MEDICAL CANNABIS: WHAT YOU NEED TO KNOW

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MultiCare Regional Cancer Center
What we’ll talk about:

• History of medical use of cannabis

• Effectiveness for managing some issues

• Forms of use: pros and cons

• Contraindications and adverse effects

• WA law provisions
What is Cannabis…?

- Dangerous Drug?

OR

- Natural Medicine?
Cannabis is...

- A plant From the *Cannabaceae* family:
  - Hops
  - Hackberry

- With many names:

(Russo 2007)
Its rise…

- Long history of medicinal use
  >3,000 years ago: Egypt, China
  1st – 2nd century CE: Pen-ts’ao Ching

- Intro to Western Medicine: 1839

(Russo 2007; Backes 2014)
And its fall...

- 1937: banned in all US States
- 1942: Removed from USP
- 1970: Schedule 1 classification
  “no accepted medical use”

(NIH-NCI; Backes 2014)
Its resurgence…

State Cannabis Programs

(Map source: National Conference of State Legislatures)
The Endocannabinoid System

- Receptors: CB1 (nervous system) & CB2 (immune cells)
- Endocannabinoids


Battista 2012, Vemuri & Makriyannis 2015
What’s so special about Cannabis?

- **Phytocannabinoids:**
  - “...any plant-derived natural product capable of either directly interacting with cannabinoid receptors or sharing chemical similarity with cannabinoids, or both.”
  - 110+ in cannabis

- **Properties:**
  - Pain-relieving
  - Anti-anxiety
  - Anti-seizure
  - Anti-nausea
  - Anti-inflammatory
  - Anti-oxidant
  - Anti-tumor
  - Neuroprotective

*And the list goes on!*

(Gertsch et al. 2010; Pacher et al. 2006; Ahmed et al. 2015; Russo 2011)
Cannabinoids and Their Therapeutic Effects

RAW

THCA
- Anti-cancer
- Anti-inflammatory
- Anti-emetic
- Appetite Stimulant
- Bronchodilator
- Neuroprotective

THCV
- Anti-inflammatory
- Appetite Suppressant
- Bone Stimulant

CBDA
- Anti-cancer
- Anti-inflammatory

CBDA
- Anti-inflammatory

CBGA
- Anti-age
- Anti-inflammatory

CBG
- Anti-cancer
- Anti-inflammatory

HEATED

THC
- Anti-allergic
- Anti-bacterial
- Anti-cancer
- Anti-inflammatory
- Appetite Stimulant
- Bronchodilator
- Neuroprotective

CBD
- Anti-allergic
- Anti-bacterial
- Anti-cancer
- Anti-inflammatory
- Anti-emetic
- Anti-nausea
- Anti-psychotic
- Anti-convulsant
- Anti-depressant
- Anti-infectious
- Antioxidant
- Bone Stimulant

CBC
- Anti-inflammatory
- Anti-fungal

CBG
- Anti-cancer
- Anti-fungal

AGED

CBNA
- Anti-inflammatory

CBN
- Anti-allergic
- Anti-convulsant
- Anti-inflammatory

Δ-8 THC
- Anti-anxiety
- Anti-emetic

CBL
- Anti-inflammatory

CBLA
- Anti-inflammatory

[Image: Courtesy Steep Hill Halent]
# The “Most Studied” Cannabinoids

<table>
<thead>
<tr>
<th>Cannabinoid:</th>
<th>Receptor Activity:</th>
<th>Major Effects:</th>
<th>Associated Rx drug:</th>
</tr>
</thead>
</table>
| THC:        | CB1: nervous system (strong)  
             CB2: immune cells (weak) | Psychoactive  
             Anti-nausea  
             Pain relief  
             Anti-spasmodic  
             Anti-inflammatory | Marinol (dronabinol)  
                    Cesamet (nabilone)  
                    Sativex (nabiximols)  
                    Levonantradol |
| CBD:        | CB1: nervous system (weak)  
             CB2: immune cells (weak) | Pain relief  
             Neuroprotective  
             Anti-seizure  
             Anti-anxiety  
             Anti-nausea | Sativex (nabiximols)  
                    Epidiolex (cannabidiol) |

(Russo 2011)
Terpenoids:

- Essential oil components
- Characteristic aroma
- Pharma effects

- Limonene
- Myrcene
- Pinene
- Linalool
- Caryophyllene(s)
- Nerolidol
- Phytol

(Russo 2011)
### Some Terpenoid Activities:

<table>
<thead>
<tr>
<th>Terpenoid</th>
<th>Noted Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limonene</td>
<td>anti-anxiety, anti-depressant</td>
</tr>
<tr>
<td>Myrcene</td>
<td>anti-inflammatory, sedative</td>
</tr>
<tr>
<td>Pinene</td>
<td>anti-inflammatory, bronchodilator</td>
</tr>
<tr>
<td>Linalool</td>
<td>anti-anxiety, anti-convulsant</td>
</tr>
<tr>
<td>Caryophyllenes</td>
<td>anti-inflammatory, anti-fungal</td>
</tr>
<tr>
<td>Nerodilol</td>
<td>sedative, anti/protozoal</td>
</tr>
</tbody>
</table>

Russo 2011
Terpenoid Analysis

PhytoPrint™
The “Entourage Effect”

Cannabinoids

Terpenoids
Reviewing the Evidence

Available studies will include:
- Synthetic THC (dronabinol, nabilone)
- Extracted THC +/- CBD
- Less often: “whole cannabis”
## Cancer: Nausea/Vomiting

<table>
<thead>
<tr>
<th>Cannabinoid</th>
<th>Control</th>
<th>Results</th>
<th>Reference</th>
</tr>
</thead>
</table>
| Dronabinol  | Anti-nausea meds & Placebo | More effective  
Preferred | Tramer et al. 2001 |
| Levonantradol | Anti-nausea meds | Dronabinol: decreased nausea, was preferred  
NS  
NS | Rocha et al. 2008 |
| Nabilone | Anti-nausea meds | 80%: ↓ nausea  
78%: people: preferred | Ware et al. 2008 |
| Levonantradol | Ondansetron & Placebo | Dronabinol: 71%  
Ondansetron: 64%  
Placebo: 15% | Parker et al. 2011 |
Appetite

- **Dronabinol vs. Megestrol acetate** (Jatoi et al. 2002)
  - Improved appetite:
    
    Megace 75% vs. Dronabinol 49%

- Advanced cancer patients
Appetite

- **THC+CBD vs. THC vs. Placebo** 
  (Strasser et al. 2006)
  - No Difference

  *Very low dose studied (2.5 mg THC)*
Smoked Cannabis

- P>0.001 for trend

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Grade</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>None</td>
<td>+37%</td>
</tr>
<tr>
<td></td>
<td>Mod</td>
<td>-38%</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>+1%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>None</td>
<td>+23%</td>
</tr>
<tr>
<td></td>
<td>Mod</td>
<td>-23%</td>
</tr>
<tr>
<td>Anorexia</td>
<td>None</td>
<td>+36%</td>
</tr>
<tr>
<td></td>
<td>Mod</td>
<td>-38%</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>+2%</td>
</tr>
<tr>
<td>Weight loss</td>
<td>None</td>
<td>+35%</td>
</tr>
<tr>
<td></td>
<td>Mod</td>
<td>-32%</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>-5%</td>
</tr>
</tbody>
</table>

(Bar-Sela et al. 2013)
Taste and Smell

• **THC vs. placebo** (Brisbois et al. 2011)
  - Chemosensory response:
    - Significant improvement: 36% THC vs. 15% placebo

  - “Food tastes better”:
    - 55% THC, 10% placebo (p = 0.04)

• Pre-meal Appetite score:
  - THC > placebo

• Pilot study: n= 11 (THC), 10 placebo
## Pain/neuropathy:

<table>
<thead>
<tr>
<th>Cannabinoid</th>
<th>Pain</th>
<th>Results</th>
<th>Notes</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixed</td>
<td>CA, other</td>
<td>Canna &gt; Effective than placebo</td>
<td>Significant Adverse effects</td>
<td>1</td>
</tr>
<tr>
<td>Mixed</td>
<td>Neuro, other</td>
<td>15/18 trials: sig, modest effect</td>
<td>No severe AEs, no dropouts; placebo or active control</td>
<td>2</td>
</tr>
<tr>
<td>Mixed</td>
<td>CA, other</td>
<td>27/38 RCTs: sig relief</td>
<td>Placebo or active control</td>
<td>3</td>
</tr>
<tr>
<td>Cannabis</td>
<td>Neuro</td>
<td>6 RCTs: All = sig relief</td>
<td>3 studies: clinically meaningful relief</td>
<td>4</td>
</tr>
</tbody>
</table>

## Smoked Cannabis

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Grade</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>None</td>
<td>+23%</td>
</tr>
<tr>
<td></td>
<td>Mod</td>
<td>+3%</td>
</tr>
<tr>
<td></td>
<td>Sev</td>
<td>-26%</td>
</tr>
</tbody>
</table>

(Bar-Sela et al. 2013)
Cannabis a “Cancer Cure”?  

- Limited Preclinical Evidence:  
  - *In vitro, In vivo*  
  - 1 small study: GBM  

- Potential? *maybe*  

- Certainty? No
What we know:
Cannabis Administration Routes:
Inhalation (Smoking & Vaping)

- Onset: 5 – 10 minutes
- Duration: 2-4 hours
- Bioavailability: 10-35%

- Vaping: less toxic byproduct

(Grotenhermen 2003; Huestis 2007; MacCallum & Russo 2018)
Caution…

• What is a “dab”?
  • Inhalation of volatile “concentrate”
  • Extracted via solvents, liquid gas, CO2

• Safety concerns:
  • Residual solvents: >80% samples
  • Pesticides: 33% samples
    • Paclobutrazol: not listed with EPA for use on food crops

• Avoid as medicine

(Raber et al. 2015)
Caution…

• Risk to the severely immunocompromised patient…
  • Bacteria, molds on green bud
  • Few case reports: aspergillus via inhaled cannabis
    *can be fatal

• Sterilization?

(Ruchlemer 2015)
Oromucosal: Sprays, Tinctures

- **Onset:** ~15 – 45 minutes (average)
- **Duration:** 6 - 8 hours
- **Bioavailability:**
  - Highly variable
  - Inhaled > OM >/= oral
  - *Less first-pass metabolism*
  - Increases with food

(Guy & Robson 2003, MacCallum & Russo 2018)
Oral Ingestion: Edibles, Capsules

- Onset: 1 - 3 hours
- Duration: 6 - 8 hours
- Bioavailability: variable, 4-20%

*First-pass metabolism: 11-OH-THC
  - Potent psychoactive
  - Reduces bioavailability THC

- More difficult to determine dose

(Grottenhermen 2003; Huestis 2007; MacCallum & Russo 2018)
A word of Caution…

• Labeling inaccuracies…

• Content analysis:
  • 17% accurately labeled
  • 23% under-labeled (had >THC content!)
  • 60% over-labeled

• Contributes to:
  • Overdosing
  • Difficulty dosing

(Vandrey et al. 2015)
Rectal: Suppositories

• Favored for absorption, no first-pass metabolism
  
  • Peak concentration: 1-8 hours
  • Bioavailability: ~2 X that of oral
  
• Availability?
• Avoid during chemo

(Huestis 2007; Grotenhermen 2003)
Skin

• Creams, Ointments
  • Few Studies

• Transdermal Patch
  
  *Preclinical research*
  • Animal model → plasma for 48 hrs
  • CBD, CBN → 10 fold higher

• More research needed

www.hc-sc.gc.ca/dhp-mps/marihuana
Contraindications:

- Allergy
- Pregnancy & breastfeeding
- CVD, Respiratory
- Hepatic, Renal
- Mental health hx
  - schizophrenia, bipolar d/o, depression

(Kahan 2014, Sachs 2015, Health Canada)
Precautions:

• Hx CVD, Angina

• HTN

• Asthma, COPD

(Kahan 2014, Sachs 2015, Health Canada)
Adverse Effects:

**Most Common:**
- Drowsiness/fatigue
- Dizziness
- Anxiety
- Nausea
- Cognitive effects (confusion, disorientation, hallucination, impaired memory)
- Cough/phlegm/bronchitis (with smoking)

**Common:**
- Euphoria
- Blurred vision
- Headache

**Rare:**
- Hypotension
- Psychosis/paranoia
- Rapid heart rate
- Hyperemesis
- Diarrhea
- Loss of coordination

(MacCallum 2018)
Lessening the Side Effects:

- When THC:CBD @ ~ 1:1
  - ↓ anxiety, memory issues

- Terpenoids
  - Beta-caryophyllene: ↓ pain, inflammation
  - Linalool, limonene: ↓ anxiety
  - Myrcene: sedating, ↓ pain
  - Pinene: ↓ memory issues

(Russo & Guy 2006; Morgan et al. 2010; Russo 2011)
Cannabis-Drug Interactions:

Drug effects increased by cannabis:

- THC:
  - Alcohol
  - Benzodiazepines (Ativan, Valium, Xanax, Restoril, etc.)
  - Opiates: codeine, fentanyl, morphine

- CBD (high dose):
  - Clobazapam – will need dose reduction

(MacCallum & Russo 2018)
WA Medical Law:

- Medical authorization from:
  - MD, DO, ARNP, PA, ND

- Over 18: good for 1 year
- Under 18: good for 6 months

- Qualified 18-20 yrs old: only enter medical endorsed store

**DOES NOT PROTECT:**
- federal law violation; employer policies; landlord policies; DUI
Common Qualifying Conditions: WA

- Cancer
- Muscle spasms/spasticity disorders, including MS
- Glaucoma
- HIV/AIDS
- Cachexia (wasting)
- Epilepsy, Seizure disorders
- Pain, unrelieved by standard treatments, meds
- Nausea (unrelieved)
- IBD, including Crohn’s
- Renal failure on dialysis
- PTSD
- TBI

(procon.org)
Why get a medical “card”?

- Can designate a provider to purchase and/or grow
  - Up to 4 plants

However, only purchase per rules for non-patients (if not in database)

- Affirmative Defense:
  * If possess not more than 4 plants, 6 usable ounces

- Access Medical Product:
  - Tested for: potency, foreign matter, bacteria, residual solvents, mycotoxins
Why be in the database?

• Allows purchase:
  • 3x the recreational limit
  • High THC product (if available)
  • Grow 6 plants
  • Minus sales/use tax

• Allows possession of:
  • 6 to 15 plants (as auth’d)

• Participation in cooperative
Why be in the database?

- WA state arrest protection
  - Card must be
    - presented if questioned
    - kept with supply
  - Must be in compliance with law

- Info NOT shared with federal government
  - unless convicted for violating WA law

www.doh.wa.gov/youandyourfamily/marijuana/medicalmarijuana
In Summary:

• Cannabis
  • has a long history of medical use
  • may be effective for some conditions

• There are pros/cons:
  • to use of various forms, related to difference in effects

• Research, talk with your medical team

• Awareness of WA law is important
Resources:

- WA State Dept of Health
  - “You and Your Family, Medical Marijuana”

- International Association for Cannabis as Medicine
  - cannabis-med.org – database of studies

- Americans for Safe Access
  - Safeaccessnow.org

- “Chronic Relief” by Nishi Whitely

- “Cannabis Pharmacy” by Michael Backes