MEDICAL MARIJUANA USE AND ABUSE

Paula Christianson-Silva RN, MS, ANP-BC
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Objectives

Based on the current body of research-based evidence, you will be able to:

1. State the primary clinical indications for medical marijuana use.
2. Describe the primary adverse health effects of marijuana.
3. Counsel patients on the clinical implications of marijuana use and legalization.
Background Information

Purple – 2 states with legalized cannabis

Dark Green – 8 states with medical cannabis and decriminalization laws

Light Green – 7 states with medical cannabis laws

Medium Green – 6 states with decriminalization laws
Marijuana Legislation - CA

first state to establish a medical marijuana program
allows people with cancer, AIDS and other chronic illnesses the right to grow or obtain medical marijuana when recommended by a physician (MD or DO)
does not affect federal law – DEA Schedule 1 Controlled Substance

Proposition 36 / The Substance Abuse and Crime Prevention Act of 2000
allows qualifying defendants convicted of non-violent drug possession offenses to receive probation if they agree to participate in and complete a licensed community drug treatment program.

Senate Bill 420 / The Medical Marijuana Protection Act of 2003
established an identification card system for medical marijuana patients issued through the CA Dept of Public Health, County Public Health Departments
allows for formation of non-profit patient collectives
Marijuana Legislation - CA

Proposition 19 / The Regulate, Control & Tax Cannabis Act  November 2010
Defeated 46% to 54%

would have legalized marijuana and allowed local governments to tax and regulate the sale of marijuana and its related activities

Senate Bill 1449  signed September 2010, effective January 1 2011

reduced charge of possession of up to one ounce of cannabis from a misdemeanor to a violation, with a $100 fine and no mandatory court appearance or criminal record
U.S. Research is limited due to classification as DEA Schedule I Controlled Substance, controlled by the National Institute on Drug Abuse, not the Food and Drug Administration.
Clinical Indications for Marijuana Use

Anorexia & cachexia

EBP

In advanced HIV disease -
2 studies demonstrated effectiveness of Dronabinal 1,2

In advanced cancer -
Jatoi et al (2002) – Megestrol more effective than Dronabinol 3

Cannabis-In-Cachexia-Study-Group (2006); multicenter, double blind, placebo-controlled – oral cannabis extract and tetrahydrocannabinol not significantly effective 4
Clinical Indications for Marijuana Use

Multiple Sclerosis

Possible benefit for pain, spasticity and depression, not statistically significant
Clinical Indications for Marijuana Use

Chemotherapy induced nausea & vomiting

EBP

10 studies – 1980s and early 90s

Cannabinoids more effective than placebo and are at least comparable to other antiemetics

Since 5-HT3 receptor antagonists (Zofran/ondansetron) introduced, not recommended in clinical guidelines 6
Clinical Indications for Marijuana Use

<table>
<thead>
<tr>
<th>Anecdotal Reports</th>
<th>Possible Uses for:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chronic Neuropathic Pain</td>
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<td></td>
<td>Chronic Musculoskeletal Pain</td>
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<tr>
<td></td>
<td>ALS</td>
</tr>
<tr>
<td></td>
<td>Migraine Headaches</td>
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<td>Other severe nausea</td>
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<table>
<thead>
<tr>
<th>Clinical Guidelines</th>
<th>Not recommended over traditional therapy for:</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Glaucoma 7</td>
</tr>
</tbody>
</table>
Clinical Indications for Marijuana Use

“Serious Medical Condition” means all of the following:

- Acquired immune deficiency syndrome (AIDS)
- Anorexia
- Arthritis
- Cachexia
- Cancer
- Chronic Pain
- Glaucoma
- Migraine
- Persistent muscle spasms, including but not limited to, spasms associated with multiple sclerosis
- Seizures, including, but not limited to, seizures associated with epilepsy
- Severe nausea
Clinical Indications for Marijuana Use

Any other chronic or persistent medical symptom that either:

Substantially limits the ability of the person to conduct one or more major life activities as defined in the Americans with Disabilities Act of 1990 (Public Law 101-336).

If not alleviated, may cause serious harm to the patient’s safety or physical or mental health.
Adverse Health Effects of Marijuana Use

Evidenced Based Practice (EBP)
Cannabis contains over 400 compounds, 60 cannabinoids

Primary psychoactive cannabinoid is delta-9-tetrahydrocannabinol (THC)

THC binds to protein, accumulates in fatty tissue and is slowly released

THC easily crosses BBB and binds to CB1 receptors in brain and CB2 receptors in brain and immune cells

Repeated stimulation of CB1 receptors causes desensitization and down regulation

THC is metabolized by multiple hepatic enzymes, excreted in urine and feces

Reduced bioavailability with oral ingestion due to hepatic first pass metabolism
Fig. 2 Distribution of THC in the body. The distribution of THC after a single administration in plasma and body tissues. Note the biphasic' disappearance in plasma. The rapid phase (in minutes) indicates a rapid uptake of the drug by fat-containing tissues. The slow phase (in days) shows the release of THC by these tissues (Nahas, 1975). THC, tetrahydrocannabinol.
**Adverse Health Effects of Marijuana Use**

<table>
<thead>
<tr>
<th>Pulmonary</th>
<th>Smoke contains 3X tar of cigarette smoke 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBP</td>
<td>Multiple studies:</td>
</tr>
<tr>
<td></td>
<td>No association between long-term use and airflow obstruction</td>
</tr>
<tr>
<td></td>
<td>Short-term bronchodilation effect</td>
</tr>
<tr>
<td></td>
<td>Irritant effect — increase in cough, sputum production, wheezing, bronchitis, asthma exacerbation, cystic fibrosis exacerbation 10</td>
</tr>
</tbody>
</table>

Moore et al (2005); US epidemiologic study — higher rates of COPD 11
Studies That Reported Effects of Long-term Marijuana Inhalation on Respiratory Complications

<table>
<thead>
<tr>
<th>Source</th>
<th>Study Design</th>
<th>No. of Subjects</th>
<th>Results</th>
<th>Control for Confounding</th>
<th>Mean Generic Quality Score</th>
<th>Mean Exposure and Disease Specific Quality Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bloom et al.(1)</td>
<td>Cross-sectional</td>
<td>990</td>
<td>Multivariable analysis shows association between intensity and duration of nontobacco cigarettes and cough, phlegm, and wheeze</td>
<td>Tobacco</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>Henderson et al.(2)</td>
<td>Case series</td>
<td>200</td>
<td>Cannabis smokers complained of pharyngitis (n = 150), rhinitis (n = 20), chronic bronchitis (n = 20), and asthma (n = 4)</td>
<td>None</td>
<td>4.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Moore et al.(3)</td>
<td>Cross-sectional</td>
<td>672</td>
<td>Marijuana use associated with respiratory symptoms: chronic bronchitis, coughing on most days, phlegm, wheezing, and chest sounds without a cold</td>
<td>Tobacco</td>
<td>17.5</td>
<td>3</td>
</tr>
<tr>
<td>Sherrill et al.(4)</td>
<td>Observational cohort</td>
<td>1802</td>
<td>Marijuana smoking associated with cough, phlegm, and wheeze</td>
<td>Tobacco</td>
<td>13.5</td>
<td>3</td>
</tr>
<tr>
<td>Taylor et al.(5)</td>
<td>Cross-sectional</td>
<td>943</td>
<td>Marijuana use associated with wheezing apart from colds, exercise-related shortness of breath, nocturnal waking with chest tightness, and morning sputum production</td>
<td>Tobacco</td>
<td>12.5</td>
<td>3</td>
</tr>
<tr>
<td>Taskin et al.(6)</td>
<td>Cross-sectional</td>
<td>446</td>
<td>Marijuana smokers had increased rates of chronic cough, sputum production, wheeze, and more than 1 prolonged episode of bronchitis during the previous 3 y compared with the nonsmokers</td>
<td>Tobacco</td>
<td>11.5</td>
<td>3</td>
</tr>
<tr>
<td>Gasti et al.(7)</td>
<td>Case-control</td>
<td>200</td>
<td>44% of asthma group compared with 20% of control group admitted to or tested positive for recent cannabis use (OR, 3.14; P&lt;.001). In acute bronchospasm group, 82% admitted to recently using cannabis substances compared with 55% of controls (OR, 3.63; P&lt;.02). No difference in proportions of asthma and control groups that reported marijuana use.</td>
<td>None</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>Tennant et al.(8)</td>
<td>Case series</td>
<td>36</td>
<td>Marijuana smokers complained of increased amounts of dyspnea and excess sputum production</td>
<td>None</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Boulogouris et al.(9)</td>
<td>Cross-sectional</td>
<td>82</td>
<td>Verbal hoarseness was detected in 4 of 44 hashish users and 2 of 36 controls, two of 44 users and 1 of 38 controls had signs of emphysema.</td>
<td>None</td>
<td>8</td>
<td>1.5</td>
</tr>
<tr>
<td>Chopra et al.(10)</td>
<td>Cross-sectional</td>
<td>124</td>
<td>Langhitas, pharyngitis, bronchitis, dyspnea, asthma, irritating cough, hoarse voice, and dryness of the throat were more common in those who smoked higher daily dose of marijuana</td>
<td>None</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Mehndiratta and Wu(11)</td>
<td>Cross-sectional</td>
<td>75</td>
<td>Cannabis smokers complained of weight loss, cough, dyspnea, and poor sleep</td>
<td>None</td>
<td>8</td>
<td>1.5</td>
</tr>
<tr>
<td>Polen et al.(12)</td>
<td>Cross-sectional</td>
<td>902</td>
<td>Marijuana smokers reported more days ill with cold, flu, or sore throat in past year than nonsmokers</td>
<td>Tobacco</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>Stern et al.(13)</td>
<td>Cross-sectional</td>
<td>173</td>
<td>In patients with cystic fibrosis, 70% of marijuana users noted immediate and 6% noted long-term improvement in symptoms; 30% of users noted immediate and 40% noted long-term worsening of symptoms.</td>
<td>None</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Tennant and Prendergast(14)</td>
<td>Case series</td>
<td>31</td>
<td>39% of marijuana smokers complained of m fully described.</td>
<td>None</td>
<td>4</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Abbreviation: OR, odds ratio.

### Adverse Health Effects of Marijuana Use

<table>
<thead>
<tr>
<th>Cancer</th>
<th>EBP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Known carcinogens</strong>&lt;br&gt;Direct association to Lung Cancer not proven;&lt;br&gt;3 studies demonstrated premalignant effect on bronchial epithelium 12,13&lt;br&gt;5 studies with conflicting evidence on association with Head and Neck Cancer14&lt;br&gt;Chacko et al - Increased rate of TCCA of Bladder with marijuana users, tobacco use possible confounding variable 15</td>
<td></td>
</tr>
</tbody>
</table>
Adverse Health Effects of Marijuana Use

Central Nervous System

EBP

Large meta-analysis and an epidemiologic study – no long term cognitive deficits 16, 17

Neuroimaging studies – decreased volume of amygdala and hippocampus, cumulative effect 18

Definite short term effect on attention, performance, memory and psychomotor speed; 9 studies associated it with an increased risk for MVA, especially fatal collisions 19
Adverse Health Effects of Marijuana Use

Published July 2012 –
1037 participants followed birth-age 37
Neuropsychological decline in adolescent-onset cannabis users, not restored by abstinence 37
Fig. 4 Effect of smoking a cannabis cigarette containing 20 mg tetrahydrocannabinol (THC) on pilot performance in a flight simulator landing task (Leirer et al, 1991). -- {blacksquare} - -, 20 mg THC; --[UNK]--, placebo.
Adverse Health Effects of Marijuana Use

Psychiatric EBP

Significant evidence that marijuana causes psychosis, probably through effect on dopamine release 20

Conflicting evidence on exacerbation of symptoms or relapse in known psychotic illness 21

No evidence for increased risk of Depression 22

No evidence of decreased motivation as measured by Apathy Evaluation Scale (Barnwell et al 2006) 23
Intoxication – tachycardia, little or no change in BP 24; high doses – bradycardia, hypotension

Reports of reversible EKG abnormalities

Possible danger to elderly of severe postural hypotension 25

Mittleman et al (2001); large MI study – MI rarely triggered by marijuana; risk 5X higher within one hour of smoking 26
Adverse Health Effects of Marijuana Use

Immune System

EBP

Suppresses immune functions
Effect on infection rates not studied 27
Victoria

Original Medical Marijuana Plant
Adverse Health Effects of Marijuana Use

Men -
- Decreases testosterone production
- May decrease libido and lead to erectile dysfunction and gynecomastia 28
- May decrease sperm count and motility leading to infertility 29

Women -
- Chronic use increases prolactin levels leading to galactorrhea 30
Large prospective study (Thomson et al 2008) – associated with higher incidence of periodontal disease at age 32; researchers controlled for tobacco use, dental hygiene and dental care.
Adverse Health Effects of Marijuana Use

Yazulla (2006) – causes corneal vasodilation and decreased intraocular pressure 32
Adverse Health Effects of Marijuana Use

Prenatal effect –

Ottawa Prenatal Prospective Study (1999) – no significant association to growth measures at birth; children of heavy users (6 joints per week) had smaller head circumference at all ages 33

Johns Hopkins (1990) – no association with prematurity or congenital abnormalities 34

Avon Longitudinal Study (2002) – 12,000 women; no association with preterm birth, NICU admission or mortality; slight decreased birth weight in weekly users, but not occasional users 35
Adverse Health Effects of Marijuana Use

Warren et al (2005) – negative correlation between BMI group and percent marijuana use 36
## Adverse Health Effects of Marijuana Use

<table>
<thead>
<tr>
<th>DSM-IV</th>
<th>Example</th>
<th>ICD-9 codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabis intoxication</td>
<td>(Drug-Induced Delirium)</td>
<td>292.81</td>
</tr>
<tr>
<td>(Cannabis withdrawal)</td>
<td></td>
<td>none</td>
</tr>
<tr>
<td>Cannabis abuse, unspecified</td>
<td></td>
<td>305.20</td>
</tr>
<tr>
<td>Cannabis dependence, unspecified</td>
<td></td>
<td>304.30</td>
</tr>
<tr>
<td>Cannabis dependence, in remission</td>
<td></td>
<td>304.33</td>
</tr>
</tbody>
</table>

Discussion Questions

- Is medical marijuana sometimes prescribed when not clinically indicated?
- Does marijuana lead to use of other drugs?
- Is marijuana as harmful as cigarettes and alcohol?
- When, if ever, should you recommend marijuana to a patient?
- If marijuana becomes legal, will it be safer?
- Other?
References


Thank you

Paula Christianson-Silva RN, MS, ANP-BC
pchristianson-silva@nursing.arizona.edu
silvafamily@yahoo.com