

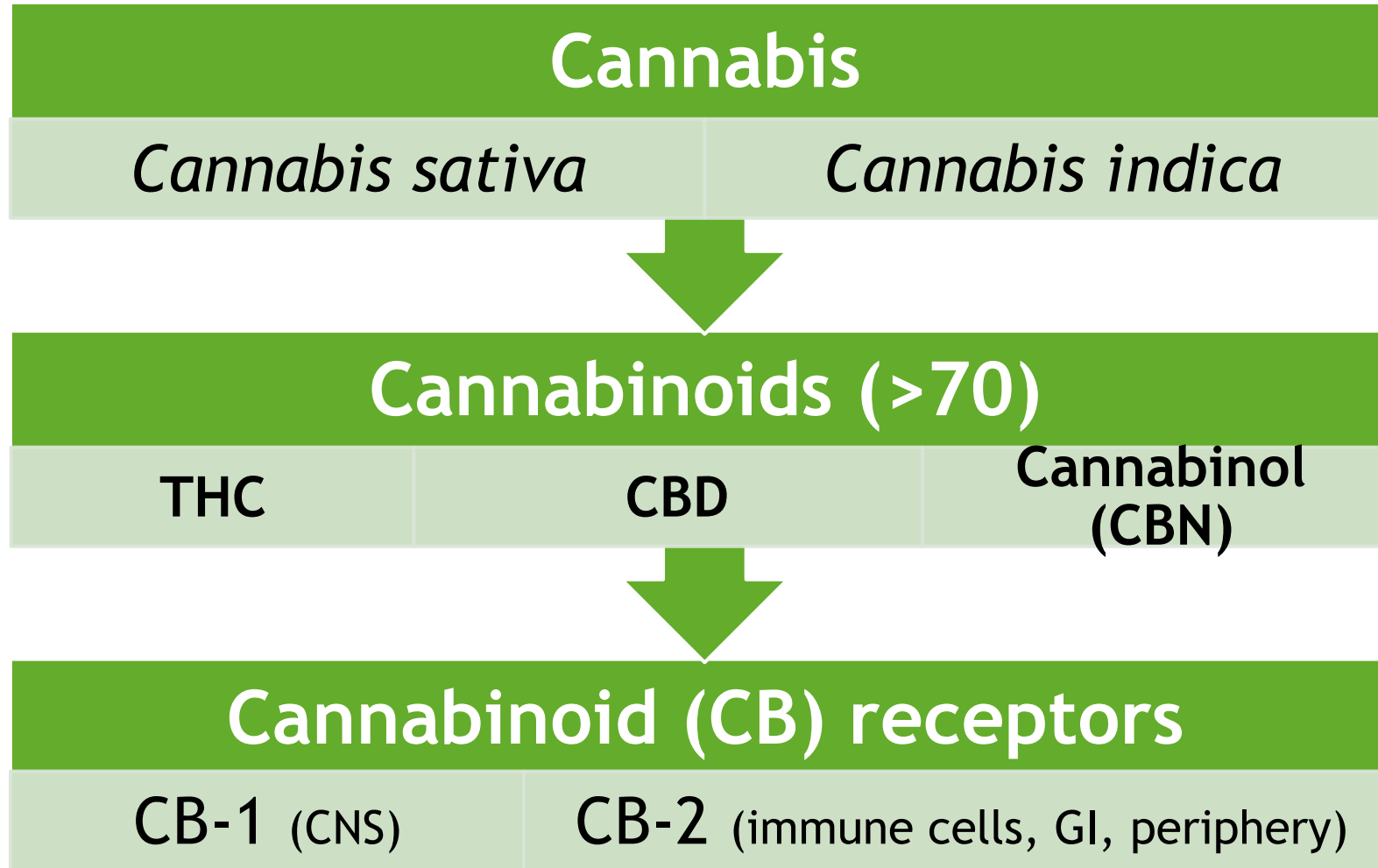
# The Effects - known & unknown - of Marijuana in Older Adults

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# Learning Objectives

1. Review various dosing strategies for medical marijuana and describe the pharmacokinetic differences between products.
2. Examine adverse effects of medical marijuana.
3. Evaluate evidence using medical marijuana for the treatment of common conditions in older adults.

# Cannabis: The Basics



# Endocannabinoid System (ECS)

- ▶ **Goal: homeostasis**
- ▶ Endocannabinoids:
  - ▶ Substances our body makes naturally
- ▶ CB receptors:
  - ▶ CB1 - primarily brain, central & peripheral nervous system, tissues
  - ▶ CB2 - immune cells, peripheral tissues

CB1 receptors are primarily found in the brain and central nervous system, and to a lesser extent in other tissues.

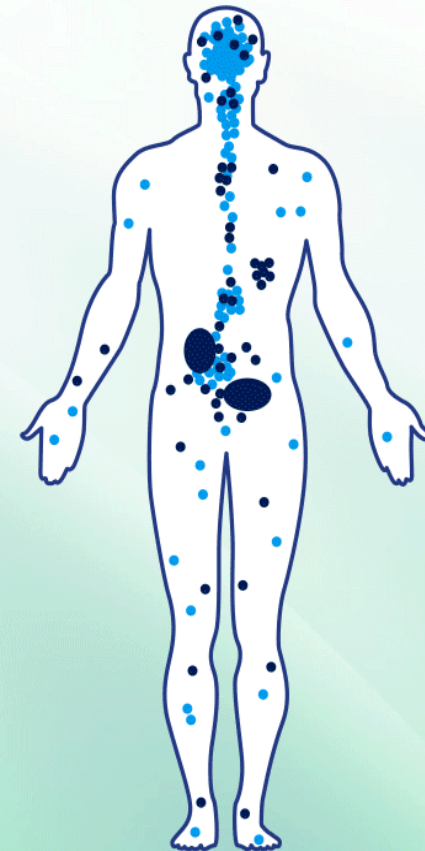


CBD does not directly "fit" CB1 or CB2 receptors but has powerful indirect effects still being studied.



CB2 receptors are mostly in the peripheral organs especially cells associated with the immune system.

Receptors are found on cell surfaces



# CBD vs. THC

CBD	THC
Non-psychoactive; decreases psychoactive effects of THC	Psychoactive
Low affinity for CB1 & CB2 receptors	Stimulates CB1 receptors in brain; CB2 to a lesser extent
Potent inhibitor of P450 enzymes (CYP3A4, 2C19, 2D6)	50% metabolized in the liver to 11-OH-delta-9- THC

# Cannabinoid Metabolism

- ▶ CBD metabolized by:
  - ▶ CYP3A4
- ▶ Inhibits:
  - ▶ CYP2C19
- ▶ THC metabolized by:
  - ▶ CYP3A4
  - ▶ CYP2C9
- ▶ Inhaled induces:
  - ▶ CYP1A2
  - ▶ Induce CYP3A4 (?)

# Drug Interactions & Considerations

- ▶ Warfarin
  - ▶ **INR fluctuations with inhaled formulations**
- ▶ CNS depressants
  - ▶ **Alcohol, barbiturates, benzodiazepines**
- ▶ Anticholinergics
- ▶ Caution with protein-bound medications
  - ▶ **Glipizide, loop diuretics, statins**

# CBD vs. THC

Effects	THC	CBD
Anticonvulsant	+	++
Muscle relaxant	++	+
Psychoactive	++	--
Anxiolytic/antipsychotic	--	++
Sedation	+	--
Tachycardia/hypertension	+	--
Appetite stimulant	+	--
Antioxidant	+	++



# Adverse Effects of Cannabis

## Acute

CV: tachycardia, hypertension, palpitations

Respiratory: coughing, wheezing, increased sputum production

CNS: disorientation, dizziness, euphoria, dry mouth, slowed reaction time, impaired coordination, anxiety, psychosis

## Chronic

Bone health: reduced bone mineral density

Respiratory: symptoms of chronic bronchitis, impair alveolar macrophages

CNS: depression, impaired memory, impaired attention and decision-making

Reproduction: decreases testosterone

# Contraindications & Warnings

## ▶ Contraindications:

- ▶ Acute psychosis and other unstable psychiatric conditions

## ▶ Warnings:

- ▶ Cardiovascular (may exacerbate arrhythmia), immunological, liver and renal impairment

# Cannabis Delivery Methods

- ▶ Inhaled (vaporized, smoking)
- ▶ Oral (edibles, oils, tinctures, spray)
- ▶ Topical (creams, gels, patches)

# Inhaled Formulations

- ▶ Immediate onset
- ▶ Peak effect within 30 minutes
- ▶ Last up to 2 hours
- ▶ Easier to dose since effects are immediate
- ▶ Vaporization preferred over smoking

# Oral Formulations

- ▶ Variable onset
  - ▶ 60 minutes to 6 hours
- ▶ Last up to 8 hours
- ▶ Difficult to dose, start low go slow
- ▶ Can re-dose if no effect after 90 minutes
- ▶ THC is more potent when eaten

# Power Couple of Cannabis: CBD + THC

- ▶ THC activates CB1 and CB2 receptors
  - ▶ Typical starting dose 2.5-5 mg (naïve), 20-10 mg (chronic)
- ▶ CBD enhances activity of serotonin 5-HT<sub>1a</sub>, α1 and α3 glycine receptor; activates nuclear peroxisome proliferator-activated receptor-γ (PPAR-γ) at high concentrations
  - ▶ Starting dose 5-10 mg; studies have used 5-800 mg/day
- ▶ In combination, CBD reduces the psychoactivity of THC
  - ▶ Best if the CBD component is higher (10:1)












# Topical Formulations

- ▶ 15 to 45 minute onset
- ▶ Last up to 2 hours
- ▶ Repeat dose as needed
- ▶ External use only
- ▶ CBD absorbs better than THC

# Current Cannabinoid Medications

	<b>Dronabinol (Marinol)</b>	<b>Nabilone (Cesamet)</b>	<b>Nabiximols (Sativex)</b>
<b>FDA Approved?</b>	Yes	Yes	No
<b>Medical Use</b>	N/V for cancer treatment, appetite stimulant for AIDS, analgesic for neuropathic pain in MS	N/V treatment in patients undergoing cancer treatment	Neuropathic pain and spasticity in MS, analgesic treatment in patients with cancer (mod-severe pain)
<b>Cannabis Properties</b>	Synthetic THC	Synthetic THC	CBD:THC (1:1)
<b>Doses</b>	2.5-20 mg/day	1-6 mg/day	2-12 sprays/day



Indication	Cannabinoid	# Studies/pts	Results	GRADE
Pain	Smoked THC, NBX	28/2454	 	Low-moderate
Spasticity in multiple sclerosis	NBX, NB, Dronabinol, THC/CBD capsules	4/2280	 	Low-moderate
Chemotherapy-related N/V	Dronabinol, NBX	28/1772		Low
Weight gain in HIV	Dronabinol	4/255		Low
Psychosis	CBD	2/71		Low
Sleep apnea	NB	1/22		Low
Anxiety	CBD	1/24		Very low
Depression	NBX	No direct study	 	Very low
Glaucoma	THC & CBD capsules, CBD spray	1/6	unknown	Very low

# Survey Data

- ▶ 2897 medical cannabis patients in California with 828 using cannabis for pain
  - ▶ 60 years+ (15%)

## Results from 828 patients

97% reported decrease in opioid dose

88% experienced side effects from opioids

92% reported cannabis side effects are more tolerable

80% reported cannabis more effective than opioids for pain

93% prefer cannabis to opioids

# Chronic Pain

- ▶ Prospective study of patients 65 years and older receiving medical cannabis
- ▶ 2736 patients
- ▶ Average age: 75 years (12% were 85 years +)
- ▶ 1822 patients using for pain
- ▶ Routes: oil (37%), smoking (24%), vaporization (6%)
- ▶ Follow-up at 1 and 6 months
  - ▶ Assess adverse events, treatment satisfaction, changes in symptoms and drug regimens

# Chronic Pain: Results

- ▶ Pain reduced from a median of 8 to 4 at 6 months
  - ▶ Prior to treatment: 573 (66.8%) reported pain 8-10
  - ▶ 6 months: 65 (7.6%) reported pain 8-10 ( $p < 0.001$ )
- ▶ 286 reported adverse events
  - ▶ Dizziness (9.7%)
  - ▶ Dry mouth (7.1%)
- ▶ 275 patients reported 1 or more falls 6 months *prior* to treatment
  - ▶ 113 reported falling within the 6 months of treatment ( $p < 0.001$ )
- ▶ 143 patients (18.1%) stopped or reduced opioid use

# Alzheimer's Disease

Study (# patients)	Cannabinoid	Results
Retrospective (40)	Dronabinol	↓ Pittsburgh Agitation Scale & Clinical Global Impression (CGI) scores
Open-label (11)	Cannabis oil	↓ CGI, caregiver distress, & neuropsychiatric inventory (NPI) domains
Randomized (50)	THC tablet or placebo	No differences in NPI

# Insomnia

- ▶ Randomized, double-blind, crossover trial in 29 patients with fibromyalgia and chronic insomnia
  - ▶ Ages 29-76 (mean 50 years)
  - ▶ Nabilone (0.5-1 mg) or amitriptyline (10-20 mg)
- ▶ Primary outcome:
  - ▶ Sleep quality measured by Insomnia Severity Index
- ▶ Results:
  - ▶ Nabilone superior [95% CI, 1.2-5.3]
- ▶ Adverse events:
  - ▶ More common with nabilone (dizziness, nausea, dry mouth)

# Patient Counseling

- ▶ Avoid driving:
  - ▶ 3-4 hours after smoking or vaporizing
  - ▶ 6 hours after oral consumption
- ▶ 2013 State of Colorado Legislature defined **5 ng/mL** of THC in the blood as “intoxicated”

# Questions?

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