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

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Presenter Disclosures for Betsy Reynolds, RDH, MS

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Agenda:

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

A word or two about hemp

The many benefits of hemp:

Industrial products

- Oil paints
- Varnishes
- Printing inks
- Fuel
- Solvents
- Coatings

Foods

- Hemp seed hearts
- Hemp seed oil
- Hemp protein powder
- Food supplements

Textiles

- Clothing
- Diapers
- Handbags
- Denim
- Shoes
- Fabrics

Industrial Textiles

- Rope
- Canvas

- Tarps
- Carpeting
- Caulking
- Moulding

Paper

- Printing
- Newsprint
- Cardboard
- Packaging

Building Materials

- Fibreboard
- Insulation
- Acrylics
- Fibreglass substitute

Across Europe, awareness was growing about the extensive damage that had been done to medieval timber-frame buildings in the post-war period through ill-advised repairs using ordinary Portland cement—using this material to replace the vapour-permeable earth-and-lime mortars and natural cements in historic buildings prevented the buildings' fabric from 'breathing'

This in turn led to the retention of moisture within the fabric—resulting in damage to the timber frames

Introducing Hempcrete

- ✓ It was discovered that the stem of the hemp plant—made up of highly durable cellulose capable of going from wet to dry and vice versa almost indefinitely without degrading—was the ideal aggregate to add to lime mortars to allow for breathability
- ✓ Of added benefit, since a great deal of air is trapped inside a hempcrete wall (both within the hemp itself and within the matrix of the hemp shiv in the cast material), hempcrete proved to be a good insulating material

According to the World Health Organization, **147 million people use cannabis**—making it the most widely used drug in the world

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 Cannabis in Canada

The 1800's

1801:

The Lieutenant Governor of Upper Canada distributed hemp seeds to farmers in an effort to stimulate industry

1822:

The provincial parliament of Upper Canada allocated 300 pounds for machinery to process hemp and incentivize domestic hemp producers

The 1920's

1923:

The Narcotics Drug Act Amendment Bill introduced the Act to Prohibit the Improper Use of Opium and Other Drugs

Cannabis was deemed illegal in Canada as a result and joined opium, cocaine and morphine as banned substances

The 1960's

1962:

Cannabis gained popularity and the number of cannabis convictions escalated to 2,300 by 1968

1969:

The Canadian government formed the Royal Commission of Inquiry in the Non-Medical Use of Drugs (known as the Le Dain Commission), to investigate the non-medical uses of cannabis

The 1970's

1971:

The first pro-cannabis smoke-in was held in Vancouver's Gastown ('Grasstown') district on Water Street—known the 'Gastown Riot' or the 'Battle of Maple Tree Square'

1972:

The Le Dain Commission released a report on cannabis with recommendations that the federal government remove criminal penalties for the use and possession of cannabis

In spite of the commission's report, no steps were taken to decriminalize cannabis

The 1990's

1996:

Terrence Parker is arrested for cannabis possession, cultivation, and trafficking after he was caught growing cannabis to control his epileptic seizures—he appealed to the Canadian Charter of Rights and Freedoms

In 2000, the Ontario Court of Appeal ruled that the prohibition of cannabis use infringed on Terrance Parker's right to life, liberty and security of the person—rendering cannabis prohibition unconstitutional

The 2000's

2001:

The Canadian government enacted the Marihuana for Medical Access Regulations (MMAR) which allowed licensed patients to grow their own cannabis or access it from licensed growers

2003:

The first federal marijuana decriminalization measure which aimed to reduce the possession of up to 15 grams of cannabis to a civil fine was introduced—the bill died (mostly due to pressure from the U.S. Drug Enforcement Administration)

2004:

An identical decriminalization measure was introduced and was also defeated

2005:

City authorities in Vancouver drafted a plan entitled 'Preventing Harm from Psychoactive Drug Use' in an attempt to regulate cannabis sales through the Four Pillars Drug Strategy

2006:

Prime Minister Stephen Harper announced a new national anti-drug strategy that was designed to impose mandatory prison sentences for cannabis dealers and anyone charged with growing more than 500 plants

Those convicted were to face a two-year minimum sentence—maximum penalties for producing cannabis increased from 7 to 14 years in jail

2011:
Justice Donald Taliano ruled that the MMAR and the prohibitions against the possession and production of cannabis were constitutionally invalid and ordered that the government fix the program accordingly
2013:
The government implemented the Marihuana for Medical Purposes Regulations (MMPR)—creating a commercially licensed industry for the production and distribution of medicinal cannabis in the process
2015:
Owen Smith, a cannabis baker from Victoria BC, was charged with the possession of cannabis-infused cookies—the Supreme Court of Canada ruled that restricting legal access to only dried cannabis flower violated the constitutional rights of medical patients after Smith appealed the charges
As a result, licensed producers were now allowed to produce cannabis oils and patients were allowed to possess and alter different forms of cannabis
2016:
Neil Allard challenged the MMPR for suspending personal production licenses from patients and requiring patients to access cannabis solely through licensed producers
The Federal Court of Canada ruled in Allard's favor, and revised the law yet again with the Access to Cannabis for Medical Purposes Regulations (ACMPR)
2017:
The Government of Canada proposed the Cannabis Act designed to legalize the possession, use, cultivation, and purchase of limited amounts of cannabis by adults 18+ years of age
2018:
The Cannabis Act went into effect—legalizing cannabis for adult use nationwide

Cannabis Legalization and Regulation

As of 17 OCT 2018, cannabis use is legal—the Cannabis Act created the strict legal framework for controlling the production, distribution, sale and possession of cannabis across Canada
For more information, please visit: http://www.justice.gc.ca/eng/cj-jp/cannabis/

Goals of the Cannabis Act:

- Keep cannabis out of the hands of youth***
- Keep profits out of the hands of criminals
- Protect public health and safety by allowing adults access to safe, legal cannabis

Age Restrictions

- No person may sell or provide cannabis to any person under the age of 18
- The Cannabis Act created two new criminal offences:
- Giving or selling cannabis to youth
- Using a youth to commit a cannabis-related offence
- With maximum penalties of 14 years in jail!

The Cannabis Act helps discourage youth cannabis use by prohibiting:

- Products that are appealing to youth
- Packaging or labelling cannabis in a way that makes it appealing to youth
- Selling cannabis through self-service displays or vending machines
- Promoting cannabis, except in narrow circumstances where young people could not see the promotion

- Penalties for violating these prohibitions include a fine of up to $5 million or three years in jail

Cannabis edible products and concentrates are legal for sale as of October 2019 (approximately one year after the enactment of the Cannabis Act)

While federal, provincial and territorial governments share responsibility for overseeing the proposed new system, the Cannabis Act was designed to protect public health through creating strict safety and quality regulations—including public education efforts*** to raise awareness about safety measures and any potential health risks

The Government of Canada has committed close to $46 million over the next five years for cannabis public education and awareness activities—these are to inform Canadians (especially youth) of the health and safety risks of cannabis consumption

The Federal government's responsibilities are to set:

- Strict requirements for producers who grow and manufacture cannabis
- Industry-wide rules and standards, including:
- Types of cannabis products available for sale
- Packaging and labelling requirements for products
- Standardized serving sizes and potency
- Prohibitions on the use of certain ingredients
- Good production practices
- Tracking requirements of cannabis from seed to sale to keep it out of the illegal market
- Restrictions on promotional activities

Provinces and territories are responsible for developing, implementing, maintaining and enforcing systems to oversee the distribution and sale of cannabis

Provinces and territories will also be able to add their own safety measures

Examples include:

- Increasing the minimum age in their province or territory (but not lowering it)
- Lowering the personal possession limit in their jurisdiction
- Creating additional rules for growing cannabis at home, such as lowering the number of plants per residence
- Restricting where adults can consume cannabis, such as in public or in vehicles

To monitor cannabis consumption before and after the legislative change, Statistics Canada has been conducting the **National Cannabis Survey ('CNS')** every three months in order to provide the latest information about cannabis use in Canada—analyses of data for the first three quarters of 2019 are available at: https://www150.statcan.gc.ca/n1/daily-quotidien/190815/dq190815a-eng.htm?HPA=1

Some CNS Highlights: (15 AUG 2019)

- The National Cannabis Survey found 16% of Canadians above the age 15 have consumed cannabis in the past three months—that percentage remains virtually unchanged when compared to use rates before legalization
- Nunavut had the highest rate of use at 32% while Quebec had the lowest at 10%—use in Newfoundland and Labrador was the same as the Canadian average at 16%
- Lighting up is still the most popular way to consume cannabis—two thirds of users prefer to smoke cannabis compared to other methods
- According to the CNS report, men are almost TWICE as likely to use cannabis as women—men are also more likely to buy cannabis, whereas women tend to receive it from friends and family

How does cannabis work?

Endocannabinoid System

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

The endocannabinoid (EC) system is a unique communications system in the brain and body that affects many important functions

A bit of background:

- 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

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-1β, 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

Cannabis plants produce cannabigerolic acid (CBGA), the precursor to the three main cannabinoid lines:

- Tetrahydrocannabinolic acid (THCA)
- Cannabidiolic acid (CBDA)
- Cannabichromenic acid (CBCA)

Specific enzymes in the plant break CBGA down and 'direct' it toward one of the three lines

Cannabigerol ('CBG')

First discovered by researchers in the 1960's, CBG is the precursor from which all other cannabinoids are synthesized—which is why it is often referred to as the 'mother' or 'stem cell' of cannabinoids

This unique property imbues CBG with enormous therapeutic promise—making it a subject of great interest for researchers and consumers alike

Some CBG Findings: (Source: https://www.leafly.com/news/cannabis-101/what-is-cbg-cannabinoid)

- CBG is thought to be particularly effective in treating **glaucoma** due to the reduction of intraocular pressure seen in the stimulation of the numerous endocannabinoid receptors found in ocular structures
- CBG was found to be effective in decreasing the inflammation characteristic of **inflammatory bowel disease** in animal studies

  Canada has one of the highest rates of inflammatory bowel disease in the world—the 2018 Impact of Inflammatory Bowel Disease in Canada report is the first wide-ranging examination of the disease and its impact on Canada since 2012--Source: Crohn's and Colitis Canada; information retrieved on 1 OCT 2019 at: https://crohnsandcolitis.ca/About-Us/Resources-Publications/Impact-of-IBD-Report

  In the six years that elapsed between reports, researchers uncovered new findings about the disease, about the people who are living with it, and how Canada can take strides to better care for those affected

  Key Report Findings:

  ✓ 270,000 Canadians are living with inflammatory bowel disease (IBD)

  ✓ The direct annual cost of caring for Canadians with IBD is estimated at $1.28 billion

- ✓ By 2030, the number of Canadians with IBD is expected to rise to 400,000 (approximately 1% of the population)
- ✓ Seniors (aged 65 and over) with Crohn's or colitis are the fastest growing group of Canadians with IBD
- ✓ Seniors with Crohn's or colitis face complications of longer disease duration and caring for age-related simultaneous conditions such as diabetes and cardiovascular disease
- ✓ Canadians with Crohn's or colitis in rural areas are less likely to receive gastroenterologist care—negatively impacting consequences on long-term outcomes
- ✓ There are over 7,000 Canadian children (under age 18) living with Crohn's or colitis
- ✓ The prevalence of Crohn's and colitis in Canadian children has risen more than 50% in the last 10 years
- ✓ Children with Crohn's or colitis have different disease complications, respond differently to treatments, and are at a greater risk of side effects of medication as compared to adults

- CBG is also a potent neuroprotectant and is currently being evaluated for its ability to combat ailments like **Huntington's Disease**
- CBG is showing great promise as a **cancer fighter** by apparently blocking receptors that cause cancer cell growth
  - ✓ CBG was shown to inhibit the growth of colorectal cancer cells in animal studies
  - ✓ Additionally, CBG inhibited tumors and chemically-induced colon carcinogenesis
- European research shows evidence that CBG is an effective antibacterial agent—particularly against methicillin-resistant Staphylococcus aureus (MRSA)
- In a study that looked at the effects of five different cannabinoids on bladder contractions, CBG tested best at inhibiting muscle contractions—making it a potential therapeutic option in preventing bladder dysfunction disorders
- The potential health benefits of non-intoxicating CBG are extensive—it is thought to help regulate mood thanks to its ability to boost anandamide as well as act as a GABA reuptake inhibitor

Scientists are excited about these initial CBG results and are promoting future research with CBG alone or CBG in combination with other cannabinoids

One more thing:

- Despite the medical appeal and consumer demand there is one big hurdle to face: CBG is notoriously expensive to produce
- It takes thousands of pounds of biomass to create small amounts of CBG isolate—that is because most hemp only contains minute percentages of CBG (some hemp strains contain 20% CBD in the crop)
- If the CBG content of the same crop is only 1%, that means it would be necessary to extract 20 times the amount of biomass to get the same amount of CBG out

THC

Out of the individual cannabinoids found in cannabis, 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 activates the brain's reward system—regions that govern the response to healthy pleasurable behaviors such as sex and eating
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
But cannabinol (CBN) is much more than simply a degraded, less potent cannabinoid derived from THC—while it is barely present in cannabis flowers and it is nowhere near as psychoactive as THC, the cannabis industry is catching on to the fact that CBN has therapeutic effects that benefit people who are sensitive to THC
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
- 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/.
- Researchers studied the feeding patterns of rats after administering cannabinol—the treated rats were quicker to eat, ate more and for longer durations of time; the research concluded CBN was **a viable non-psychoactive appetite stimulant**--Source: Farrimond JA et al: Cannabinol and cannabidiol exert opposing effects on rat feeding patterns; results appearing in

Psychopharmacology (Berl). 2012 Sep; 223(1):117-29. Accessed on 1 OCT 2019 at: https://www.ncbi.nlm.nih.gov/pubmed/22543671

- Research showed that cannabinol is capable of slowing the onset of symptoms from **ALS** in animal models--Source: Weydt P et al: Cannabinol delays symptom onset in SOD1 (G93A) transgenic mice without affecting survival; 2005; Amyotrophic Lateral Sclerosis, 6:3, 182-184. Accessed 1 OCT 2019 at: https://www.tandfonline.com/doi/abs/10.1080/14660820510030149

The research on cannabinol (especially in human trials) is currently lacking—as investigations continue, even more beneficial applications for CBN may be uncovered

Cannabidiol (CBD)

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

CBD is classified as a 'non-psychotropic 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 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

CBD has 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
- Schizophrenia affects about 1% of Canadians—that's about 40,000 people in British Columbia
- 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

Cannabidiol is promoted for a wide range of medical conditions—the Clinicians' Guide to Cannabidiol and Hemp Oils was published in the journal Mayo Clinic Proceedings (access the report at: **https://www.mayoclinicproceedings.org/article/S0025-6196(19)30007-2/pdf**)

As consumer interest in CBD grows ahead of the 17 OCT legalization of cannabis edibles, extracts and topicals, common questions about its health claims for seizures, pain and other conditions need to be addressed

The State of CBD in Canada

Health Canada assigns a drug identification number (DIN) to all drug products evaluated and authorized for sale in Canada—to qualify, a drug manufacturer needs to provide information including dosing, strength and how medication should be taken

Currently, there are two cannabis-related drugs that have a DIN and are authorized for sale in Canada:

- Nabilone
- Sativex

Nabilone—a synthetic tetrahydrocannabinol product—is approved to treat nausea

Sativex, which is manufactured from whole botanical extracts and contains THC and CBD, is added to treatments aimed at relieving spasticity in adults with multiple sclerosis

Epidiolex is the only CBD-related treatment approved by the U.S. Food and Drug Administration (FDA)—it is used to treat severe forms of epilepsy; Epidiolex is not listed in Health Canada's database of medications approved for use in Canada

KEY POINT: No CBD-specific product has a DIN!!!

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)

Edibles

Headliners: Canadians Can Expect Tight Supply When Cannabis Edibles Become Legal mid-December; Source: As reported by Kathleen Harris; CBC News; posted 14 JUN 2019; accessed 20 AUG 2019 at: https://www.cbc.ca/news/politics/edibles-legalize-cannabis-rules-1.5175689

Health Canada released new regulations on the sale and use of cannabis edibles, beverages, topicals and extracts which will be on the legal market as early as mid-December 2019

Officials say the regulations (which include strict packaging and labelling requirements) are designed to limit the appeal of cannabis products and reduce the risk of food-borne illness or over-consumption

Some of the Regulations:

- Cannabis-infused alcoholic beverages and cannabis products containing tobacco, nicotine or caffeine will be prohibited
- Health Canada will maintain strict rules on labelling to prevent companies from making the products more attractive to young people
- The packaging and labelling must have a clear cannabis symbol, a health warning listing the product's tetrahydrocannabinol (THC) and cannabidol (CBD) content, limited use of logos and colours, and child-resistant packaging

The Canadian market for next-generation cannabis products is worth an estimated $2.7 billion annually—with edibles contributing to more than half of sales--Source: Deloitte report; as reported by CBC; accessed online 20 AUG 2019 at: https://www.cbc.ca/news/business/edibles-market-deloitte-1.5159882

“I've heard from the industry and people say, 'You know, we could make more money if you did this or relaxed these regulations.' But quite frankly, that's not our motivation. Our motivation is, and will always be, to protect our kids, protect health and safety of Canadians, to keep our communities safe and displace that illicit market that has developed over decades in this country.”--Source: Border Security and Organized Crime Reduction Minister Bill Blair; in a statement to CBC 14 JUN 2019

Edible Primer:

- Edibles are foods, drinks, lozenges, tinctures, candies, mints, etc. that are infused with cannabis flower or concentrates—the main benefits of edibles are that the user can feel the effects without having to smoke or vape and the effects generally last longer
- 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
    - This THC metabolite activates CB1 cannabinoid receptors in the brain and It induces a ‘high’ more potently than THC itself

A couple of things to keep in mind:

- The ‘right’ dose varies between people—factors such as previous cannabis use, hormones, and sensitivities will affect the appropriate dose of edible cannabis product
- BEST PRACTICE: Use a very low dose to begin with GRADUALLY add product as necessary

Vaping

Headliners: The Vape Wars are Coming: Companies prepare for the next battle in the cannabis market; Source: Peter Armstrong; reporting for CBC News; posted 29 JUL 2019; accessed 21 AUG 2019 at: https://www.cbc.ca/news/business/legal-cannabis-vaping-partnership-1.5226342

With the next wave of cannabis legalization looming, the cannabis business is once again booming—and many think this phase may be dominated by technology (specifically, vape pens)

Like edibles, beverages and extracts, cannabis vaping products will be for sale legally in Canada in mid-December 2019

Which explains why Canadian cannabis company Auxly Cannabis Group Inc. has teamed up with British tobacco giant Imperial Brands in a deal worth more than $120 million—Imperial gets a foothold in the cannabis market and Auxly gets exclusive access to Imperial's vape technology and research

The partnership accelerates Auxly's plan to go heavily into the recreational market—particularly, the vape category, which [the company] think[s] will be very large--Source: Chuck Rifici; outgoing CEO; Auxly

No need to worry about Chuck

In fact, analysts say vaping could become the driving force of the recreational cannabis market

From the market data south of the border and anecdotally across Canada in unlicensed dispensaries, people seem to disproportionately choose vape devices—part of that, is the ease and discretion of using a vape pen

Once legal, the pens will come with pre-loaded cartridges of cannabis extract—with the push of a button, the extract is vaporized and instead of smoke, the user inhales vapour

U.S. Federal officials call vaping an ‘epidemic of youth use’ and estimate that the number of high school students who use vaping devices has risen about 75% in the past year to about 3 million students—overtaking tobacco products in popularity

One of the most popular is JUUL—packaged to look like a sleek computer flash drive that can be tucked into a fist or pocket and charged in a USB port
The U.S. Centers for Disease Control and Prevention (CDC) reported 530 confirmed and probable cases of lung injury related to e-cigarettes as of 17 SEP 2019—that number increased to 805 as of 27 SEP 2019!
While no single device, ingredient, additive or pathway to illness has been identified in the U.S. investigation, most of the affected individuals reported using tetrahydrocannabinol (THC, the main component in cannabis that gives users a high) or both THC and nicotine
The U.S. investigators said vaping products carrying THC or vitamin E acetate mixed with THC oil from the illicit market were the villain behind the rash of serious lung issues, stating:
'Of the patients who reported what products they used, THC-containing products were the most prominent link across patients, with only 16% reporting using only nicotine-containing products.'--
Source: Anne Schuchat; CDC principal deputy director

Headliners: Quebec Resident Confirmed as First Canadian Case of Vaping-Related Illness; Source: CBC News; posted 27 SEP 2019; accessed 1 OCT 2019 at: https://www.cbc.ca/news/canada/montreal/vaping-related-illness-quebec-1.5299487rcv

A Quebec resident was diagnosed with Canada's first case of a severe vaping-related breathing illness—the patient (in their 50's) reported vaping for a few months in an attempt to quit smoking
In Canada, the definition of a vaping-related severe pulmonary illness case includes the following criteria:

- Symptoms such as shortness of breath, cough, chest pain, with or without vomiting, diarrhea, abdominal pain, fever
- History of vaping or dabbing (using THC concentrates like oil or wax) 90 days prior to symptom onset
- Pulmonary infiltrate, which is a substance denser than air, such as pus, blood, or protein in the lungs
- Negative results on tests for a lung infection
- No evidence in medical records of alternative plausible diagnoses

In September 2019, Dr. Horacio Arruda, provincial director of public health for Quebec's Health Ministry issued a warning about the risks of developing a pulmonary illness as a result of vaping and stated:
'…what they know is there is a link between the illness and people who vape.'

Worth Noting:

- Anyone who has used an e-cigarette or vaping products, and has experienced these symptoms is advised to consult a health-care professional

Canada is enforcing stricter regulation on cannabis derivatives and will take into account the emerging health risks associated with cannabis vaping and ban additives including vitamins and coloring agents (Source: Health Canada)

Headliners: Vapes Need Same Restrictions as Tobacco, Medical Groups Tell Federal Parties; Source: CBC News; posted 19 SEP 20 19; accessed 1 OCT 2019 at: https://www.cbc.ca/news/health/vaping-thursday-1.5289485

A group of health organizations in Canada called for immediate political action in dealing with the '…urgent need for vaping products to be given the same advertising and flavour restrictions as tobacco'
The 18 SEP 2019 appeal came was presented at a news conference in Ottawa from representatives of:

- Action on Smoking and Health
- Canadian Cancer Society
- Canadian Medical Association
- Canadian Lung Association

- Coalition québécoise pour le contrôle du tabac
- Heart & Stroke
- Ontario Campaign for Action on Tobacco
- Physicians for a Smoke-Free Canada

The groups said manufacturers are allowed to entice youth and non-smokers with attractive flavours, give the products away and have no obligations for nicotine limits or health warnings on packages as in this case for tobacco

Let's Talk Flavour

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

Good News!

- Facing mounting government pressure and a public backlash over an epidemic of teenage vaping, JUUL Labs announced 13 NOV 2018 that it would suspend sales of most of its flavored e-cigarette pods in retail stores and would discontinue its social media promotions—the San Francisco-based company has more than 70% of the e-cigarette market share

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 cannabis

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 U.S. 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 cannabis

Some of the highlights of the NAS report:

Medical Benefits

- 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

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 cannabis 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

Health Risks

Cancer

- 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 cannabis use is associated with **heart attack and stroke**

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

Asthma and other chronic respiratory problems

- Evidence suggests that smoking cannabis 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

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

- 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
- The Society of Obstetricians and Gynaecologists (SOGC) reported evidence-based studies which demonstrated how cannabis could harm growth and development of babies if used while pregnant or breastfeeding

Potential effects include:

- ✓ Pre-term labour
- ✓ Low birth weight
- ✓ Lower IQ scores
- ✓ Impulsivity and hyperactivity in childhood

- The SOGC reported that about 70% of pregnant and nonpregnant women in the U.S. who were surveyed believed there was slight or no risk of harm from using marijuana once or twice a week
- 'We know from studies that frequent use of cannabis during pregnancy—daily or near daily use—does increase risk of adverse outcomes including risk for low birth weight as well as adverse effects on cognition and behaviour in children and adolescents that persists to early adulthood. This contributes to poor academic achievement. This risk is independent of alcohol or tobacco use. It does hinge on smoking cannabis. We don't know too much about what happens if a pregnant woman is using via the other ways of consumption. We also don't know too much about risks that are specific to breastfeeding. If a woman is using cannabis while breastfeeding it's most likely she was using cannabis while pregnant. We do know that THC, one of the important psychoactive compounds of cannabis does get into the breast milk. It is transferred to the infant, metabolized and excreted, so there is definitely the potential for that affecting brain development.'--Source: Sarah Konefal, Canadian Centre on Substance Use and Addiction
- Researchers at the Ottawa Hospital looked at data from the Better Outcomes Registry and Network (BORN) Ontario database which studied a total of 10,731 women who reported using cannabis while pregnant—1.2% of pregnant women were using cannabis in 2012 compared to 1.8% in 2018
- Cannabis use in pregnancy has increased since 2012—research published in the Canadian Journal of Public Health found that imbibing in cannabis during pregnancy is a trend that is expected to continue now that recreational cannabis is legal across Canada

Headliners: The Great Health Experiment; As reported by Bruce Barcott and Michael Scherer; appearing in Marijuana Goes Mainstream; special TIME edition adapted from: Weed the People: The Future of Legal Marijuana in America (2015)

Dr. Yasmin Hurd, a well-respected neuroscientist specializing in addiction, has been conducting interesting research on the effects of early-exposure to regular doses of THC in animal models

The findings of one of her experiments was disconcerting—the offspring of rats that had been exposed to regular THC-dosing demonstrated an increased tendency to select behavior with heroin as a reward when compared to non-THC exposed rats' offspring

The researchers found that the neuronal circuitry of the rats with drug-using parents was altered—the behavioral changes associated with these alterations extended to the 'grandkids' of the THC-exposed laboratory animals

'This data tells us we are passing on more things that happen during our lifetimes to our kids and grandkids. I wasn't expecting these results, and it is fascinating.'--Source: Hurd

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/

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

Cannabis inhibits those prefrontal cortex functions

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

One thing to keep in mind:

- Cannabis has been identified as a 'toxin accumulator'—meaning that toxins from growing media or soil may leach into the plant
- Heavy metals, certain pesticides, and other harmful substances may concentrate in the cannabis plant and contaminate the end product

Cannabis Use in the Elderly

Across Canada, seniors (mostly baby boomers in their mid-50s to early 70s) are adding cannabis-rich tinctures, oils and capsules to their medicine cabinets—even adults in their 70s, 80s and 90s are trying cannabis for the first time in hopes that the plant will ease chronic pain, insomnia, depression and anxiety after pharmaceutical drugs have failed

In the United States, seniors have become the fastest-growing demographic of cannabis users—this trend is likely going to be the case in Canada

The world's oldest woman, Fulla Nayak (who passed away at the ripe old age of 125), credited her longevity to daily use of ganja and palm leaf wine—not only did Nayak live a long life, she could stand and walk on her own until the day she passed away

An occasional cold was her most serious medical condition

Oral Health Effects of Cannabis 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

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

Addiction Potential of Cannabis

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

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

Cannabis Updates

Cannabis Capsule

- Cannabis—like all medicaments—is neither 'all good' nor 'all bad'
- What we do know, is that research into cannabis use needs to continue to elucidate systemic and oral effects of this product to maximize use potential