a pill to make things better, both contributed to the growth in antidepressant use over this time period.’--Source: Dr. Seth Mandel; director of psychiatry; Northwell Health's Huntington Hospital (Huntington, NY)

2-arachidonoylglycerol (2-AG)

As the most abundant endocannabinoid, 2-AG is a full agonist for cannabinoid receptors (CB1 and CB2)—although, as a potent immune modulator, 2-AG is often recognized as the primary agonist for the CB2 receptor

CB2 receptors occur mainly in peripheral locations of the cells and organs associated with the immune system and are involved in control of inflammatory reactions—upon stimulation by 2-AG, inhibition of the release of proinflammatory cytokines and increased release of anti-inflammatory cytokines is seen--Source: Zubrzycki M et al: A New Face of Endocannabinoids in Pharmacotherapy; accepted for

publication 16 DEC 2013; accessed on 26 OCT 2017 at:

http://www.jpp.krakow.pl/journal/archive/04_14/articles/02_article.html

2-AG was shown to inhibit the overexpression of inflammatory cytokines such as tumor necrosis factor alpha (TNF- α), IL-1 β , and inducible nitric oxide synthase (iNOS)—Source: Ben Li et al: Endocannabinoid 2-arachidonoylglycerol protects inflammatory insults from sulfur dioxide inhalation via cannabinoid receptors in the brain; appearing in Journal of Environmental Sciences; Volume 51, January 2017, Pages 265–274. Accessed on 26 OCT 2017 at:

<http://www.sciencedirect.com/science/article/pii/S1001074216302340>

Complex tasks coordinated by the body and brain (such as appetite, sleep, and pain perception) are also influenced by 2-AG because of its effects on the CB1 receptors

Summary of 2-AG Functions:

- Immune function***
- Bone health***
- Pain***
- Mood
- Metabolism
- Reproduction
- Memory
- Movement
- Sleep
- Neuroprotection

Anandamide (AEA)

Anandamide serves many functions in the body—one of its main functions is to control local inflammatory responses

Anandamide is quickly constructed in synaptic spaces and rapidly reduces the release of inflammatory cytokine molecules—this sets off a chain reaction and results in the shut down of long term potentiation ('LTP') of pain

Not only does anandamide have anti-inflammatory and analgesic properties, but this endocannabinoid also modifies broad categories of brain responses throughout sensory and motor circuits—aiding in sleep, appetite regulation, anxiety, anti-cancer cell spread, hormone regulation, brain neuroplasticity and emotional regulation

Anandamide stimulates the brain in its pleasure centers and creates a state of bliss—in fact the person who discovered this molecule named it 'anandamide' because in the ancient Sanskrit language 'ananda' means 'bliss'

On March 24, 1992, Lumír Hanuš, a Czech analytical chemist working in Israel with American pharmacologist William Devane, isolated bliss-inducing anandamide—the first known endocannabinoid in the human brain

Here's the KEY:

- There is a great overlap in pleasure and pain circuits—when pleasure molecules such as anandamide are released, they dominate pain chemistry
- Consciously pursuing the experience of pleasure and happiness is a wonderful way to counteract pain

Phytocannabinoids

Phytocannabinoids are cannabinoids that occur naturally in the cannabis plant

Of over 480 different compounds present in the cannabis plant, about 85+ have been identified as cannabinoids—the most well-known of these compounds is the delta-9-tetrahydrocannabinol (Δ^9 -THC) which is the main psychoactive ingredient in the plant

Out of the individual cannabinoids found in marijuana, THC is the only one that produces powerful, intoxicating, psychoactive effects

Endogenous cannabinoids such as anandamide function as neurotransmitters because they send chemical messages between neurons throughout the nervous system

KEY: THC's chemical structure is very similar to anandamide—this similarity in structure allows THC to be recognized by the body and to alter normal brain communication

Because the endocannabinoid system plays a critical role in neuronal functioning, interfering with it can have profound effects

- For example, THC is able to alter the functioning of the **hippocampus** and **orbitofrontal cortex**—areas of the brain that enable a person to form new memories and shift his or her attentional focus
 - Because of this, using marijuana can cause impaired thinking and interference with a person's ability to learn and perform complicated tasks
- THC also disrupts functioning of the **cerebellum** and **basal ganglia**—these areas of the brain regulate balance, posture, coordination, and reaction time
 - For this reason, use of marijuana may impair driving and may cause problems with playing sports or engaging in other physical activities
- THC also activates the **brain's reward system**—regions that govern the response to healthy pleasurable behaviors such as sex and eating
 - When consumed, THC releases the signaling chemical dopamine at levels higher than typically observed in response to natural stimuli—this flood of **dopamine** contributes to the pleasurable 'high' that those use who recreational marijuana seek

There are a few key differences between THC and anandamide—namely, THC lasts a lot longer than natural endocannabinoids do

- Anandamide actually begins to break down in a matter of minutes after binding to a cell—THC's half-life can last several days in frequent users

Other phytocannabinoids such as **cannabidiol (CBD)** and **cannabinol (CBN)** are gaining the interest of researchers due to a variety of healing properties

Cannabinol (CBN)

Cannabinol (CBN) is the product of degradation by oxidation of THC—when THC is exposed to oxygen and heat, it breaks down to CBN

Although only mildly psychoactive, evidence has suggested that CBN offers a variety of therapeutic benefits—including promoting sleep, stimulating appetite, stimulating bone growth, preventing glaucoma, and providing antibacterial, anti-inflammatory and analgesic effects

Of all the cannabinoids, CBN has been shown to be the most sedative—making it a potential therapeutic option for those with insomnia, sleep apnea or other sleep disorders

Evidence demonstrated that when CBN was applied topically, it was effective against MRSA--Source: Appendino, G., Gibbons, S., Giana, A. Pagani, A., Grassi, G., Stavri, M., Smith, E., and Rahman, M.M. (2008, August). Antibacterial cannabinoids from Cannabis sativa: a structure-activity study. Journal of Natural Products, 71(8), 1427-30. Retrieved from <http://pubs.acs.org/doi/pdf/10.1021/np8002673>.

CBN has been shown to have anti-inflammatory effects—leading some to speculate that it could assist in the treatment of inflammatory diseases and disorders like multiple sclerosis, rheumatoid arthritis, diabetes, allergic asthma, and Crohn’s disease--Source: Croxford, J.L., and Yamamura, T. (2005, September). Cannabinoids and the immune system: potential for the treatment of inflammatory diseases? *Journal of Neuroimmunology*, 166(1-2), 3-18. Retrieved from [http://www.jni-journal.com/article/S0165-5728\(05\)00160-8/fulltext](http://www.jni-journal.com/article/S0165-5728(05)00160-8/fulltext)

As a weak agonist of both CB1 and CB2 receptors, CBN is thought to reduce the risk of osteoporosis and other bone diseases and support bone health--Source: Idris, A.I., van’t Hof, R.J., Greig, I.R., Ridge, S.A., Baker, D., Ross, R.A., and Ralston, S.H. (2005, July). Regulation of bone mass, bone loss and osteoclast activity by cannabinoid receptors. *Nature Medicine*, 11(7), 774-9. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1430341/>.

Cannabidiol (CBD)

CBD is the second to THC as the most discussed cannabinoid in marijuana

CBD is classified as a ‘non-psychoactive cannabinoid’—meaning it does not contribute to the euphoria associated with certain strains of cannabis

It is, however, psychoactive because it crosses the blood-brain barrier

CBD works its by inhibiting the enzyme fatty acid amide hydroxyls (FAAH) that is responsible for breaking down anandamide—this increases the amount of natural endocannabinoids present in the system

Unlike THC, CBD can be administered at relatively high doses without undesired psychological side effects

For medical marijuana users, CBD offers an opportunity to treat many diseases without the mental side-effects of getting high—CBD is considered an especially attractive option for treating children with illnesses that can be treated with marijuana

Headliners: A Primer About Cannabidiol and the Benefits of CBD; Source: Dr. David Bearman; contributor; Huffington Post: posted 2 MAR 2017; accessed on 30 OCT 2017 at:

https://www.huffingtonpost.com/entry/cannabidiol-cbd-a-primer_us_58b7129ee4b0ddf654246290

Studies demonstrated that cannabidiol (CBD) was neuroprotective against both excitatory transmitter- (glutamate) and oxidant- (hydroperoxide) induced neurotoxicity—conditions caused by stroke,

traumatic brain injury (TBI), or being placed on a heart-lung machine during cardiac bypass surgery

CBD has also shown promise in treating anxiety, depression and **schizophrenia**—it increases levels of the neurotransmitter serotonin and anandamide which reduces pain and anxiety

- German researchers showed in 2012 that giving CBD to schizophrenic patients reduced psychotic symptoms such as hallucinations and disordered thinking
- About 100,000 people in the United States will be diagnosed with schizophrenia this year

CBD has garnered much interest in its **effects on cancer**

Based on current research, CBD has demonstrated positive effects in treating these types of cancer:

- Breast
- Glioma
- Leukemia
- Lymphoma
- Lung
- Thyroid
- Colon

‘Collectively, the non-psychoactive plant-derived cannabinoid CBD exhibits pro-apoptotic and anti-proliferative actions in different types of tumours and may also exert anti-migratory, anti-invasive, anti-metastatic and perhaps anti-angiogenic properties. On the basis of these results, evidence is emerging

to suggest that CBD is a potent inhibitor of both cancer growth and spread.'--Source: Massi, Paola et al: Cannabidiol as Potential Anticancer Drug; British Journal of Clinical Pharmacology 75(2) (2013): 303–312. PMC. Web. 30 Oct. 2017

In early 2014, a CNN documentary by Sanjay Gupta, M.D. pointed out the **anti-epileptic properties of CBD**

Additionally, the American Epilepsy Society (AES) reported in February 2017 that CBD was effective in combating epilepsy—with the substance exhibiting acute efficacy in treating the condition within children

Routes of Administration

Different routes of cannabinoid administration have different effects

Inhaled THC enters capillaries in the lungs, passes into general circulation through the pulmonary arteries and goes directly to the brain without passing through the liver

- The cannabinoids then cross the blood-brain barrier to affect the endocannabinoid receptors (CB1)
- In addition, when cannabis is burned new compounds are created not found in the raw or dried plant
- On the first pass through the liver, 85% of THC is metabolized—part of the cannabis is metabolized to **11-hydrox-THC**
- This THC metabolite activates CB1 cannabinoid receptors in the brain and it induces a 'high' more potently than THC itself

Vaporizing or 'vaping' of cannabis has gained in popularity over the last several years—just as e-cigarettes have

- Essentially, vaping is the heating of cannabis without burning—the heat releases the active ingredients into a vapor that is then released into the air in a fine mist created by a vaporizer device
- 'Since combustion does not occur, smoke is not created'

Vaping Device Components

- Rechargeable lithium battery
A cartridge containing desired vaping solution (with or without flavorings)
- A microchip activates the battery when the e-cigarette is puffed—causing the atomizer to create heat which in turn vaporizes the liquids in the sponge to create vapor
- Atomizer

Studies have shown that people who vape cannabis perceive it to have health benefits and find it to be safer and less harmful to their health than smoking

In a recent 2014 study of about 100 subjects who both smoked and vaporized, users identified four advantages to using a vaporizer over smoking marijuana: perceived health benefits, better taste***, no smoke smell, and more effect from the same amount of marijuana--Source: Malouff JM et al:

Experiences of marijuana-vaporizer users. *Subst Abus.* 2014;35(2):127-8. accessed on 31 OCT 2017 at: <https://www.ncbi.nlm.nih.gov/pubmed/24821347>

Let's Talk Flavor

- In addition to solvents, vaping products also contain chemical flavorings and food preservatives from the vaping liquid
- Although most of these additives received a 'GRAS' or 'generally recognized as safe' designation by FDA, the designation is based on tests of the compounds when they are ingested—not inhaled

- Even the Flavor Extracts Manufacturers Association argues that it would be ‘false and misleading’ to claim that food-grade flavorings are inherently safe to vape
- Researchers are reporting that certain vaping flavorings can harm lung cells—after exposing human lung cells to various doses of 13 flavorings for either 30 minutes or 24 hours, five of the flavorings (hot cinnamon candies, banana pudding [southern style], kola, vanilla and menthol tobacco) tested caused harmful effects
- Detrimental effects included reduced cell replication and, at higher doses, spurred cell death
- Measured for the first time in the Monitoring the Future survey in 2014, students were asked about what they vaporized the last time they used a vaping device—a significant majority (over 60% across all grades) reported vaporizing ‘just flavoring’

When **ingested orally**, THC and other cannabinoids are absorbed from the small intestine over several hours

- THC and the other constituents are then carried to the liver, where THC is metabolized by subclasses of cytochrome P450 enzyme system (‘mixed function oxidase system’)—about 85% of the THC is metabolized on its first pass through the liver
- Orally consumed cannabinoids take about 45-75 minutes before enough of the plant constituents are in the bloodstream to exert a therapeutic effect
- Additionally, there is a greater effect of a THC metabolic breakdown product—11-hydroxy-THC
- Consumers can use cannabis-infused oil, butter, or syrup to create edibles such as brownies, lollipops or beverages

Transdermal patches with incorporated cannabis deliver cannabinoids directly into the bloodstream without passing through the liver—avoiding the ‘higher high’ caused by ingesting edibles

Tinctures of liquid cannabis are often administered sublingually where cannabinoids are introduced directly to the bloodstream

Oral and Systemic Ramifications of Cannabis Use

Headliners: Marijuana's Health Effects? Top Scientists Weigh In; Dr. Marie McCormick; lead investigator and chair of the NAS committee; as reported by Patricia Neighmond for NPR; 12 JAN 2017; results appearing in National Academies of Sciences, Engineering and Medicine; accessed 24 OCT 2017 at: <http://www.npr.org/sections/health-shots/2017/01/12/509488977/marijuanas-health-effects-scientists-weigh-in>

A report by the National Academies of Sciences, Engineering and Medicine analyzed more than 10,000 studies to see what could conclusively be said about the health effects of marijuana

Despite the drug's increasing popularity conclusive evidence about its positive and negative medical effects is hard to come by

According to the report, the lack of evidence is at least partly because the federal drug enforcement agency's designation of the drug as a Schedule I substance—having ‘no currently accepted medical use and a high potential for abuse’—entails so many restrictions that it has been difficult for researchers to do rigorous research on marijuana

Medical Benefits

Pain relief

- Regarding chronic pain, there is evidence that patients who are treated with cannabis or cannabinoids ‘are more likely to experience a significant reduction in pain symptoms’
- Researchers stated that for adults with muscle spasms related to multiple sclerosis, there is ‘substantial evidence’ that short-term use of certain oral cannabinoids can improve symptoms

- For adults with chemotherapy-induced nausea and vomiting, ‘there is conclusive evidence’ that certain oral cannabinoids are effective in preventing and treating those ailments

Health Risks

There is **no evidence** that smoking marijuana **increases the risk for cancers** often associated with tobacco use, such as lung and head and neck cancers

More research is needed to determine whether marijuana use is associated with **heart attack and stroke**

- ‘Some evidence suggests smoking marijuana may trigger a heart attack among individuals with diagnosed heart disease’

There was also **some evidence** that smoking marijuana **during pregnancy** was linked to lower birth weight in the offspring

Headliners: Pregnant and Smoking Pot—with Risks Unclear; Source: As reported by Catherine Saint Louis; New York Times News Service; appearing in the Idaho Statesman; 3 FEB 2017

- Often pregnant women presume that cannabis has no consequences for developing infants but preliminary research suggests otherwise: THC can cross the placenta to reach the fetus and can also be present in breast milk
- Almost 4% of mothers-to-be reported that they had used marijuana in the past month in 2014—compared with 2.4% in 2002
- Young mothers-to-be were particularly likely to turn to marijuana: Roughly 7.5% of 18- to 25-year-olds said they had used marijuana in the past month in 2014, compared with 2% of women ages 26 to 44
- The American Academy of Pediatrics and the American College of Obstetricians and Gynecologists both advise against prenatal cannabis use because of its links to cognitive impairment and academic underachievement

Asthma and other chronic respiratory problems

- Evidence suggests that smoking marijuana on a regular basis is associated with more frequent chronic bronchitis and worse respiratory symptoms
- However, it was unclear whether the drug increases the risk of developing asthma or chronic obstructive pulmonary disease

Injury or death

- In terms of risk to life and limb, the NAS committee found that driving under the influence of cannabis ‘increase[d] the risk of being involved in a motor vehicle accident’

The report also cited evidence that **increasing numbers of young children may be accidentally ingesting marijuana products** now—particularly in states where cannabis use is legal

Substance abuse disorders

The evidence that marijuana is a **gateway drug** to trying other drugs—including tobacco—was ‘**limited**’ There was ‘**moderate evidence**’ that there was a link between cannabis use and the development of **substance dependence** or **abuse problems** with alcohol, tobacco and illicit drugs

The evidence suggested that initiating marijuana use at a younger age ‘increase[d] the likelihood of developing dependency, which can affect academic performance and social interactions’

‘The adolescent brain is very sensitive to these kinds of substances. So they continue to use it—and may use it in increasing amounts—and are at risk for developing problematic cannabis use. Many health questions remain to be answered by better research. The increased legal availability of cannabis products in many states, and their increased potency make that rigorous research more important than ever.’--Source: Dr. Marie McCormick

Headliners: Adolescents May Suffer Long-Term Consequences from Marijuana Use; As reported by Lauren Glendenning for y the Healthy Futures Initiative; SummitDaily; accessed 24 OCT 2017 at: <http://www.summitdaily.com/news/adolescents-may-suffer-long-term-consequences-from-marijuana-use/>

According to the American Psychological Association (APA), the brain is extremely sensitive to damage from drug exposure throughout adolescence because the brain—especially the prefrontal cortex—is still developing until a person's early to mid-20s

The brain's **prefrontal cortex**—responsible for important functions such as impulse control, attention, focusing, organization and personality—is the last area of the brain to fully develop

Marijuana inhibits those prefrontal cortex functions

THC attaches to the brain's cannabinoid receptors and interferes with the brain's ability to function properly—the cannabinoid receptors are immature during adolescence

The endocannabinoid system is important for cognition, neurodevelopment, stress response and emotional control

According to a report by Colorado Department of Public Health and Environment, there is substantial evidence that adolescents who use marijuana weekly or more often are less likely to graduate from high school—study investigators found moderate evidence that teens and young adults who use frequently are more likely to have ongoing impairment of cognitive and academic abilities for at least 28 days after use

Teenagers might hear about the supposed benefits of marijuana— things like medicinal uses or its calming effects on those who suffer from anxiety—but information about its potentially harmful effects on young people is not widely discussed

The legal age to use marijuana in Alaska is 21—some scientists and health professionals think even that is too young because the brain is not fully developed

The Law in Alaska: Question and Answer Time

This overview details what is legal in Alaska for personal-use marijuana—however, cities and communities are allowed to pass even stricter laws (visitors and residents should review local laws prior to purchasing or using cannabis products)

Can I smoke or consume pot while in the park with my friends?

- Not in Alaska—the current law bans all public use of any form of marijuana, not just smoking
- Since marijuana is illegal federally, it cannot be used on federal land (such as national parks and national forests)

Can I use marijuana while I am cruising around town?

- Use of marijuana while operating any motorized vehicle (including cars, snowmachines, boats, ATVs, and airplanes) is not allowed
- If impaired by cannabis ingestion, the driver will receive a DUI if operating any aircraft or watercraft (whether motorized or not)

So where can I use marijuana?

- Private property is best, however, some property owners or homeowners' associations may have policies that prohibit marijuana use—check local laws and with hotel owners and landlords prior to consuming marijuana

Can I grow my own product?

- Adults aged 21+ can possess (28 gram limit), grow, and give away as many as six marijuana plants—however, only three of the plants can be mature and flowering at any one time

Can I take marijuana out of the state?

- It is illegal to leave Alaska with any marijuana products

Headliners: When Retirement Comes With a Daily Dose of Cannabis; Hu, W; reporting for the NY Times; 19 FEB 2017; accessed on 31 OCT 2017 at:

<https://www.nytimes.com/2017/02/19/nyregion/retirement-medicinal-marijuana.html>

From retirement communities to nursing homes, older Americans are increasingly turning to marijuana for relief from aches and pains

Many have embraced it as an alternative to powerful drugs like morphine—marijuana is less addictive and with fewer side effects

In a medical marijuana education and support club started by residents of Rossmore Walnut Creek (a retirement community east of San Francisco) has grown to 530 members—so many that it has changed meeting rooms three times

‘I would be in a lot worse shape if I wasn’t using cannabis, both physically and mentally.’--Source: Anita Mataraso, 72; a grandmother of six who is the program director and takes marijuana daily for arthritis, nerve pain, and other ailments

Oral Health Effects of Marijuana Use

Headliners: Periodontal and Oral Manifestations of Marijuana Use; Rawal SY et al; J Tenn Dent Assoc. 2012 Fall-Winter; 92(2):26-31; accessed 16 OCT 2017 at:

<https://www.ncbi.nlm.nih.gov/pubmed/23420976>

Researchers concluded that chronic marijuana use may result in gingival enlargement with clinical characteristics similar to phenytoin-induced enlargement

Headliners: Associations Between Cannabis Use and Physical Health Problems in Early Midlife: A Longitudinal Comparison of Persistent Cannabis vs Tobacco Users; Madeline H. Meier, PhD et al; results appearing in JAMA Psychiatry. 2016;73(7):731-740; accessed at:

<https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2526003>

To test associations between cannabis use of over 20 years and a variety of physical health indexes at early midlife, researchers examined over 1000+ study participants

Cannabis use for up to 20 years was associated with periodontal disease[s] but was not found to be associated with other physical health problems in early midlife such as lung function, systemic inflammation, and metabolic health

‘Although we found that cannabis users were generally no worse off than nonusers on almost all health indexes, they did have worse periodontal health. Cannabis use was associated with attachment loss, which can result in tooth loss. A similar association was observed for tobacco use, consistent with previous research. Tobacco’s effect on periodontal disease is thought to be mediated through increased inflammation and vasoconstriction, which may or may not be the case for cannabis. Cannabis use was not associated with systemic inflammation...but prior research has shown that cannabis use can induce **vasoconstriction***.**’--Source: Research statement

Headliners: Marijuana Use: Relevance to Clinical Practice; Interview with Dr. Jose Lança; posted 18 JAN 2017; accessed on 23 OCT 2017 at: <http://oasisdiscussions.ca/2017/01/18/marijuana/>

Dr. Jose Lança, MD, PhD, Assistant Professor of Pharmacology (University of Toronto) spoke with Dr. Chiraz Guessaier about the use of marijuana in dentistry as well as its impact on dental practice

Common adverse oral effects of cannabis use noted by Dr. Lança:

- Gingival hyperplasia
- Erythematous edema of the uvula
- ‘Nicotine’ stomatitis
- Increased periodontal disease
- Increase caries risk
- Oral papilloma

- Leukoplakia
- Alveolar bone loss

Headliners: Consumption of Cannabis and Effects on Periodontal Oral Health; Source: Suellan GY and Fine JB; appearing in the CDA Journal; 45(9): SEP 2017; accessed OCT 2017 at: https://www.cda.org/Portals/0/journal/journal_092017.pdf

When comments by researchers on this study, it was stated that the investigation 'did not provide data on the use of other illicit drugs in study population and that the association should take into account potential confounding by other substances that can affect oral health'

Xerostomia

Cannabis can and does cause excessive oral dryness—whether it is taken for recreational or medical purposes

When ingested, THC binds to endocannabinoid receptors found in the salivary glands—temporarily shutting down the lines of communication between the nervous system and the saliva-producing glands in the process

Saliva contains organic compounds that are mostly proteins or peptides that contribute significantly in protecting us

Nutrients needed for the synthesis of these compounds pass from the capillaries surrounding the glands into the acini cells

Two salivary compounds that deserve a second look:

- Lactoferrin
- Histatin

Lactoferrin

- Lactoferrin is a substance belonging to a family of chemicals called cytokines that are responsible for coordinating immune responses involved in preventing disease and infection
- Lactoferrin has the unique ability to bind to iron—an essential mineral used not only by host cells but also a wide array of pathogens and tumors depend on iron for reproduction and growth
- Presented with an infectious challenge or tumor, a healthy body will respond by producing lactoferrin in copious quantities in the vicinity of the infection or tumor where it binds systemic iron and renders it unavailable to the bacteria or malignant cells
- Lactoferrin does not remove iron from the body itself and, over time, degrades to release the iron back into the body
- Another attribute of lactoferrin involves its antimicrobial ability—special sections of lactoferrin molecules are themselves directly toxic to bacteria, yeast and molds
- Lipopolysaccharide (LPS), a pathogen produced by periodontal bacteria, not only stimulates the progress of periodontal disease but also increases the level of cholesterol and triglycerides in the blood
- It also appears that lactoferrin inhibits replication of some viruses—including HIV and some of the herpes family of viruses
- In addition, lactoferrin has demonstrated positive control of *Candida albicans* —especially when combined with fluconazole in treating resistant candidiasis in HIV+ patients

Histatin

- Histatins are a family of salivary proteins with bactericidal and fungicidal activities that contribute to the innate defense of the oral cavity
- Histatins are present in the serous granules of the parotid and submandibular glands
- Histatins are important for the initial stage of wound healing in which fast wound coverage is important for healing without infection, inflammation, or fibrosis development
- Histatin's presence in acquired pellicle prevents adhesion by *Streptococcus mutans*

- Histatins play a MAJOR role in inhibition of candidiasis

Cannabis Headliners

Headliners: Case Study Shows Chronic Marijuana Use Associated With Hypopituitarism; Pinsker R: Abstract #825; presented at: the AACE Annual Scientific and Clinical Congress; May 1-5, 2013; Phoenix, AZ; posted 3 MAY 2013; accessed 24 OCT 2017 at: <https://cushieblog.com/2013/05/03/case-study-shows-chronic-marijuana-use-associated-with-hypopituitarism/>

Results of a case study presented at the American Association of Clinical Endocrinologists 22nd Scientific and Clinical Congress demonstrated that smoking marijuana may result in serious endocrine complications

The subject of the case presented to the emergency department with dyspnea on exertion, increasing fatigue and loss of libido with no previous radiation exposure or head trauma

Labs revealed low total T3; high T3 resin reuptake; low total T4; normal free T4 and low TSH

After being started on cortisone 25mg in the morning and 12.5mg at bedtime and levothyroxine 25 mcg daily, the patient's fatigue and edema improved significantly

'Hypothalamic-Pituitary-Thyroid Axis' is critical for thyroid function—if one component is compromised, thyroid function is affected

Another example glandular axis relationship is the Hypothalamic-Pituitary-Adrenal Axis ('HPA Axis')

Headliners: New Study Confirms Cannabis Improves Immunity in HIV Patients; As reported by Steve Elliott; study results appearing in Drug and Alcohol Dependence; posted 25 SEP 2017; accessed 24 OCT 2017 at: <https://herb.co/2017/09/25/cannabis-improves-immunity-hiv/>

Researchers reported that HIV patients who tested positive for past exposure to cannabis had higher CD4+ and CD8+ counts than those who tested negative for the herb

A team of scientists from Virginia State University and University of Florida Center for AIDS/HIV Research looked at variances in the lymphocyte count among HIV patients whose urinalysis tested positive for THC and those who tested negative for THC

After adjusting for demographic and HIV-related covariates, THC-positive patients had significantly higher CD4+ and CD8+ counts than their THC-negative counterparts

The research findings were in line with previous research that demonstrated daily marijuana users had higher CD4+ cell counts and lower viral load than their non-using and infrequent using counterparts

The study findings suggested a potentially immune-bolstering beneficial role to marijuana beyond just palliation

In a 17-month study, Dr. Patricia E. Molina and her team of researchers from Louisiana State University administered concentrated THC to 4-to-6-year-old male rhesus monkeys who were SIV-positive—the simian version of HIV—twice daily

Examination of intestinal tissue before and after the THC exposure showed large decreases in tissue damage in the stomach and a significant increase in the numbers of normal cells

In the course of HIV infection, one of the earliest effects is that the virus quickly spreads through the body and kills a significant number of cells in the gut and intestine—damaging the gut in a way that allows HIV to leak through the cell wall of the intestines and into the bloodstream

'People with advanced HIV have intestinal disease and significant systemic inflammation that may cause progressive defects in immunity and speed the progression from HIV infection to AIDS. We think changes in the virome and bacterial microbiome damage gut epithelial cells and allow bacteria and viruses to leak into surrounding tissues and blood, contributing to inflammation.'--Source: Herbert W. Virgin IV, MD, PhD; Washington University School of Medicine (St. Louis, MO)

When THC is introduced into this environment, it activates the CB2 receptors in the intestines to build new, healthy bacterial cells blocking the virus from leaking through the cell walls

Bottom Line:

- While HIV kills the cells that protect the intestinal walls, it is believed that THC helps bring them back

Addiction Potential of Marijuana

There are many different opinions on how addictive THC is—research has shown an increasing likelihood that habitual abuse leads to addiction

Most experts agree that the addictive potential of THC increases with the level and consistency of use

THC Dependence

- THC dependence is not necessarily the same as THC addiction—physical dependence on THC manifests as withdrawal symptoms upon discontinuation with THC use because the body needs the presence of THC to function normally
- THC does present withdrawal symptoms—they can include anxiety, panic attacks, and depression

THC Addiction

- In contrast, addiction to THC is characterized by psychological symptoms of cravings and compulsive use
- The main symptom of THC addiction is the need to self-medicate in order to deal with the stressors of life
- Addiction can happen in those who start to abuse THC beyond medical reasons or who use THC to get high on a regular basis
- An estimated 9%-13% of users will develop an addiction to marijuana

Besides addiction, **long-term marijuana use** is known to cause many damages which include:

- Chronic cough, bronchitis and respiratory problems
- Diminished satisfaction with life
- Impaired cognitive functions
- Loss of memory
- Reduced motor coordination
- Risk of psychosis

Headliners: Michigan University Could be First Offering Marijuana-Based Degree; As reported by Matthew Smith; 19 OCT 2017; accessed on 31 OCT 2017 at: <http://www.wxyz.com/news/michigan-university-could-be-first-offering-marijuana-based-curriculum>

Northern Michigan University is believed to be the first in the nation to offer up a marijuana-based undergraduate degree—the degree is in **Medicinal Plant Chemistry**

According to the University:

- ‘Increasing legitimacy and legality of medicinal plants nationwide has created great demand for qualified technical personnel and great opportunity for the skilled entrepreneur in the cannabis, herbal extract, and natural product industries.’

Medicinal Plant Chemistry at Northern Michigan University is the only 4-year undergraduate degree program of its kind designed to prepare students for success in the emerging industries relating to medicinal plant production, analysis, and distribution

The required coursework provides a foundation in chemistry and plant biology, with a capstone research experience involving experimental horticulture and instrumental analysis of natural products

For more information, contact Dr. Mark Paulsen, Department Head, chemistry department