

**BCKD**<sub>18</sub>  
**BC KIDNEY DAYS**

# Practical Considerations in Medical Cannabis Administration and Dosing

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# Disclosures

- None to declare.
- That is to say, I have not invested in cannabis companies, am not employed by or am a director of any cannabis company and have not benefitted from cannabis in any way.

**Q1:** If asked, I would tell my patient that cannabis:

- A) Is both effective and safe
- B) Is something I really don't know much about
- C) Is awesome and they should try (strain name)
- D) Might help but we should discuss what symptoms it would be used for and then I could advise on how to use it.

[Results](#)

# Objectives

- Understanding cannabis routes of administration, plant types and dosing.
- Determine when cannabis may be of benefit or not for selected patients.

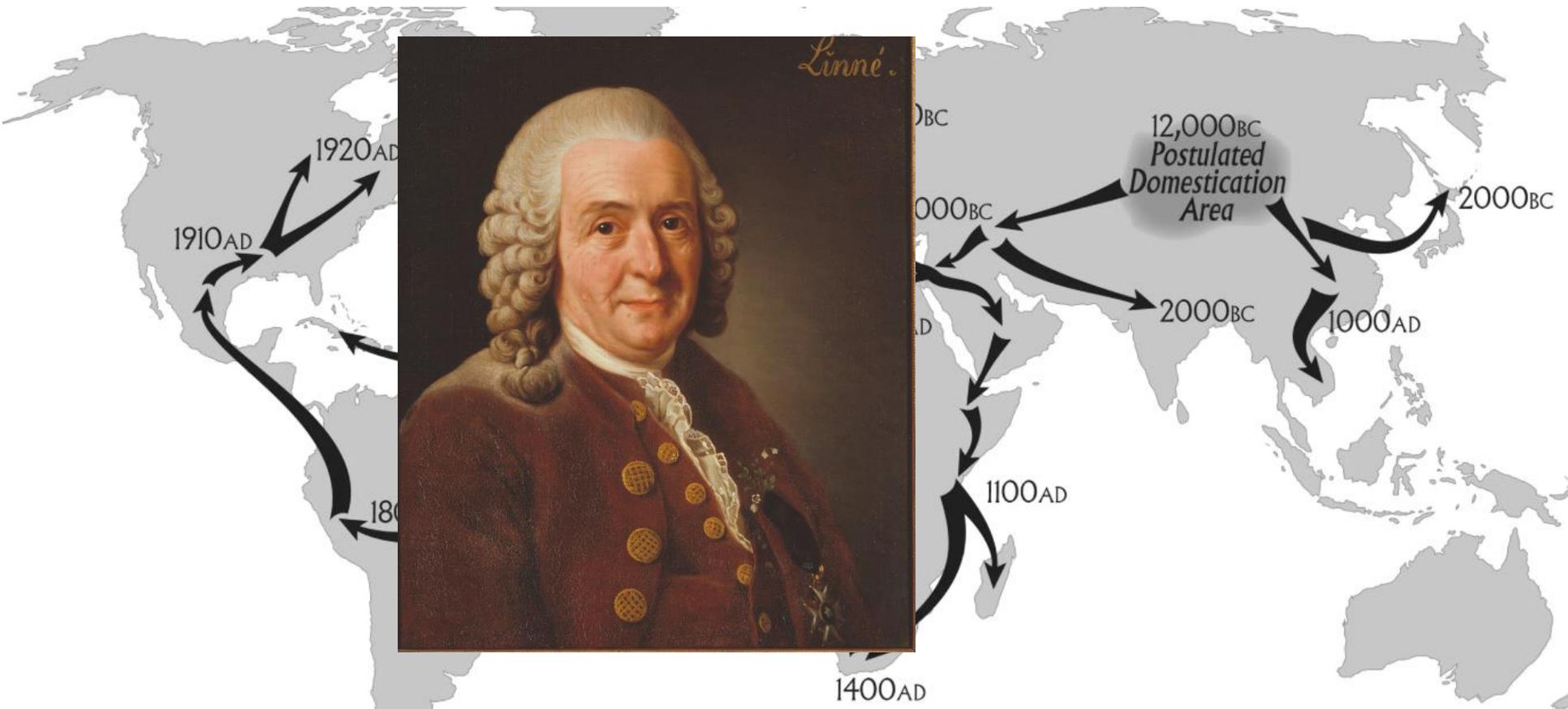
# The journey

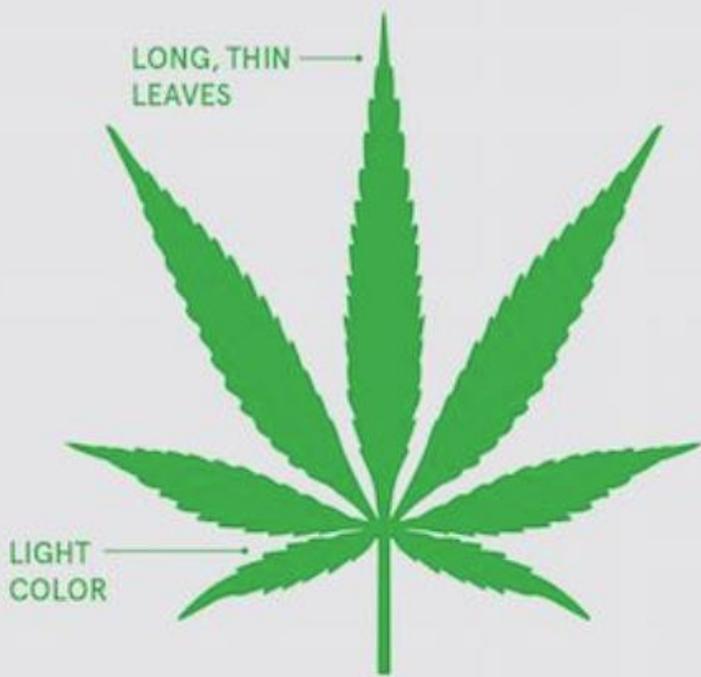
- I wish
- I worry
- I hope

# Outline

- History of the plant and mythology
- Pharmacology and finding balance
- The evidence
- Legislation
- Dosing tips
- Hope for the future

# Origins of Cannabis



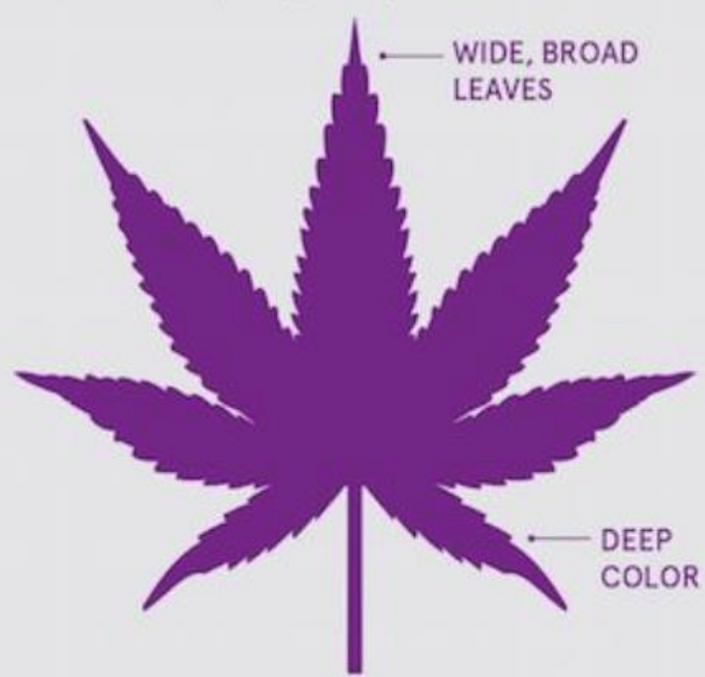


LONG, THIN  
LEAVES

LIGHT  
COLOR

**SATIVA**

VS.



WIDE, BROAD  
LEAVES

DEEP  
COLOR

**INDICA**



**RUDERALIS** is a short, hearty, wild strain with fewer leaves and low THC content. It is not used for consuming but is sometimes crossbred with indicas or sativas to produce an “autoflowering” hybrid—meaning it will produce flowers (buds) based on age rather than light cycles like sativas or indicas.

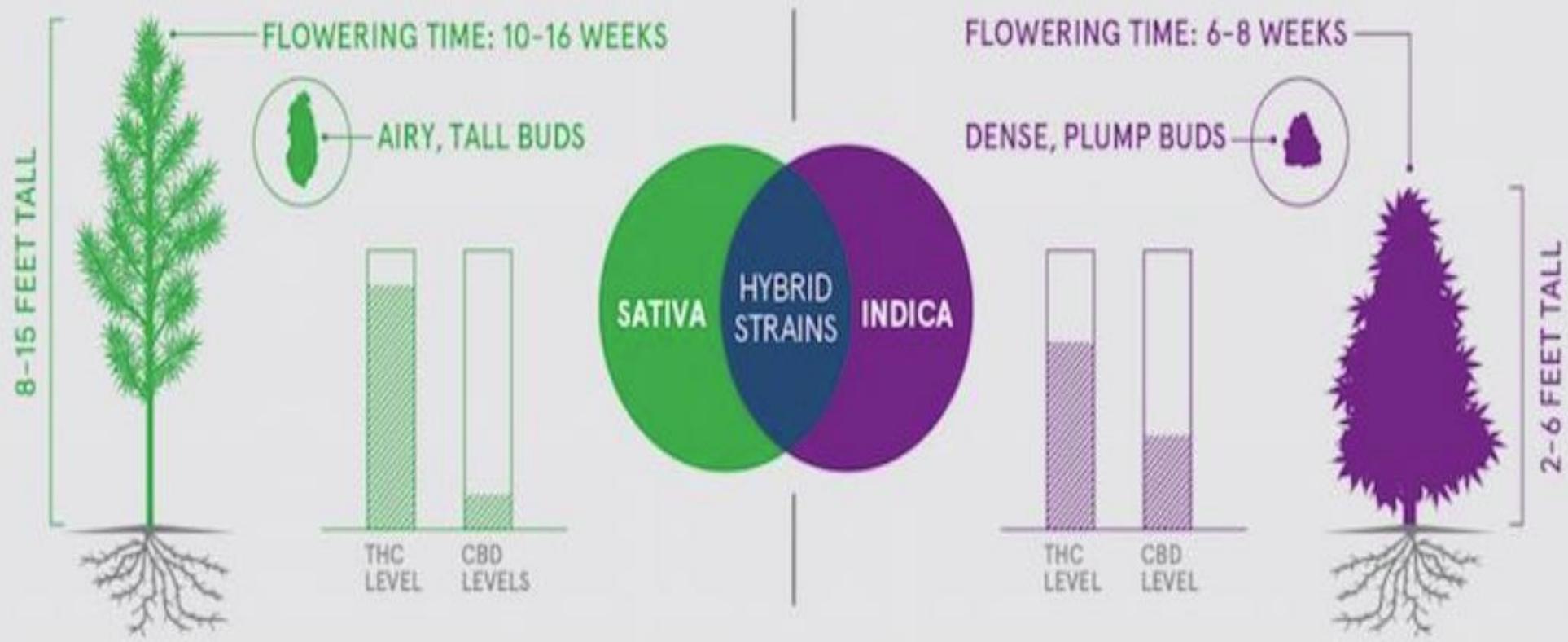


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## Q2: When describing cannabis

- A) I should always use “Indica” or “Sativa”
- B) I should never use “indica” or “sativa”
- C) I should just describe the chemovar
- D) I should just list the levels of THC, CBD and terpenes (whatever they are)

[Results](#)





DAYTIME:  
MIND/HIGH



NIGHTTIME:  
BODY/STONED

**“The clinical effects of the cannabis chemovar have nothing to do with whether the plant is tall and sparse vs. short and bushy, or whether the leaflets are narrow or broad.”**

*Ethan Russo, neurologist and cannabis researcher*

Better suited for warm climates with a long season



Sativa	Sativa	Sativa
<b>Aca</b>	<b>Pam</b>	<b>Dp</b>
Acapulco Gold	Panama Red	Durban Poison

Suitable for colder climates with shorter seasons



Indica	Indica	Indica
<b>Hk</b>	<b>Mis</b>	<b>Afk</b>
Hindu Kush	Mazar I Sharif	Afghan Kush



# The problem with Cannabis

- Genetic variation from region to region
- Common names – thousands of “strains”
- “Chemovar” (chemical variety) diversity
- History: Sativa and indica today are derived from indica

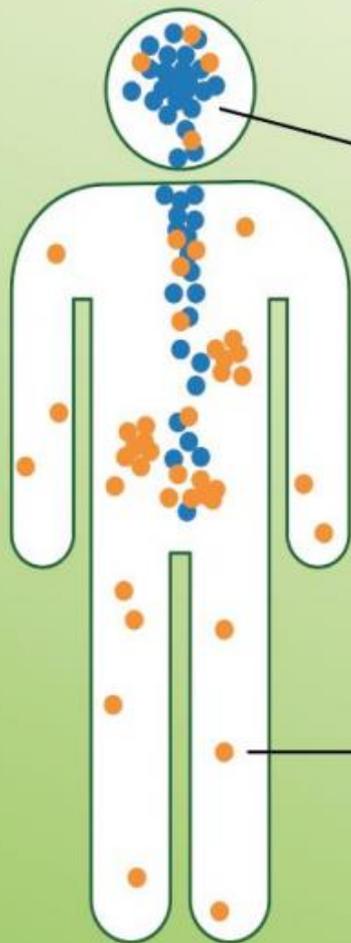
# Some interesting tidbits

- Cannabis was used medically 1840-1940
- Early 1900's - ~30% of Rx's had cannabis
- No known deaths from unaltered cannabis
- Cannabis is not the gateway drug: 80% of street opiate users started with prescription opiates
- Cannabis addiction 9%\*

# Pharmacology

- Endocannabinoids “eat, sleep, relax & forget”
- CB1 receptors = everywhere in CNS\*
- CB2 receptors = far fewer\*
- THC = ↓ pain, ↑ sleep, ↓ nausea, ↓ vomiting, ↑ hunger, ↑ euphoria, & ↑ impairment
- CBD = epilepsy, pain, inflammation, anxiety, PTSD but not insomnia

Cannabinoid receptors are widely distributed throughout the human body



## Receptors

CB1 receptors are mainly located in the brain and central nervous system but are also found in other tissues.

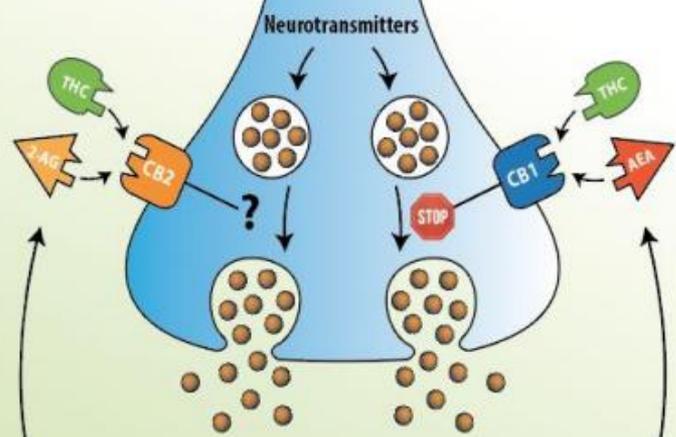


## Ligands

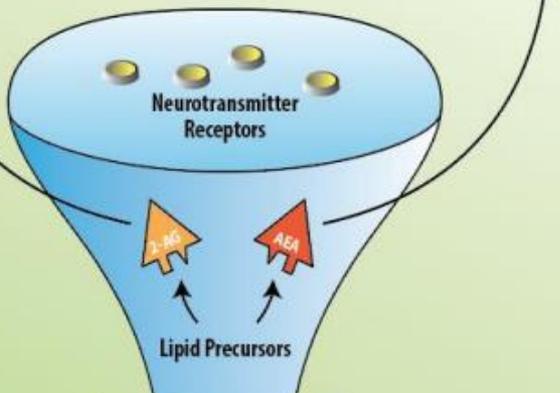


CB2 receptors are most densely found in immunological tissues and modulate cell fate.

## Presynaptic (sending neuron)



## Neurotransmitter Receptors



## Postsynaptic

B

NDMENTS



# The right balance

- THC is the lighter fluid, CBD the charcoal
- THC: CBD
- Oil - anxiety 1:4, pain 1:1
- CBD alone may not be enough
- For pediatrics, use CBD alone

# The down side:

- Adverse reactions
  - Hypotension, palpitation, dry / red eyes\*, cough\*
  - 5-10% cannabis use disorder. 0-5% psychosis
- Drug interactions
  - Increased clobazam and warfarin levels
- Diabetics and renal failure patients tend to be more sensitive to opiates & THC

# Avoid in:

- Pregnancy
- Breast feeding
- Personal or family history of psychosis
- Youth under 25 (THC component)
- Anyone driving or using heavy machinery after use

# Physiological Effects of $\Delta 9$ -Tetrahydrocannabinol and Cannabidiol

## $\Delta 9$ -Tetrahydrocannabinol (THC)

- Euphoria
- Hallucinations
- Sedation
- Aggravation of psychotic states
- Memory disturbance
- Deterioration or amelioration of motor coordination
- Analgesia
- Orthostatic hypotension
- Increase in oxygen demand
- Tachycardia
- Appetite stimulation
- Delayed gastric emptying
- Anti-emetic

## Cannabidiol (CBD)

- Sedation
- Antidystonic
- Antiepileptic
- Anti-emetic
- Anti-inflammatory
- Anxiolytic
- Antipsychotic

# Our Systematic Review 2018

Based on studies conducted in patients without renal impairment, those treated with non-synthetic cannabinoids were 43 to 300% more likely to report a  $\geq 30\%$  reduction in chronic neuropathic pain compared to placebo.

# Our Systematic Review 2018

However, there is currently insufficient evidence to recommend non-synthetic cannabinoids for other medical indications, although preliminary investigation into topical endocannabinoids for uremia-induced pruritus in end-stage renal disease is promising.

# Our Systematic Review 2018

Lastly, any benefits of cannabis may be offset by potential harms in the form of cognitive impairment, increased risk of mortality post-myocardial infarction, orthostatic hypotension, respiratory irritation and malignancies (with smoked cannabis).

## Level of evidence

An absence of evidence  
is NOT evidence of  
absence (of effect)!

Altman Douglas G, Bland J Martin. Statistics notes: Absence of evidence is not evidence of absence *BMJ* 1995; 311 :485

# Systematic review - evidence

- Chronic neuropathic pain – non renal 1A
- N&V: synthetic 1A, Chemo tx 2B, Uremia ?
- Anorexia: cancer 1A, HIV 2B, Uremia ?
- Uremic pruritus 2B (topical localized therapy)
- Insomnia ? (no studies in primary insomnia)

# State of legislation

- Medical cannabis still exists
  - Before Oct 17, no store front, simple HC form, fax & phone
  - Duration (1-365 days) Ceiling dose (1-5 g)
  - 1 g = 2 joints
  - Arrives on doorstep in 24 hours
  - New: Pharmacists can sell in store
  - Tax deductible if no 3<sup>rd</sup> party payer

# Private insurance coverage

- 2017 Loblaw asks insurers to cover MM
- Sunlife: Pain with cancer etc, CIN, MS, HIV anorexia
- Green Shield, Great West & Manulife considering
  - Manulife: recommends limit of \$1.5-2.5K/year
  - Great-West: To avoid opiates, decrease costs
- PTSD, insomnia etc.- many more people



## Medical Document Authorizing the use of Cannabis for Medical Purposes under the Access to Cannabis for Medical Purposes Regulations

Help on accessing alternative formats, such as Portable Document Format (PDF), Microsoft Word and PowerPoint (PPT) files, can be obtained in the [alternate format help section](#).

For related information, please see Health Canada's [Information for Health Care Practitioners](#).

This document may be completed by the applicant's health care practitioner as defined in the Access to Cannabis for Medical Purposes Regulations (ACMPR). A health care practitioner includes medical practitioners and nurse practitioners. In order to be eligible to provide a medical document, the health care practitioner must have the applicant for the medical document under their professional treatment. Regardless of whether or not this form is used, the medical document must contain all of the required information, (see in particular s. 8 of the ACMPR).

**Your health care practitioner may use this form to provide you authorization to use cannabis for medical purposes.** Your health care practitioner may use a different form, but the required information as per section 8 of the ACMPR (outlined below) must be included.

**Access via Health Canada licensed producers:** Should you choose to access cannabis from a licensed producer, this form must be sent directly to the licensed producer of your choice. You may choose any licensed producer who is authorized to sell to registered clients. Please see the Health Canada website for a list of licensed producers. Should you wish to switch from one Health Canada licensed producer to another a new medical document will be required as licensed producers are required to keep the original medical document on file.

**Access via production for own medical purposes:** Should you choose to produce your own cannabis, or designate someone to produce it for you, the original of this document must be sent to Health Canada with your Registration Application Form.

Patient's Given Name and Surname:

Patient's Date of Birth (DD/MM/YYYY):

Daily quantity of dried marijuana to be used by the patient:  grams / day

The period of use is  day(s) or  week(s) or  month(s).

**Note: The period of use cannot exceed one year**

Health care practitioner's given name and surname:

Profession:

Health care practitioner's business address:

Full business address of the location at which the patient consulted the health care practitioner (if different than above):

Phone Number:

Fax Number (if applicable):

Email Address (if applicable):

Province(s) Authorized to Practice in:

Health Care Practitioner's Licence number:

**By signing this document, the health care practitioner is attesting that the information contained in this document is correct and complete.**

Health Care Practitioner's Signature: \_\_\_\_\_

Date Signed (DD/MM/YYYY):

### Important Note for Authorizing Health Care Practitioner

**If the patient chooses to produce cannabis for their own medical purposes or you are not submitting this document via secure fax do not initial the box below.**

If your patient chooses to access cannabis for medical purposes via a licensed producer, this medical document can be submitted from the health care practitioner's office to the licensed producer by secure fax. If you choose to submit the medical document by secure fax, initial the statement below to acknowledge agreement.

I, the health care practitioner, acknowledge that the faxed medical document is now the original medical document and that I have retained a copy of this document for my records only.

Initial here:

[https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/dhp-mps/alt\\_formats/pdf/marihuana/info/med-eng.pdf](https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/dhp-mps/alt_formats/pdf/marihuana/info/med-eng.pdf)

# Recreational cannabis (Oct 17)

- Purchase fresh or dried cannabis, cannabis oil, plants and seeds for cultivation from either a provincially or territorially regulated retailer, or — where that option is not available — directly from a federally licensed producer;
- Possess up to 30 grams of dried legal cannabis or its equivalent in public;
- Share up to 30 grams (or its equivalent) of legal cannabis and legal cannabis products with other adults;
- Cultivate up to four plants at home (four plants total per household); and
- Prepare various cannabis products (such as edibles) at home for personal use, provided that no dangerous organic solvents are used in the process.



# Recreational use in British Columbia

- BC Liquor Distribution Branch
  - is the only wholesaler for non-medicinal cannabis
  - buys from 32 federally licensed producers
  - sold in standalone LDB stores & online by LDB
  - will licence private retail stores
  - will not include edibles to start



Health  
Canada

Santé  
Canada

*Your health and  
safety... our priority.*

*Votre santé et votre  
sécurité... notre priorité.*

## **Information for Health Care Professionals**

**Cannabis (marihuana, marijuana) and the  
cannabinoids**



**Table 4: Quick Reference of Smoked to Estimated Oral Doses of  $\Delta^9$ -THC**

<b>“Smoked Dose”† % THC in a 750 mg cannabis cigarette (Total available mg <math>\Delta^9</math>-THC)</b>	<b>Estimated Oral Dose (mg <math>\Delta^9</math>-THC)‡</b>
1 % THC (7.5 mg)	18.8 mg
2 % THC (15 mg)	37.5 mg
2.5 % THC (18.8 mg)	46.8 mg
3 % THC (22.5 mg)	56.3 mg
5 % THC (37.5 mg)	93.8 mg
7.5 % THC (56.3 mg)	140.6 mg
10 % THC (75 mg)	187.5 mg
12.5% THC (93.8 mg)	234.4 mg
15 % THC (112.5 mg)	281.3 mg
20 % THC (150 mg)	375 mg

† A “smoked dose” is defined as the total available amount (in mg) of  $\Delta^9$ -THC in a standard cannabis cigarette (750 mg joint)

‡ An oral dose is defined as the total amount (in mg) of orally ingested  $\Delta^9$ -THC

# Route

Issue	Smoking/vaporisation	Oral
Onset (min)	5–10	60–180
Duration (h)	2–4	6–8
Pro	Rapid action, advantage for acute or episodic symptoms (nausea/pain)	Less odor, convenient and discrete, advantage for chronic disease/symptoms
Con	Dexterity required, vaporisers may be expensive, and not all are portable	Titration challenges due to delayed onset

Route of Administration	Inhalation	Oral
% Dose Consumed	~ 50% (loss due to pyrolysis)	100%
Trajectory to Circulation	Lungs – Bronchi-Bronchiole - Alveoli	Stomach – Small Intestines – Portal Vein - Liver
Other Factors Affecting Uptake	Intake upon inhalation (puff duration, intake volume, holding time)	Absorption (stomach contents, metabolic rate, genetic variants in CYP 450 enzyme activity, enzyme regulation by other drugs)
First-Pass Hepatic Metabolism	Bypassed	First-Pass Hepatic Metabolism by CYP450 enzymes
Bioavailability	2 – 56%	<20%
Onset	Immediate	30 – 90 minutes
Time of Peak Plasma	5 – 10 minutes	1 – 6 hours
Duration	2 - 4 hours	4 – 8 hours

Issue	Oromucosal	Topical
Onset (min)	15–45	Variable
Duration (h)	6–8	Variable
Pro	Pharmaceutical form (nabiximols) available, with documented efficacy and safety.	Less systemic effect, good for localised symptoms
Con	Expensive, spotty availability	Only local effects

## Smoking

- Most common route of administration, but not recommended (joints, bong, pipes, etc.)
- Combustion at 600–900 °C producing toxic biproducts: tar, PAH (polycyclic aromatic hydrocarbons), carbon monoxide (CO), ammonia (NH<sub>3</sub>).
- Chronic use associated with respiratory symptoms (bronchitis, cough, phlegm), but not lung cancer nor COPD (if cannabis only).
- Patients may mix with tobacco increasing respiratory/cancer risk
- 30–50% of cannabis is lost to ‘side-stream’ smoke

## Vaporisation

- Heats cannabis at 160–230 °C. Reduced CO, but not complete elimination of PAH demonstrated to date.
- Vaporisation produces significantly less harmful biproducts vs. smoking.
- Decreased pulmonary symptoms reported compared to smoking.

## Oral

- Oils, capsules and other po routes increasingly popular due to convenience and accuracy of dosing.
- Edibles (brownies/cookies) may be more difficult to dose.
- Juicing and cannabis teas do not allow for adequate decarboxylation of raw plant
- Nabiximols oromucosal spray is currently the only cannabis-based prescription that delivers standardised dosage of CBD/THC in a 1:1 ratio with extensive research
- Tinctures and lozenges intermediate onset with limited research

# Clinical Pearls

- Start low, go slow, stay low
  - Reduces fatigue, tachycardia dizziness
  - Promotes tolerance to THC psychoactive effect
- For medical benefit, higher CBD content, low THC.
- Patients use average 1-3 g/day (<5% use >5 g/day)
- For chronic symptoms typically use long acting preps (oral)
- Hemodialysis does not appreciably remove THC/CBD/terpenes.

# Oral Dosing

- Day 1-2 = 2.5 mg THC qhs (or 1.25 mg...)
- Day 3-4 = 3.75 – 5 mg THC qhs
- Day 5-6 = ↑ 1.25-2.5 mg THC q2d until satisfied or reduce to best tolerated dose
- (CBD dose 5-20 mg PO divided BID-TID but in seizure disorders up to 2,500 mg/day)

# Oral Dosing

- Day 1-2 = 2.5 mg THC daily (or 1.25 mg...)
- Day 3-4 = 2.5 mg THC BID
- Day 5-6 = q2d titrate up to 5 mg TID or until satisfied or reduce to best tolerated dose
- >20-30 mg/day ↑ adverse effects/tolerance

# Dosing inhalations

- Variables make it harder to dose: Size of chamber, depth of inhalation, breath holding, temperature of incineration (smoked or vaped)
- Inhale once, wait 15 minutes, then once each 15-30 minutes until symptom control achieved.

# What about terpenes?

- Monoterpenoids & sesquiterpenoids
- $\beta$ -Myrcene – anti-inflammatory, analgesia, sedating
- D-Limonene – antidepressant, anxiolytic
- $\alpha$ -Pinene – anti-inflammatory, minimizes memory loss from THC
- $\beta$ -caryophyllene – anti-inflammatory, analgesic



3D chess on [Star Trek](#)  
from the episode "[Court Martial](#)")



# New cannabis classification

- Type I – THC predominant
- Type II – mixed THC:CBD content
- Type III – CBD predominant
- Terpenes contribute to the pharmacologic effects and adverse effects so this content should be known as well.



# Patterns of medicinal cannabis use, strain analysis, and substitution effect among patients with migraine, headache, arthritis, and chronic pain in a medicinal cannabis cohort

Eric P. Baron<sup>1\*</sup>, Philippe Lucas<sup>2,3,4</sup>, Joshua Eades<sup>2</sup> and Olivia Hogue<sup>5</sup>

# Methods

- Electronic survey of medicinal cannabis patients
- 2032 recruited in two days (\$10 incentive)
- Headaches, arthritis, chronic pain (42.4%)
- Methods, frequency, quantity, preferred strains
- Cannabinoid and terpene profile
- ID Migraine as a validated tool

# Results (migraine n=445)

- “OG Shark” most preferred strain
- Substituted opiates for cannabis (43.4%)
  - Antidepressants 39%, NSAIDs 21%, Triptans 8.1%  
anticonvulsants 7.7%, muscle relaxers 7%
- 2032 patients total (chronic pain 42.4%)

## Preferred Cannabis Strains (top 15)

Chronic pain as primary illness	Strain	Mental Health Condition/PTSD	Insomnia/Sleep Disorder	Gastrointestinal Disorder/ Crohn's Disease
OG Shark (43; 10.5%)	BD	Jack Herer (52; 10.8%)	Lemon Sour Diesel (20; 13.8%)	Island Sweet Skunk (8; 9.8%)
	1.1%)	Island Sweet Skunk (50; 10.4%)	OG shark (15; 10.4%)	Jack Herer (8; 9.8%)
CBD House Blend (34; 8.3%)	; 7.4%)	White Widow (46; 9.6%)	Skywalker OG (13; 9%)	Black Tuna (7; 8.5%)
	nd	Jean Guy (41; 8.5%)	Pink Kush (12; 8.3%)	Afghani (6; 7.3%)
Pink Kush (34; 8.3%)	lend	Lemon Sour Diesel (37; 7.7%)	Jack Herer (10; 6.9%)	Warlock CBD (6; 7.3%)
	.1%)	Pink Kush (35; 7.3%)	White Widow (9; 6.2%)	White Widow (6; 7.3%)
Skywalker OG (29; 7.1%)	; 5.4%)	OG Shark (34; 7.1%)	Afghani (8; 5.5%)	CBD House Blend (5; 6.1%)
	esel	Sweet Skunk CBD (30; 6.2%)	Indica House Blend (7; 4.8%)	Sweet Skunk CBD (5; 6.1%)
Master Kush (28; 6.8%)	8; 5.4%)	Afghani (28; 5.8%)	Sweet Skunk CBD (7; 4.8%)	OG Shark (5; 6.1%)
	unk	Skywalker OG (24; 5%)	Island Sweet Skunk (7; 4.8%)	OG Shark (5; 6.1%)
Warlock CBD (28; 6.8%)	(8; 5.4%)			

Strain	Terpenes (%)								Cannabinoids (%)			
	$\alpha$ -Pinene	$\beta$ -Myrcene	D-Limonene	Linalool	$\beta$ -Caryophyllene	Humulene	Trans-nerolidol	Bisabolol	THCA	THC	CBDa	CBD
OG Shark	0.022	0.194	0.191	0.136	0.263	0.078	0.023	0.107	22.8	21.4	0.1	0
Afghani	0.024	0.101	0.036	0.033	0.132	0.055	0.032	0.066	16.9	15.6	0.1	0
Skywalker OG	0.037	0.217	0.208	0.159	0.319	0.149	0.024	0.110	24.2	22.9	0.2	0
Lemon Sour Diesel	0.127	0.235	0.037	0.026	0.169	0.067	0.022	0.026	19.9	18.3	0.1	0
Jack Herer	0.369	0.612	0.023	0.021	0.132	0.039	0.046	0.013	18.8	17.9	0.2	0
Jean Guy	0.031	0.066	0.069	0.063	0.156	0.047	0.050	0.052	18.1	17.3	0.1	0
White Widow	0.032	0.093	0.195	0.006	0.106	0.032	0.034	0.051	20.1	18.7	0.1	0
Pink Kush	0.019	0.187	0.178	0.148	0.317	0.093	0.058	0.124	27.7	25.8	0.1	0
Master Kush	0.045	0.168	0.192	0.203	0.353	0.169	0.039	0.130	28	25.6	0.1	0
Sweet Skunk CBD	0.054	0.162	0.042	0.014	0.051	0.019	0.015	0.028		9.1		11.2
Headband	0.028	0.238	0.230	0.138	0.318	0.094	0.065	0.124	25.1	23.4	0.1	0
Black Tuna	0.026	0.139	0.149	0.077	0.267	0.088	0.033	0.054	21.8	0.2	0.1	0
Warlock CBD	0.050	0.298	0.199	0.051	0.173	0.102	0.023	0.032	11.4	11	12.6	11.4
Cannatonic	0.059	0.152	0.038	0.022	0.099	0.032	0.015	0.035	10.9	9.4	7.6	7.5
Blueberry	0.000	0.333	0.000	0.052	0.324	0.089	0.021	0.023		21.7		0.1

# Summary

- Cannabis likely has a role in renal patients
- We need more evidence to help our patients
- We should have an organized way to ask our patients what works for them (a study)
- We can cautiously recommend medical cannabis for neuropathic pain

## Q3: I think I can now

- A) Tell my patients about cannabis
- B) Recognize that there is way too much to know about cannabis to talk with patients
- C) Listen to patients experiences with cannabis and continue my learning
- D) Advocate for renal specific research

[Results](#)



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**THANK YOU**

