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Cannabinoids and What Oral Healthcare Professionals Need to Know

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Our Clinician:



Dr. Mark Donaldson BSP, RPH, PHARMD, FASHP, FACHE received his baccalaureate degree from the University of British Columbia and his Doctorate in Clinical Pharmacy from the University of Washington. He completed a residency at Vancouver General Hospital, and has practiced as a clinical pharmacy specialist, clinical coordinator and director of pharmacy services at many healthcare organizations in both Canada and the United States. He is currently the Associate Principal of Clinical Pharmacy Performance Services for Vizient, in Whitefish, Montana.

Dr. Donaldson is a Clinical Professor in the Department of Pharmacy at the University of Montana in Missoula, and Clinical Associate Professor in the School of Dentistry at the Oregon Health & Sciences University in Portland, Oregon. He has a special interest in dental pharmacology and has lectured internationally to both dental and medical practitioners. He has spent the last 25 years focusing on dental pharmacology and dental therapeutics, and is a leader in the field.

Dr. Donaldson has published numerous peer-reviewed works and textbook chapters. He currently serves on the Editorial Board for the Journal Healthcare Executive and the Journal of the American Dental Association, and is a reviewer for over ten other different journals. He is board certified in healthcare management and is the Past-President and current Regent of the American College of Healthcare Executives' Montana Chapter. Dr. Donaldson was named as the 2014 recipient of the Bowl of Hygieia for the state of Montana and is the 2016 recipient of the Dr. Thaddeus V. Weclaw Award. This award is conferred by the Academy of General Dentistry upon an individual who has made outstanding contributions to the medical, dental and pharmacy literature. In 2019, Dr. Donaldson was conferred by the Canadian Dental Association (CDA) in Ottawa with the, "Special Friend of Canadian Dentistry Award." This award is given to an individual outside of the dental profession in appreciation for exemplary support or service to Canadian dentistry and/or to the profession as a whole.

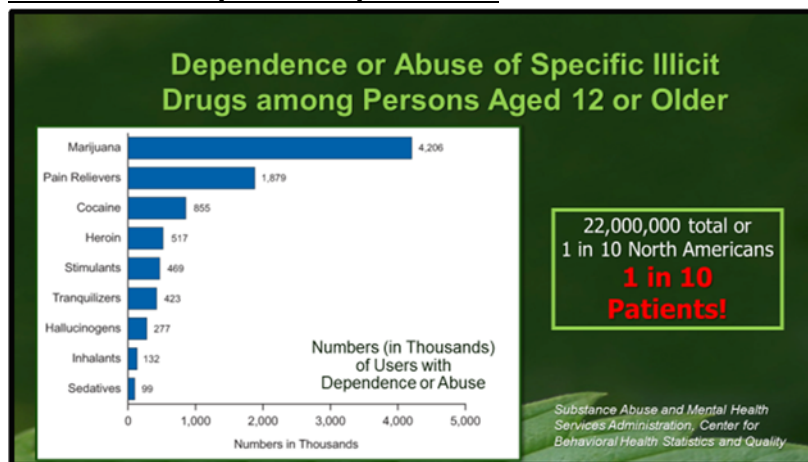
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Grand Rapids, MI

Medical Cannabinoids, Illicit Drugs and Dentistry

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What is the scope of the “problem”?



Reasons noted for refusing to reveal information on a health history form	
Unimportant information	17%
Privacy	62%
Afraid of refusal of treatment	7%
Other	14%

McDaniel TF, Miller D, Jones R, Davis M. Assessing patient willingness to reveal health history information. *J Am Dent Assoc.* 1995;126(3):375-9.

- 23% of respondents would be reluctant to note current drug abuse on a medical history questionnaire!

In the United States, thirty-three states and the District of Columbia currently have passed laws broadly legalizing marijuana in some form (as of September 2022). The District of Columbia and 11 states -- Alaska, California, Colorado, Illinois, Maine, Massachusetts, Michigan, Nevada, Oregon, Vermont and Washington -- have adopted the most expansive laws legalizing marijuana for recreational use. Most other states allow for limited use of medical marijuana under certain circumstances. Some medical marijuana laws are broader than others, with types of medical conditions that allow for treatment varying from state to state. Louisiana, West Virginia and a few other states allow only for cannabis-infused products, such as oils or pills. **In Washington State, as of December 6, 2012, the Uniform Controlled Substances Act is in force (RCW 69.50). The Cannabis Patient Protection Act went into effect July 1, 2016 (RCW 69.51A). Neither dentists nor chiropractors are allowed to authorize the use of medical marijuana**

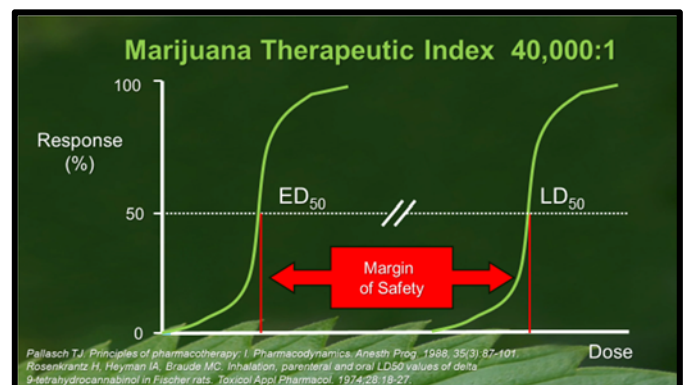
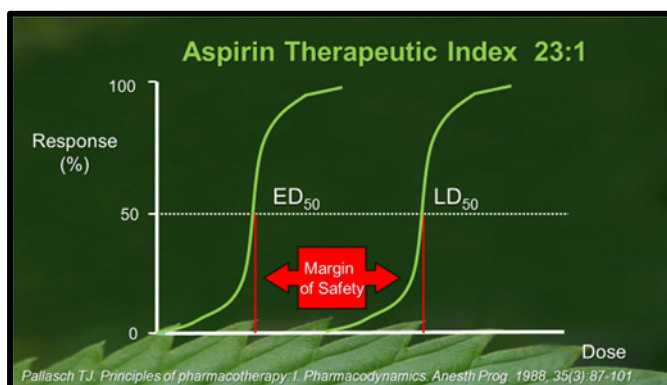
What are Cannabinoids?

- Species: Pure or hybrid varieties of Cannabis.
- C. Indica and C. Sativa, C. Ruderalis (Ruderalis is not used for medical or recreational purposes)
- Approximately 24 plant strain varieties, hybrids are very common
- All have varying THC:CBD ratios and varying concentration of other cannabinoids and other bioactive molecules depending on:
 - Genetics
 - Potency
 - Benefits
 - Skill Level
 - Flower Time

Other Notes or Questions to Ask:

- Cannabis plants contain up to 500 distinct chemical compounds, including over 100 “cannabinoids.” The term “phytocannabinoid” distinguishes natural cannabis-derived cannabinoids from synthetic cannabinoids (Hanus, *et al. Nat Prod Rep.* 2016;33:1357-1392).
- The two major cannabinoids are:
 - **Δ^9 -Tetrahydrocannabinol (Δ^9 -THC, often simplified to “THC”)**
 - **Cannabidiol (CBD)**
- Recreational cannabis typically has a greater THC:CBD ratio while medical cannabis can vary from high THC:CBD to high CBD:THC ratios.
- *Cannabis sativa* with little THC (< 0.3%) is cultivated as “hemp”, for use in food, textiles, etc.
- Other active cannabinoids and metabolites may contribute to biological activity, including:
 - Δ^8 -Tetrahydrocannabinol (Δ^8 -THC)
 - Cannabinol (CBN)
 - Cannabidivarin (CBDV)
 - 11-hydroxy- Δ^9 -Tetrahydrocannabinol (11-OH-THC)
 - many others
- There are also hundreds of potentially bioactive flavonoids and terpenes that have the potential to cause or modulate the pleasurable, medicinal, or adverse effects of cannabis (Hanus, *et al. Nat Prod Rep.* 2016;33:1357-1392).
- Cannabis plants have 2 genders:
 - “Males” grow fast and tall and have little THC
 - “Females” produce flowers rich in cannabinoids
- THC concentrations peak when female plant flowers. At the floral stage, oils high in phytocannabinoids are secreted and concentrated on trichomes (small “hairs” rich in resin). This is when cannabis plants are harvested and non-flowering portions of the plant are removed.
- Most cannabinoids in the cannabis plant are in a carboxylated (i.e., acidic) form such as THCA not THC, and CBDA not CBD. THCA breaks down (e.g., decarboxylates) into THC very slowly over time as cannabis product dries (slow) or very quickly as the plant material is heated. There is very little evidence that carboxylated cannabinoids have any biological activity (i.e., eating the plant does not get you high).
(Wang M, *et al. Cannabis Cannabinoid Res.* 2016;1:262-71.)

Are Cannabinoids Safe?



Lethal Smoked Dose: “1500 pounds smoked within 15 minutes” (Annas. *N Engl J Med.* 1997 Aug 7;337(6):435-9).

Other Notes or Questions to Ask:

"Federal authorities should rescind their prohibition of the medical use of marijuana for seriously ill patients and allow physicians to decide which patients to treat. The government should change marijuana's status from that of a Schedule I drug ... to that of a Schedule II drug ... and regulate it accordingly."

AMA Editorial: The New England Journal of Medicine, January 30, 1997.

Marijuana Safety



Unfortunately with the rise in THC content (3% in the 1980s and 15%+ in 2018), there are some dire consequences to include:

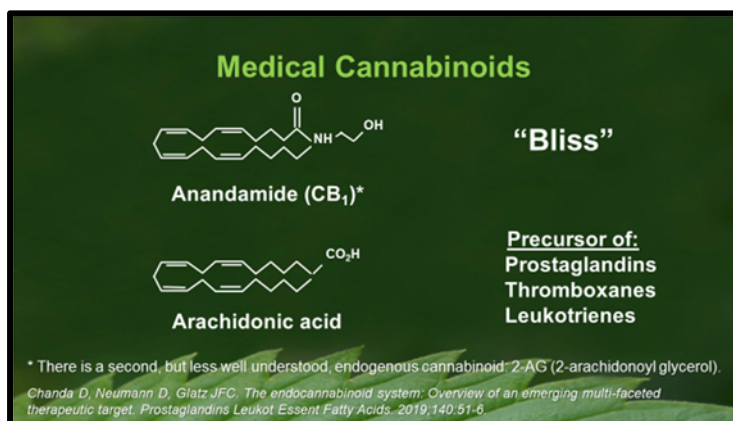
- Increase in percentage of fatal motor-vehicle accidents
- Increase in driving while under the influence of drug

Consider the most recent published evidence from Colorado:
Roberts BA. Legalized Cannabis in Colorado Emergency Departments: A Cautionary Review of Negative Health and Safety Effects. West J Emerg Med. 2019 Jul;20(4):557-572.

Are Cannabinoids Effective (and how do they work)?

- Marijuana contains over 400 chemicals and hundreds more are produced when smoked. Over 100 are cannabinoids with Delta-9-tetrahydrocannabinol (THC) being the most psychoactive, and is most often used as a marker to gauge potency.
- These phytocannabinoids interact with a cannabinoid system of receptors in humans to produce different effects. The discovery of the endocannabinoid system was the result of, "reverse engineering." First, we radiolabeled THC molecules to see where they would naturally concentrate in the body: in areas of the limbic system also known as the "reward center" (nucleus accumbens, caudate nucleus, prefrontal cortex and the cerebellum). From this information we were able to locate and eventually clone CB1 receptors in 1990. These receptors are concentrated in areas within the "reward system" of the human brain and help explain cannabinoid actions in the hippocampus such as memory interference and action in the cerebellum which may be responsible for the cannabinoids ability to cause incoordination and loss of balance. CB1 also seems to be important in mediating pain relief, body temperature and gut activity (Zou, et al. *Int J Mol Sci* 2018;19:833).
- At these very specific receptors, cannabinoids inhibit adenylate cyclase via both brain and peripheral G-protein-coupled cannabinoid receptors which leads to increased levels of dopamine in the nucleus accumbens. Opioids and cannabinoids share common signaling pathways in the brain and can interact to promote each other's reinforcing properties.

Other Notes or Questions to Ask:



The CB2 receptor was first cloned in 1993 and shares only 44% identity with CB1. It is present in lymphocytes and the monocyte/macrophage population of the spleen but not the brain. CB2 appears to be confined to the immune system and may mediate the chemical communications between different types of immune cells or between sensory fibers and blood cells

Zou S and Kumar U. Cannabinoid receptors and the endocannabinoid system: Signaling and function in the central nervous system. Int J Mol Sci 2018;19:833

- **THC** exerts the most psychoactive effects of cannabis and some peripheral/physical effects, including effects on pain, appetite, emotions, thought processes and others. It is a "partial agonist" at both CB1 and CB2 receptors.
- **CBD** antagonizes or modulates CB receptors which explains why it is a "non-psychoactive" or "non-euphoric" cannabinoid. It has analgesic, anti-inflammatory, anxiolytic, and other effects on the body. CBD may activate serotonin and adrenergic receptors, ion channels, transcription factors, and blocks other types of receptors.
- **Δ8-Tetrahydrocannabinol (Δ8-THC)** less well characterized compared to THC. It may contribute to the psychoactive and adverse effects and therapeutic effects (and possibly anti-emetic effects).
- **Cannabinol**, also not well-characterized and is estimated to have ~10% of the activity of THC.
- **11-hydroxy-Δ9-Tetrahydrocannabinol** is one of the major psychoactive metabolites of Δ9-THC and is produced by the first-pass effect in the liver when THC is consumed orally. This hydroxyl radical is three times more psychoactive than THC and may explain many of the paranoid and anxiety-type reactions displayed in people who consume edibles versus those individuals who inhale cannabinoids.

Lucas CJ, et al. Br J Clin Pharmacol. 2018;84:2477-82

Other potentially important cannabinoids:

- CBG (cannabigerol)
- CBC (cannabichromene)
- THCV (tetrahydrocannabivarin)
- CBDV (cannabidivarin)
- CBGV (cannabigerivarin)
- CBCV (cannabichromevarin)
- Many others. . .

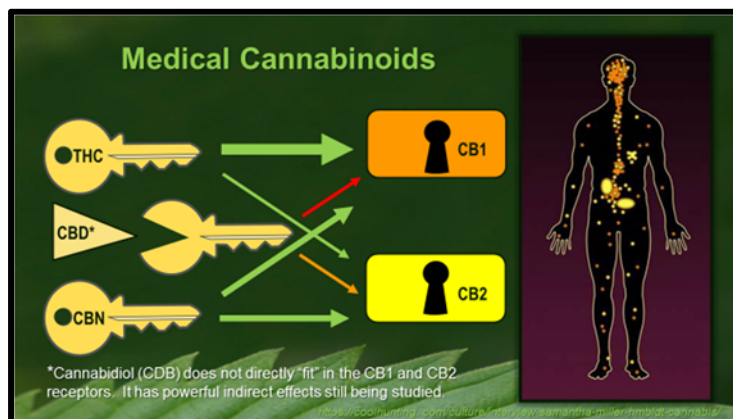
Hanus, et al. Nat Prod Rep. 2016;33:1357-1392.

Looking through history and folklore, marijuana has been considered important in treating a variety of ailments including:

Poor appetite, pain, seizures, insomnia, spasticity, depression, rheumatism, migraines, menstrual cramps, PMS symptoms, constipation, and others.

In the modern era, many guidelines have approved marijuana for the following indications even though the medical evidence of benefit may still be unclear: cancer, cachexia (appetite stimulation), HIV/AIDS, chronic pain, spasticity / MS, glaucoma, peripheral neuropathy, epilepsy, Crohn's disease, Hospice admit (comfort care).

Other Notes or Questions to Ask:



Medical Cannabinoid Products

Dronabinol (Marinol®) - 1992 - Purified THC indicated for the treatment of refractory CINV and as an appetite stimulant in patients with anorexia due to AIDS or cancer.

- It is only approved in adults and elderly and has not been studied in adolescents and children.
- It is available as 2.5, 5, 10 mg oral capsules and the average wholesale price (AWP) is about \$2.36/mg.

Nabilone (Cesamet®) - 1985 - Synthetic THC – two methyl groups are added to the methyl chain and one methyl group on the ring system is replaced with an oxygen molecule). It is indicated for prophylaxis and treatment of CINV.

- It is only approved in adults and elderly although it has an off-label indication in adolescents and children.
- It is available as 1 mg oral capsules and the average wholesale price (AWP) is about \$21.00/mg.

Sativex® (Nabiximols) by Bayer (GW Pharmaceuticals) - 2005 – is a 50:50 mixture of tetrahydrocannabinol (THC and cannabidiol (CBD). Each buccal spray contains 2.7mg THC and 2.5mg CBD.

- It is an oromucosal Spray, indicated in adult patients with moderate to severe spasticity due to multiple sclerosis who have not responded adequately to other anti-spasticity medication and who demonstrate clinically significant improvement in spasticity related symptoms during an initial trial of therapy.
- The dose is titrated for efficacy and side effects. It is available in Canada and 18 other countries, but not yet available in the US (although clinical trials are ongoing in the US for cancer pain).
- Peppermint-flavored, extracted from cannabis plants and costs around \$282 CAD per bottle

Epidiolex® (Cannabidiol) by GW Pharmaceuticals - 2018 – is an oral, strawberry-flavored solution of Cannabidiol 100mg/mL without THC.

- Studies in children with epilepsy (age range 1 month to 18 years) have proved effective in Dravet Syndrome and Lennox-Gastaut Syndrome.
- Typical doses are 2.5-20mg/kg/day as bid.
- This is the first FDA-approved prescription CBD Drug (C-V) and is only available in the USA at this time and the average wholesale price (AWP) is about \$14.82/mL (\$1482/bottle) – USD\$ (10 doses for a 50kg patient getting 20mg/kg/day)

THC:CBD ratios

- The unregulated market is driven to produce/sell cannabis with high THC and low CBD. This has led to an increase in THC in cannabis (3% to 15%+).
- The regulated system typically labels products with %THC and %CBD, all products contain some amount of THC.
- Medical strains are selected to provide a range of ratios, from low to high THC:CBD ratios and these must be listed on the labeling of products.
- There are a number of unregulated Cannabidiol (CBD) Oil products which are a form of concentrated cannabis extract, usually sticky and viscous in appearance and administered orally. They are typically prepared with whole cannabis plant, the addition of a solvent, then heat is applied, followed by filtering and cooling. They can also contain 20 to 80% THC depending on strain. The typical solvents used are: petroleum ether, ethanol, naphtha (butane/hexene), and olive Oil (Organic). Naptha can be hazardous and some, such as hexane and benzene, may be neurotoxic. Both naphtha and petroleum-ether are considered potential cancer hazards according to their manufacturers. While the most prominent delivery method of marijuana is inhalation, the second most popular formulation is the cannabidiol oil, and it is quickly gaining popularity – especially in the pediatric space.

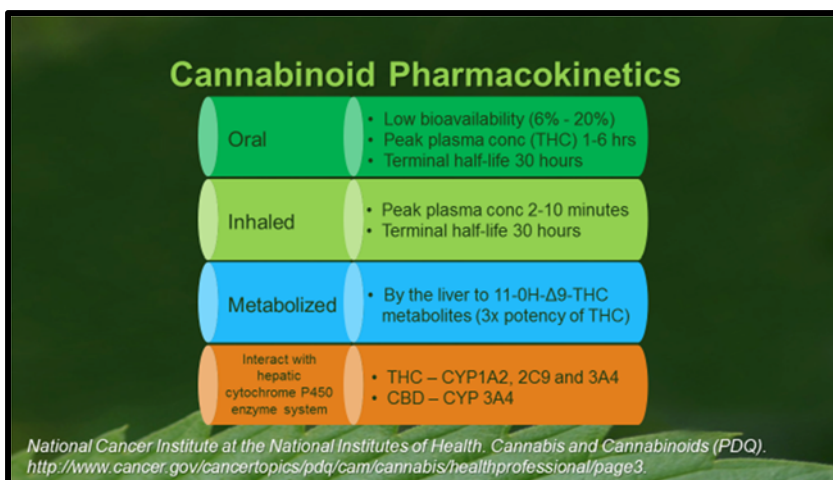
Other Notes or Questions to Ask:

Cannabis Precautions

Avoid driving for at least:

- Inhalation: 4 hours
- Ingestion: 6 hours
- If euphoria: 8 hours
- Impairment may last 24 hours

*Cannabis for Medical Purposes
Evidence Guide, Information for
Pharmacists and Other Health
Professionals. CPhA, Jan 25, 2018.*



Cannabinoid Pharmacodynamics	
CNS depressant and alcohol	•Enhanced sedative, respiratory, psychomotor effects
Sympathomimetics	•Additive tachycardic effects
Anticholinergic agents	•Additive tachycardic effects, possible increased blood pressure
Other possible interactions	•Disulfiram/fluoxetine (hypomania), warfarin (INR elevation)
Induces CYP 1A2 (smoked formulation)	•Increased substrate metabolism (e.g., local anesthetics, diazepam) •Percentage double when combined with tobacco smoking

Cannabinoid Side Effects

In general cannabinoids can cause the following effects, both desirable and undesirable:

- Dizziness
- Drowsiness
- Short-term memory loss
- Euphoria
- Dry mouth
- Blurred Vision, Dry eyes
- Reddening of the conjunctiva
- Mydriasis, Photophobia
- Weight Gain
- Vomiting

There are some more serious side effects to include: severe anxiety, psychosis, respiratory depression, altered central nervous system responsiveness, increased heart rate and vasodilation. These cannabis risks are higher in people aged <25 and can further lead to long-term impairment of cognition, suicidal ideation, cannabis use disorder, and certainly an earlier onset of psychosis when used before age 25.

Fischer, et al. Am J Public Health. 2017;107:e1-12.

Cannabis Respiratory Effects

While respiratory issues are generally considered long-term risks, smoke has the same contents as tobacco smoke (i.e., carbon monoxide, bronchial irritants, ↑ tar, ↑ carcinogens). In fact, 3-4 marijuana cigarettes is equivalent to 20 tobacco cigarettes given the fact that they have no filter and the user usually has a deeper inhalation. It has been suggested that water pipes and vaporizers may increase safety but recent data has shown that this may not necessarily be the case. There are increasing reports on the negative effects of e-cigarette ingredients and their notable deterioration on oral health, as well as explosions while vaping and burn injuries from e-cigarettes leading to disfigurement of oral soft tissues.

Versteeg, et al. Int J Dent Hyg. 2008 Nov;6(4):315-20.

Other Notes or Questions to Ask:

A vaporizer heats cannabis product (dried, flowering portion of the plant) to above the volatilization point of cannabinoids, but below the combustion point. Cannabinoids start to vaporize around 160°C through to 230°C (THC first, then CBD, and others). The assumption then is that this is a “healthier” alternative to smoking, since vaporizers heat the material at a much lower temperature (when compared to smoking) and that the active compounds contained in the plant material produce an aromatic vapor (instead of smoke): volatilization versus combustion.

Pomahacova, et al. Inhale Toxicol. 2009;21:1108-12.

Emerging dosage forms, including the cannabinoid-containing e-cigarette liquids, are now available for purchase online but are not regulated, lack quality control, expiry date, and conditions of preservation and there is essentially no toxicological or clinical data. E-cigarettes are battery-powered devices that work by heating a liquid to generate an aerosol that the user inhales. The liquid in the e-cigarette, called e-liquid, is usually made up of propylene glycol, glycerin, flavorings, water, and THC +/- nicotine.

The temperature control of E-cigarettes may be less controlled and hotter than traditional vaporizers. Propylene glycol (PG) acts as a carrier for the e-liquid and when used orally, the breakdown products include acetic acid, lactic acid, and propionaldehyde, which are all toxic to enamel and soft tissues. In addition, PG is a hygroscopic product, which means water molecules in saliva and oral tissue will bond to the PG molecules, leading to tissue desiccation. The result of this is xerostomia leads to an increase in cavities, gum disease, and other oral health issues.

The other major component of e-liquids are glycerin and flavorings. Vegetable glycerin (VG) is a colorless, odorless, viscous, and sweet-tasting liquid. It serves as a humectant, solvent, and sweetener. VG is 60% as sweet as sucrose and is not metabolized by cariogenic bacteria, and is therefore thought not to cause cavities. However, studies have shown that the combination of VG with flavorings produces a four-fold increase in microbial adhesion to enamel and a two-fold increase in biofilm formation. In addition, a 27% decrease in enamel hardness was demonstrated when flavorings were added to e-liquid as compared to unflavored controls.

Kim, et al. PLoS One. 2018;13(9):e0203717.

Although the percentage of nicotine is much lower (0.3%–1.8%) than traditional tobacco products, one electronic cartridge (200–400 puffs) can equal the smoking of two to three packs of regular cigarettes. The dangerous effects of nicotine on gum tissue are well known as nicotine affects gingival blood flow as it is a vasoconstrictor. It also affects cytokine production, neutrophil function, and other immune cell function as well as decreasing connective tissue turnover. All of this results a much higher chance of developing gum disease and tooth loss.

The first known case of a fatal e-cigarette explosion occurred in May 2018 when an e-cigarette exploded in a St. Petersburg, Florida man’s face. More recently, a 24-year-old man from Texas was killed when his vape pen exploded, and part of the device wound up severing his jugular vein (January 29, 2019). Although these types of sensationalized deaths are rare with e-cigarettes and vaping pens the explosions of these pens are not. The problem lies within the vape pen and the lithium batteries overheating and exploding. A recent report shows that there were 2,035 e-cigarette explosions and burn injuries in the United States between 2015 and 2017—more than 40 times the initial estimate by the US government. These injuries are serious and often lead to disfigurement of oral soft tissue.

Electronic cigarette fires and explosions in the United States 2009–2016. Lawrence A. McKenna Jr. Research Group. National Data Fire Center. United States Fire Administration. U.S. Department of Homeland Security.

The health risks associated with smoking are many. Each year, 430,000 North Americans die of smoking-related illnesses, more than all American deaths in wars in the 20th century combined; around the world, 5 million people die each year.

Other Notes or Questions to Ask:

Smoking both tobacco and marijuana synergistically increases the risk of respiratory symptoms (2.5x) and COPD (3x).

Tan WC, Lo C, Jong A, Xing L, Fitzgerald MJ, Vollmer WM, Buist SA, Sin DD; Vancouver Burden of Obstructive Lung Disease (BOLD) Research Group. Marijuana and chronic obstructive lung disease: a population-based study. CMAJ. 2009 Apr 14;180(8):814-20. iCapture Centre for Cardiovascular and Pulmonary Research, St. Paul's Hospital and the University of British Columbia, Vancouver, Canada.

- The incidence of tobacco smoking in Canada is 20%
- The incidence of marijuana smoking in Canada is 16% (27% in those people younger than 34)
- Prior to the legalization of marijuana the incidence of COPD in Canada was 4%
- COPD is on the rise and it is a true contraindication to the use of nitrous oxide
- Cannabis also ↑ carboxyhemoglobin concentrations

Other Oral Effects of Cannabis

- Xerostomia
- Periodontal disease – possibly b/c of immunosuppression, heavy smokers have a 3x increased risk of periodontal disease
- “Cannabis stomatitis” – chronic use may cause inflammation of the oral epithelium (similar to nicotine stomatitis).
- Leukoedema – may progress to leukoplakia
- Increased risk of mouth and neck cancers
- Synergistic risk when combined with tobacco smoking
- Increased prevalence and density of *Candida albicans*.

Cannabis Cardiovascular Effects

- Dose-related tachycardia of up to 50% increase in heart rate and myocardial oxygen demand
- THC increases catecholamine release which leads to increased demand on the heart (careful with epinephrine)
- Tolerance may develop within 1 week
- Generalized vasodilation (hypotension after 1 week)
- ↑ carboxyhemoglobin concentrations

Cannabis Other Effects

- Cannabis used to treat nausea/vomiting in chemotherapy
- Can also cause chronic vomiting (hyperemesis)
- Related to chronic use in recreational users
- Repeated episodes of nausea and vomiting
- Abdominal pain that requires emergency management
- Nausea relieved by a hot shower
- Stops with cessation of cannabis, recurs if cannabis use restarted
- Case reports of death from cannabis hyperemesis

Richards JR. J Emerg Med. 2018 Mar;54(3):354-363.

What do Oral Healthcare Providers really need to know?

Dentists may prescribe medications and controlled substances **ONLY FOR DENTAL-RELATED** conditions. Under no circumstances may a dentist prescribe anything whatsoever outside the course of his/her practice of dentistry.

Other Notes or Questions to Ask:

The Cannabis for Medical Purposes Evidence Guide, Information for Pharmacists and Other Health Professionals (CPhA, Jan 25, 2023. Available at: https://www.cfpc.ca/Release_Dried_Cannabis_Prelim_Guidance/) begins with three general principles:

Recommendation 1

There is no research evidence to support the authorization of dried cannabis as a treatment for pain conditions commonly seen in primary care, such as fibromyalgia or low back pain (Level III). Authorizations for dried cannabis should only be considered for patients with neuropathic pain that has failed to respond to standard treatments (Level I).

Recommendation 2

If considering authorizing dried cannabis for treatment of neuropathic pain, the physician should first consider a) adequate trials of other pharmacologic and non-pharmacologic therapies and b) an adequate trial of pharmaceutical cannabinoids (Level I).

Recommendation 3

Dried cannabis is not an appropriate therapy for anxiety or insomnia (Level II).

One recent report has suggested a role for cannabidiol for oral mucositis since the control of oxidative stress may prevent and alleviate oral mucositis. Studies have demonstrated that cannabidiol is safe to use and possesses antioxidant, anti-inflammatory and analgesic properties, however, more studies are needed before this can be considered an evidence-based recommendation (and oral cannabinoids have not yet been approved for prescribing).

Cuba, et al. J Clin Pharm Ther. 2017 Jun;42(3):245-250.

Cannabis and Dentistry Conclusions

- The use of cannabis, particularly marijuana smoking, has been associated with poor quality of oral health.
- The etiology has been complicated by the number of associated factors with frequent users, including high tobacco, alcohol, and other drug use; poor oral hygiene practices; and infrequent visits to dentists.
- Cannabis use also leads to xerostomia which can contribute to a number of oral health conditions.
- Further, the main psychotropic agent, THC, is an appetite stimulant, which often leads users to consume cariogenic snack foods.
- Regular cannabis users are known to have significantly higher numbers of caries than nonusers, particularly on normally easy-to-reach smooth surfaces.
- Leukoedema is more common among cannabis users than non-users but it is unclear whether associated irritants, such as orally inhaled smoke, rather than cannabis itself, may be contributing causes.
- Smoking marijuana is associated with gingival enlargement, erythroplakia and chronic inflammation of the oral mucosa with hyperkeratosis and leukoplakia, sometimes referred to as “cannabis stomatitis” that can develop into malignant neoplasias.
- It has been reported that a synergistic effect between tobacco and cannabis smoke may increase oral and neck cancer risk for people who smoke both.
- The risk and aggressiveness of cancers associated with cannabis appear to be higher in younger (i.e., <50 years old) users.
- Immunosuppressive effects of cannabis, especially in association with oral papillomavirus in smokers, may contribute to these increased risks of cancer.

Other Notes or Questions to Ask:

- The immunosuppressive effects of cannabis may contribute as well to a higher prevalence of oral candidiasis compared to non-users (hydrocarbons in cannabis provide an energy source for *Candida*).
- The generally poor oral hygiene among many cannabis smokers may promote candidiasis colonization.
- Viable microbiota may be transmitted from contaminated marijuana, which could further exacerbate a pathogenic oral environment.
- A number of studies have suggested a direct relationship between cannabis use and periodontal disease, including a 2019 systematic review (*J Periodontal Res.* 2019 Aug;54(4):311-317).
- Significantly higher rates of periodontitis are observed among frequent users compared to non-users, with significantly higher numbers of sites with high pocket depths ($\geq 4\text{mm}$) and attachment loss.
- Periodontitis may occur at an earlier age in marijuana users than the general population with chronic periodontitis.
- In a histometric experiment, laboratory rats exposed to marijuana smoke had a significant increase in alveolar bone loss due to periodontitis, despite research that has indicated that specific cannabinoids, such as the non-psychoactive cannabidiol (CBD), may prevent bone loss.
- Avoid treating active (currently intoxicated) users: euphoria, hyper-activity, tachycardia, paranoia, delusions and hallucinations.
- Increased anxiety, paranoia and hyperactivity may heighten the stress experience of a dental visit – caution if sedatives are to be considered given their synergistic effects.
- Increased heart rate and other cardiorespiratory effects of cannabis make the use of epinephrine potentially life-threatening.

Cannabis and Screening Tools

- CUDIT-R
- ASSIST
- Severity of Dependence Scale
- E-TOKE
- Additional screening tools include: CAGE-AID and the Modified ORT
- <https://www.cpha.ca/cannabis-screening-tools>

Dental Considerations with Illicit Drug Users

	Cardiovascular Effects	Respiratory Effects	Xerostomia	Interaction with local anesthesia	Interaction with vasoconstrictors	Interaction with narcotic analgesics
Cannabis	+	++	++	-	+	-
Cocaine	++	+	++	+++	+++	+++
Narcotics	++	++	++	-	-	+++
METH	+++	+	+++	-	+++	+++

Other Notes or Questions to Ask:

Cocaine

- Cocaine is one of the alkaloids present in the leaves of *Erythroxylon coca*.
- Main psychoactive constituent is benzoylmethylecgonine.
- The principal method of administration is snorting.
- Interferes with reabsorption of Dopamine and stimulates pleasure centers of brain.
- Cocaine powder (cocaine hydrochloride) is made from the leaves of the coca plant, it is separated with alcohol, gasoline, or kerosene.
- Freebase - a method using ammonia and ether that separates the free-base molecule of cocaine, can be smoked, high potency, ↑ toxicity.
- Crack - a method that converts cocaine hydrochloride into a smokable form using bicarbonate. Results in lower potency than freebase, ↑ impurities.
- Half-life: 0.7-1.5 hrs
- Detectable in the body for up to 10 days after use. Cocaine can be found on the street using an infinite number of street names and slang. It can be snorted, injected, smoked, or eaten. The level and length of the effects depend on how the drug was induced.



Route	Onset	Peak Effect (min)	Duration (min)
Inhalation	3-5 s	1-5	20
Intravenous	20 s	3-5	20-30
Nasal	3-5 min	15	45-90
Oral	10 min	60	60
Topical	< 5 min	--	--

Dis Mon 2009;55:8-38



• Euphoria	• Paranoia
• Arousal	• Hallucinations
• Lightheadedness	• Restlessness
• Dizziness	• Aggression
• Blurred vision	• Delirium
• Tinnitus	• Vomiting
• Disorientation	• Tremors
• Dilated pupils	• Shivering
• Hyperthermia	• Insomnia
• Tachycardia	• Tachypnea

Int Dent J 2015;55:365-9

Cocaine Effects

Immediate effects: Within a few minutes a euphoric 'high' feeling occurs which can last for up to 90 minutes.

"There's no happy ending to cocaine. You either die, you go to jail, or else you run out."
- Sam Kinison

- Anesthetic effect.
- CNS excitation → CNS/Respiratory depression.
- ↑ Heart rate, ↑ oxygen demand.
- Vasoconstriction of coronary arteries causing ↓ oxygen supply.
- Peripheral vasoconstriction increases BP 15-20%.

Lethal Snorted Dose: "1.4 grams for a 70kg male."
One 'line' of cocaine ~ 50-100mg.

Cocaine Oral Effects

- Nasal Septum perforation & palatal perforation (vasoconstriction → local ischemia).
- "Saddle-nose" deformity
- Increased BP
- Local anesthetic toxicity
- Vasoconstrictor toxicity – potentially fatal
- Xerostomia
- Bruxism

Other Notes or Questions to Ask:

Narcotic: A drug derived from opium or opium like compounds, with potent analgesic effects associated with significant alteration of mood and behavior, and with the potential for dependence and tolerance following repeated administration.

Opiate: A medication or illegal drug that is either derived from the opium poppy, or that mimics the effect of an opiate (a synthetic opiate).

Heroin

- The most powerful known non-synthetic painkiller (medical name: diacetylmorphine).
- Heroin is not a naturally occurring drug, it is refined from morphine.
- Can be snorted or injected: “Chasing the dragon.”
- In its purest form, Heroin is a white powder but it is most commonly seen is brown due to impurities.
- Black tar heroin is not really heroin, but an unrefined mixture of lesser acetylated morphine derivatives.

Heroin Pharmacokinetics		
	Half-Life (mins)	Duration of action (hr)
Intravenous	3-5	2-6
Snorting	4-5	2-6
Intramuscular	5-7	2-6
Smoking	3-5	2-6

Current Clinical Pharmacology 2006;1:109-118.

Heroin Effects

- The immediate effect of intravenous heroin is often described by heroin dependents as a “flash”, a warm and intensively pleasant sensation. It is felt with IV, IN, and smoking. No flash with oral or rectal.
- The “flash” is followed by an euphoric, benumbed state, which may be more related to morphine.
- Slows down circulation and heart rate. Heroin also causes generalized vasodilation (users feel warm).
- Depresses bowel activity, which can result in constipation. First-time users often vomit.
- Respiratory Depression.
- At high doses users become drowsy. An excessive dose can produce stupor and coma, and possible death.

Lethal Injected Dose is “22 mg/kg for a 70kg male.” One “stamp bag” is 100 mg Heroin and costs \$10-\$15.

Heroin Dental Considerations

- Xerostomia.
- Drug Interactions (synergistic with any other narcotic).
- Allergic thrombocytopenia (Quinine).
- ↑ risk of endocarditis.
- ↑ risk of HIV and Hepatitis.
- 40% of IV users exposed to some form of Hepatitis.

Methadone

- Synthetic opiate in use since the 1960’s as a narcotic pain reliever and an adjunct to addiction detoxification (1mg/mL concentration).
- Methadone Pharmacokinetics.
- Syrup (Sugar-free? - Sugar-based has a high sugar content [0.9g/5mL]).
- Onset ~ 30 mins; Duration of action 24-36 hrs ; $T_{1/2}$ = 15-25 hrs.

Methadone Dental Considerations

- Xerostomia
- Increased caries rate with sugar-based formulations
- Consider fluoride supplementation
- Possibly contributes to erosion (↓ pH)
- Same systemic effects as the other opioids

Other Notes or Questions to Ask:

Consider that people who are opioid-dependent are likely to require greater analgesia post-operatively; will require a pain management plan to manage existing tolerance and to ensure provision of adequate analgesia; may have best outcomes if commenced or stabilized on maintenance pharmacotherapies pre-operatively; and May require careful management not to reinstate opioid dependence if abstinence was achieved pre-operatively (caution in recovering addicts!)

Why is Meth so popular?

In contrast to Cocaine...

- Meth is easily manufactured – precursors can be bought over-the-counter (OTC).
- The high can last up to 8 hours.
- How used: snorted, injected, smoked, swallowed

Methamphetamine can be easily produced with toxic precursors:

- | | | |
|-------------------------------|-----------------|---------------------|
| • Pseudoephedrine or Ephedrin | • Battery acid | • Anhydrous ammonia |
| • Acetone | • Iodine | • Drain cleaner |
| • Red Phosphorus | • Muriatic Acid | • Paint thinner |
| • Denatured alcohol | • Freon | • Sulfuric Acid |

Methamphetamine is the more powerful and more addictive cousin of amphetamine:

- Positive outcomes: rush, flash, enhances mood, energy, alertness.
- Duration: minutes (rush) up to 12 hours.
- Physical effects: increased heart rate, blood pressure, respiration, flush, sweating.
- Lethal Dose: “70-120mg/kg” or 4-8 grams
- Addicts may use up to 8 grams per day, fatalities reported with as little as 3 grams.

Causes massive release of neurotransmitters dopamine and norepinehrine, also blocking reuptake:

- Results in neurotransmitter depletion.
- Rapid tolerance, withdrawal symptoms.
- Psychosis, violent behavior.

Meth adverse effects

- Extremely addictive
- Can cause convulsions
- Heart irregularities
- High blood-pressure
- Fear, fatigue or
- Depression
- Restlessness
- Tremors
- Wasting
- Skin Lesions
- Impotence
- Exposure to HIV/STDs
- Hallucinations
- Desire to self-mutilate
- Paranoia
- Insomnia
- May cause coma and death

Methamphetamine – “Crank Bugs”

All Meth users suffer from what they call "Crank Bugs." Meth is manufactured with chemicals that are toxic to the human body, and once the drug is taken the chemicals remain. The body's natural reaction is to try and eliminate the toxins (usually slowly leech out through the skin). Users itch and scratch which causes the open sores

“Meth Mouth”

The phenomenon is thought to be the result of the ingredients used to make Meth, however, Studies have shown that the ingredients are most likely NOT responsible for the rapid destruction to dentition.

- Navarro et al. 2001. pH decline from 7.4 to 6.9
- Critical pH for demineralization of enamel is 5.5

Current literature suggests that “Meth Mouth” is the result of: Hyposalivation, High sugar intake, Bruxism, and Poor oral hygiene.

Other Notes or Questions to Ask:

Dental Management of the Meth patient:

- Postpone all dentistry if history of recent use.
- For Emergency Procedures:
 - No vasoconstrictor in local anesthetic preparations
 - No Narcotic-containing analgesics
- IV users have increased risk of endocarditis.
- ↑ risk of HIV and Hepatitis.

Dental Modifications for Meth Patients:

- Postpone elective care.
- No vasoconstrictor (for 24 hours after most recent use).
- Recommend avoidance of carbohydrate-rich soft drinks (e.g., water).
- Increased preventive measures.

Strategies to promote saliva flow:

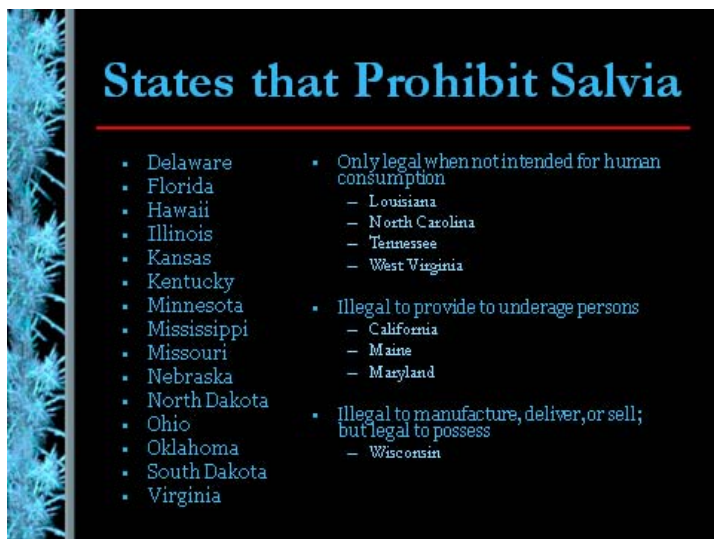
- Sugarless gum
- Saliva replacement (Moi-Stir®)
- Oral moisturizers (Optimoist®)
- Pilocarpine (Salagen®)
- Cevimeline (Evoxac®)
- Biotene® Products

The state of Oregon ranks among the top ten states nationally in per capita treatment admissions for methamphetamine. The social costs are staggering. The human costs are incalculable.

- 52% of children in foster care are there due to Meth. Cost to the State: \$12 million a year.
- 50% of adults in prison are there due to Meth-related crime. Cost to the State: \$43 million a year.
- 20% of adults in treatment are there for Meth addiction. Cost to the State: \$10 million a year.

Dental Management of the Recovering Meth patient:

- For the recovering Meth user, who is now clean, there are no contraindications to dentistry!



Salvia Divinorum

- Hallucinogenic Plant in the mint family.
- Used by the Mazatecs in Mexico for its psychoactive properties during traditional spiritual practices.
- Salvinorin A is the active agent.
- K – opioid receptor agonist.
- Hallucinations, dysphoria, delirium, dissociation.
- Can be smoked or swallowed.
- Leaves must be held in the mouth for absorption, stomach acids deactivate the drug.
- Lethal Dose: Unknown.

Khat Bush . . . Bath Salts

- Active ingredient in the leaves is cathinone.

Plant is found in East Africa and Southern Arabia and pharmacologic profile closely resembles that of amphetamine. Cause dopamine and norepinephrine release in the brain and has led to the development of cathinone-based “Designer Drugs” such as MDPV (Methylenedioxypyrovalerone).

Other Notes or Questions to Ask:

Effects very similar to amphetamine, methamphetamine, and MDMA (ecstasy). Intense cravings and as little as 5mg dose can be effective. Can be swallowed, snorted, smoked, or IV. 5-20mg is the usual dose and a 500mg packet can be purchased for as little as \$20.

Duration of action is usually 3-4 hours and side effects may last a total of 6-8 hours. While the lethal dose is unknown, typical effects consist of:

- Hallucinations
- Fever / increased body temperature
- Paranoia
- Tachycardia followed by bradycardia and hypotension
- Vasoconstriction
- Suicidal thoughts

“The LD₅₀ of MDPV is not known, although it is suggested that non-fatal overdose would be possible at relatively low doses compared to mephedrone.”

*Psychonaut WebMapping Research Group (2009). MDPV Report.
Institute of Psychiatry. Kings College: London, UK*

State and local law enforcement officials encountered MDPV in 2009 and 2010 in Iowa, Kentucky, North Dakota, Oklahoma, Texas, and Wisconsin. Currently, MDPV is not a scheduled drug under the Controlled Substances Act (CSA). However, if intended for human consumption, MDPV can be considered an analogue of a schedule I drug under the CSA. Therefore, law enforcement cases involving MDPV can be prosecuted under the Federal Analogue Act of the CSA.

Is anyone here afraid of crocodiles? How about krokodil (Russian: "Крокодил")

Russian junkies created krokodil which they made by mixing codeine with chemicals such as gasoline, red phosphorus, and hydrochloric acid, because heroin was scarce and codeine was available over the counter. Codeine is converted by the liver to desomorphine which is the most active drug in this toxic mixture. It is around 8-10 times more potent than morphine and is described as having a fast onset and a short duration of action, with relatively little nausea or respiratory depression compared to equivalent doses of morphine.

The high associated with krokodil is akin to that of heroin, but lasts for a much shorter period. While the effects of heroin use can last four to eight hours, the effects of krokodil do not usually extend past one and a half hours, with the symptoms of withdrawal setting in soon after.

“Krokodil” (Flesh-eating “zombie drug”) gets its name from the fact that similar to crank bugs and methamphetamine, Krokodil is notorious for producing severe tissue damage, phlebitis and gangrene (making the users skin similar to that of a crocodile); sometimes requiring limb amputation in long-term users.

The Take-Home Message

An estimated 22 million Americans-almost 10 percent of the population-suffer from chemical dependence or abuse drugs, alcohol or both, according to the latest statistics from the Substance Abuse and Mental Health Services Administration of the Department of Health and Human Services. That means 10% of YOUR patients!

Medical histories should include complete pharmacological histories with an emphasis on what constitutes a “drug” and why your patients need to tell you the truth. In this world of polypharmacology and illicit drug use, the interplay of drug interactions with traditional medical therapy is becoming more difficult every day!

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