Medical Marijuana: Is That Cannabis Dragon Really Magical?

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Loveland, Ohio

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Opening Prayer
Taking a Poll

- How many are from states that have passed laws to legalize MMJ?
- How many are from states that have not passed laws to legalize MMJ?
Industry News

- By 2016, 2.4 million people were registered as medical cannabis patients
- This industry will grow to $9 billion by 2017
Objectives

- Discuss the history of medical marijuana use and the legal landscape in Ohio
- Review cannabinoid receptor pharmacology
- Identify & manage evidence-based indications, side effects, interactions associated with the use of medical marijuana
- Discuss the role of the physician, nurse, pharmacist in patient education and monitoring of medical marijuana use
Genesis 1:29

Then God said, "I give you every seed-bearing plant on the face of the whole earth and every tree that has fruit with seed in it. They will be yours for food." - NIV

Found in the Garden of Eden?
Cannabis History

- Earliest documented use 2700 BC in China (e.g., gout, malaria, constipation, menstrual disorders, absentmindedness).

- Western medicine adopted use of cannabis as analgesic in 19th Century (William O’Shaughnessy MD in 1839). 1854 listed in U.S. Pharmacopeia.

Prior to WWI, pharmaceutical supplies of cannabis imported from India per USP requirements. From 1915-1927, some states banned cannabis. 1930’s Parke Davis, Eli Lilly manufacture, and Lloyd Brothers Cincinnati pharmacists dispense cannabis extracts for medicine.

- 1937 Marijuana Tax Act created criminal fine for recreational use/possession but affirmed right of physicians and pharmacists to prescribe and dispense medical marijuana. AMA opposed. Led to decline in MJ scripts. Fed’s 1st attempt to regulate MJ. By 1942, MJ removed from the U.S. Pharmacopeia
Specific Medicines

CANNABIS

(AMERICAN HEMP)

(A LIQUID PREPARATION)

ALCOHOL 74 PER CENT

LLOYD BROTHERS PHARMACISTS, INC.
CINCINNATI, OHIO

Water, 3 ml.

Sig: A teaspoonful of the dilution every hour. Shake the bottle before each dose.
Poisonous in Overdoses.

4 OUNCES
SPECIFIC MEDICINES

CANNABIS

(AMERICAN HEMP)

ALCOHOL 74 PER CENT

LLOYD BROTHERS, PHARMACISTS INC.
CINCINNATI
OHIO
Cannabis Regulation

- THC discovered in 1964

- U.S. Congress passed the Controlled Substances Act in 1970 in response to soaring recreational drug use. Schedule I - federally, not considered legitimate for medical use along with Heroin, LSD, Ecstasy, Methaqualone, Peyote category.

- Amount of marijuana that a person may possess for medical use varies widely from state to state.
Federal Legislation

- **July 28, 2014** HR 5226 Bill (Charlotte’s Web Medical Hemp Act) introduced by Scott Perry (R-PA), Paul Broun (R-GA), Steve Cohen (D-TN), Dana Rohrabacher (R-CA) - to amend the definition of marijuana and exclude medical marijuana from controlled substance list. Bill died in committee.

- **March 2015** US Senate passed Compassionate Access, Research Expansion, and Respect States (CARERS) Act of 2015 (S 683) to transfer medical marijuana from Schedule I to Schedule II of CSA. Ensures states with legal MMJ will have their patients’ access to drug respected by federal officials.

- **December 14, 2016** DEA issued final ruling that classified all cannabis extracts as Schedule 1 drugs including hemp cannabis.
Medical Marijuana

- **California** was the first to legalize in *1996* for AIDS wasting and cancer pain under Compassionate Use Act (Prop 215).

- **Ohio June 8, 2016** HB523 signed into law by Governor John Kasich - includes 20 indications & employer protection (25th state). In Ohio, Schedule II (regulated as ‘high potential for abuse’ like heroin).

- **Arkansas, Florida, North Dakota** in *November 2016* legalized medical use; **Montana** voted on whether to ease restrictions on existing medical marijuana law. Still not legal in **Kentucky**.

- 22 states have approved MJ use for seizure control including **Ohio**.
States with medical cannabis laws had a **24.8% lower mean annual opioid overdose mortality rate** compared with states without medical cannabis laws. **Will this be true in Ohio?**
Ohio Medical Marijuana Control Program
Ohio Medical Marijuana Control Program

September 8, 2016 – HB 523 bill signed on June 8, 2016 became effective

September 8, 2017 – rules and regulations must be completed

September, 2018 – Ohio Department of Commerce and State of Ohio Board of Pharmacy are required by law to ensure Ohio’s Medical Marijuana Control Program is fully operational no later than September, 2018 (cultivating, processing, testing, dispensing, physicians, patient and caregivers)

MMJ Ohio Advisory Committee

www.medicalmarijuana.ohio.gov
Ohio Sub. H.B. 523 Summary – Medical Marijuana Control Program

- Requires Ohio Department of Commerce and State Board of Pharmacy to administer MMCP

- Establishes MMJ Advisory Committee who will make recommendations to Department of Commerce, Board of Pharmacy, State Medical Board

- Permits patients, on recommendation of physicians, to use MMJ to treat qualifying medical conditions

- Patients must apply to Board of Pharmacy for registration

- Authorizes Department of Commerce to issue licenses to MMJ cultivators, processors, and testing labs

- Authorizes Medical Board to issue certificates to physicians seeking to recommend treatment with MMJ

- Prohibits cultivation of MMJ for personal, family, or household use

- 90-day supply – max 7.5 oz (three THC % tiers). THC plant < 35%, THC extract < 70%
Ohio HB 523

- Provides that the use or possession of medical marijuana by a registered patient in accordance with the bill’s provisions cannot be used as a reason for disqualifying the patient from medical care or from including the patient on a transplant waiting list.
- Requires that the Board of Pharmacy establish a program to assist patients who are veterans or indigent in obtaining medical marijuana.
- Specifies that it does not permit the use, possession, or administration of medical marijuana on federal land located in Ohio.
Ohio Law 2016 Allows:

<table>
<thead>
<tr>
<th>Disease</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS/HIV</td>
<td>Multiple Sclerosis</td>
</tr>
<tr>
<td>ALS</td>
<td>Pain (chronic &amp; severe or intractable)</td>
</tr>
<tr>
<td>Alzheimer’s</td>
<td>Parkinson’s Disease</td>
</tr>
<tr>
<td>Cancer</td>
<td>PSTD (weak evidence)</td>
</tr>
<tr>
<td>Crohn’s Disease</td>
<td>Sickle Cell Anemia</td>
</tr>
<tr>
<td>Chronic Traumatic Encephalopathy (CTE)</td>
<td>Spinal Cord Disease/Injury</td>
</tr>
<tr>
<td>Epilepsy or another Seizure Disorder</td>
<td>Tourette’s Syndrome</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>Traumatic Brain Injury (TBI)</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>Ulcerative Colitis</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>Any other disease or condition added by state medical board under section 4731.302 of Revised Code</td>
</tr>
<tr>
<td>Inflammatory Bowel Disease</td>
<td></td>
</tr>
</tbody>
</table>
### 17 States Allow Marijuana CBD Oil

<table>
<thead>
<tr>
<th>State</th>
<th>State</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alabama</td>
<td>South Carolina</td>
</tr>
<tr>
<td>Florida</td>
<td>Tennessee</td>
</tr>
<tr>
<td>Georgia</td>
<td>Texas</td>
</tr>
<tr>
<td>Iowa</td>
<td>Utah</td>
</tr>
<tr>
<td>Kentucky</td>
<td>Virginia</td>
</tr>
<tr>
<td>Mississippi</td>
<td>Wisconsin</td>
</tr>
<tr>
<td>North Carolina</td>
<td>Wyoming</td>
</tr>
<tr>
<td>Oklahoma</td>
<td>Idaho (approved, vetoed)</td>
</tr>
<tr>
<td><strong>Ohio</strong></td>
<td>New York (investigating in clinical trials now)</td>
</tr>
</tbody>
</table>
Introduction to Cannabis

- **Cannabis indica** and **Cannabis sativa** are the best-known species.

- A product’s chemical profile is more important than the strain of plant from which it originated.

- Products should be characterized by analytical chemistry - percentages of cannabinoids and terpenoids.
Compounds in Cannabis

- Cannabis, like all herbs, is a polypharmaceutical substance.
- 108 cannabinoids have been isolated (Hanus 2008).
- The cannabis-derived cannabinoids of most therapeutic interest are THC and cannabidiol (CBD).
  - Minor cannabinoids include cannabigerol, cannabichromene, and tetrahydrocannabinol (a short-chain C19 homolog of THC).
- Terpenoids are common, often aromatic, organic compounds found in many plants. Terpenoids found in cannabis include β-caryophyllene, myrcene, limonene, and pinene.
- As many as 420 other constituents occur in the plant (Turner et al 1980).

- phytoestrogens, flavonoids
Indication – fibromyalgia, diabetic nerve pain

Anti-inflammatory/analgesic

Active – CBD and B-carophyllene (sesquiterpene)

B-carophyllene is also found in rosemary, black pepper, oregano, cloves!

May be a selective agonist at CB2 receptors
Common Modes of Administration and Formulations

- **Inhalation by smoking or vaporization**
  - (herbal cannabis, resin, concentrates)

- **Oral**
  - (prescription cannabinoids, edibles, tinctures)

- **Oro-mucosal or sublingual**
  - (lollipops, lozenges, nabiximols)

- **Topical or Rectal**
  - (herbal cannabis, resin, concentrates)
Ohio HB 523 – Permissible Forms

- Oils
- Tinctures
- Plant Material
- Edibles
- Patches

- “Any other form approved by the Board of Pharmacy”

- Suppository and spray under debate……
Edibles
Images of a marijuana vaporizer
<table>
<thead>
<tr>
<th>Natural product Derived Compounds</th>
<th>Substance</th>
<th>Route of Administration</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabis</td>
<td>Multiple</td>
<td>Oromucosal</td>
<td>Multiple active cannabinoids</td>
</tr>
<tr>
<td>Cannabidiol (CBD)</td>
<td>Oral capsule</td>
<td>Cannabinoid extracted from Cannabis t</td>
<td></td>
</tr>
<tr>
<td>Cannador</td>
<td>Oral capsule</td>
<td>THC and CBD from Cannabis extract</td>
<td></td>
</tr>
<tr>
<td>Epidiolex® (FDA Fast Track)</td>
<td>Oil</td>
<td>Concentrated CBD from Cannabis extract</td>
<td></td>
</tr>
<tr>
<td>Nabiximol (Sativex®) (FDA Fast Track)</td>
<td>Oromucosal spray</td>
<td>THC and CBD extract from two Cannabis plant varieties</td>
<td></td>
</tr>
<tr>
<td>Tetrahydrocannabinol (THC)</td>
<td>Oral capsule Smoked Oromucosal</td>
<td>Active cannabinoid of Cannabis plant</td>
<td></td>
</tr>
<tr>
<td>THC/CBD</td>
<td>Oral capsule</td>
<td>Combination of cannabinoids</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Synthetic Compounds</th>
<th>Substance</th>
<th>Route of Administration</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ajulemic acid (AjA) (FDA PHASE II Active)</td>
<td>Oral capsule</td>
<td>Synthetic nonpsychoactive cannabinoid</td>
<td></td>
</tr>
<tr>
<td>Dronabinol (Marinol®; Syndros®) (FDA approved)</td>
<td>Oral capsule</td>
<td>Synthetic THC</td>
<td></td>
</tr>
<tr>
<td>Nabilone (Cesamet®) (FDA approved)</td>
<td>Oral capsule</td>
<td>Synthetic cannabinoid- THC analogue</td>
<td></td>
</tr>
</tbody>
</table>
Argument Against Dronabinol (Marinol) Capsules

- Approved in **1986** (chemotherapy induced N&V), expanded indication in **1992** (treatment of anorexia associated with weight loss in AIDS wasting)

- C-III, synthetic THC, very sedating, psychoactive

- Not an appropriate substitute for natural cannabis

- **No studies comparing cannabis plant cannabinoids to first line prescription drugs for CINV**
Cannabis ADME Process

- **Absorption**: varies via different routes: smoking (not Ohio approved), vaping, oral ingestion, IV, ophthalmic, transdermal, SL, rectal

- **Distribution**: 90-95% protein bound (in lipoproteins of brain, heart lung, liver, testes); 10% in RBC’s

- **Metabolism**: hepatic (allylic oxidation, epoxidation, decarboxylation, conjugation). THC oxidized by CYP2C9, CYP2C19, CYP3A4 to produce active metabolite 11-hydroxy THC and inactive 11-nor-9-carboxy THC (THC-COOH). Other metabolic paths via CYP2C8 and CYP3A2. Oral - first pass hepatic metabolism to 11-OH-Δ-9-THC.

- **Elimination**: 20-45% of THC is eliminated in urine and 65% - 80% in feces.
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Oral</th>
<th>Inhaled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>30 minutes- 1 hour</td>
<td>Seconds/minutes (9-23 minutes for 11-OH-THC)</td>
</tr>
<tr>
<td>Time to peak blood [']</td>
<td>2 hours</td>
<td>2 – 30 minutes</td>
</tr>
<tr>
<td>Maximal duration</td>
<td>2-6 hours</td>
<td>Dose dependent; 20 - 60 minutes</td>
</tr>
<tr>
<td>Variables</td>
<td>Dose/concentration, pattern of use, bioavailability</td>
<td>Dose, pattern of use</td>
</tr>
</tbody>
</table>

## THC Bioavailability

<table>
<thead>
<tr>
<th>Route of Admin</th>
<th>Bioavailability</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>10-20%</td>
<td>From package insert for Marinol: while 90-95% of the oral dose is absorbed, only 10-20% of the dose reaches systemic circulation due to high first pass metabolism and high lipid solubility</td>
</tr>
<tr>
<td>Oral</td>
<td>6%</td>
<td>Chocolate cookie prepared with 20 mg THC Reported range 2-56%</td>
</tr>
<tr>
<td>Inhalation via smoking</td>
<td>10-40%</td>
<td>No pharmacokinetic or clinical studies in humans</td>
</tr>
<tr>
<td>Inhalation via vaporization</td>
<td>10-40%</td>
<td></td>
</tr>
<tr>
<td>Transdermal</td>
<td>Unknown</td>
<td></td>
</tr>
</tbody>
</table>

Ohio State Medical Marijuana Program 2017 Reference
-- A typical marijuana joint contains 0.5 grams of marijuana
-- THC content ranges from 12% - 23% in the joint
-- A typical joint contains 60 mg - 115 mg THC

-- The standard serving size for a marijuana edible is 10 mg
**Δ-9-THC Detection**

- **Serum** - Active THC (positive at 20 ng/mL)
- **Urine** - Inactive THC-COOH-glucuronide (positive at 50 ng/mL). Answers, “has this person used cannabis over the last days or weeks?”

Levels of THC or metabolites correlate with efficacy or toxicity.
# Detected in the Urine

<table>
<thead>
<tr>
<th>THC-COOH-Glucuronide</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Single Use</td>
<td>3 Days</td>
</tr>
<tr>
<td>Moderate Use (4x/Week)</td>
<td>5 – 7 Days</td>
</tr>
<tr>
<td>Daily Use</td>
<td>10 – 15 Days</td>
</tr>
<tr>
<td>Long-Term Heavy Smoker</td>
<td>&gt;30 Days</td>
</tr>
<tr>
<td>THC - T1/2</td>
<td>2-7 Days</td>
</tr>
</tbody>
</table>
Endocannabinoid System

- Endogenous cannabinoids, cannabinoid receptors, and enzymes that synthesize and degrade endocannabinoid ligands (anandamide & 2-AG)
- Effects of cannabinoids are mediated by two G protein-coupled receptors, CB1 and CB2 (discovered 1980’s)
- Retrograde signaling, partial agonism, inverse agonism, and functional selectivity determine the cellular response to specific cannabinoid receptor ligands (endocannabinoids, plant cannabinoids, synthetic cannabinoids)
Anandamide and 2-AG (arachidonoylglycerol) are synthesized and released from post synaptic neuron terminals, travel backwards across the synaptic cleft to presynaptic neurons, and bind CB1 receptors on presynaptic terminals = retrograde signaling.

This inhibits release from excitatory and inhibitory synapses of serotonin, glutamate, acetylcholine, GABA, norepi, dopamine, and cholecystokinin.
### Partial Agonism

<table>
<thead>
<tr>
<th></th>
<th>Efficacy toward CB1</th>
<th>Efficacy toward CB2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anandamide</td>
<td>Full agonist</td>
<td>?</td>
</tr>
<tr>
<td>2-Arachidonylglycerol (2-AG)</td>
<td>Full agonist</td>
<td>?</td>
</tr>
<tr>
<td>Δ-9-Tetrahydrocannabinol</td>
<td>Partial agonist</td>
<td>Partial agonist</td>
</tr>
<tr>
<td>CBD</td>
<td>Very weak agonist/antagonist? (blocks reuptake of anandamide)</td>
<td>Very weak agonist/antagonist?</td>
</tr>
<tr>
<td>J WH-018</td>
<td>Full agonist</td>
<td>Full agonist</td>
</tr>
</tbody>
</table>
Inverse Agonism

- Receptors exist in **equilibrium between active and inactive states**

- Some receptors are in an active state, even in the absence of an agonist, when there is a low level of signaling mediated by the receptor (**basal signaling**)

- Agonists will **shift** more of the receptors to the active state, increasing signaling

- **G** proteins preferentially bind to **inactive receptors**
Cannabinoid receptors are located throughout the body but have differing effects based on location.

Cannabinoids bind reversibly and stereoselectively to the cannabinoid receptors.
Herbal MJ Alternatives

- Synthetic cannabinoids (J WH-018, J WH-073 in K2 or Spice incense) which cannot be detected in urine drug screen for THC and THC metabolites

- Products sold in gas stations, convenience stores, internet

- Urine/blood screens specific for J WH-018 metabolites
Compare Chemical Structures for JWH-018 and THC - Herbal Marijuana Alternatives

- K2 or Spice belong to a group of blends that contain a mixture of inert plant matter plus chemical grade synthetic cannabinoids sprayed on it

- Symptoms similar to marijuana PLUS sympathomimetic SXS: agitation, anxiety, HR, tremors, seizures

- Agonists at CB1 and CB2 receptors

- May be NDMA glutamatergic antagonists
<table>
<thead>
<tr>
<th>Synthetic Cannabinoids Family</th>
<th>Principal Compounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzoyleindole</td>
<td>AM-694, AM-2233, AM-679, RCS-4, RCS-8</td>
</tr>
<tr>
<td>Naphthoylindole</td>
<td>JWH-018, JWH-022, JWH-073, JWH-081, JWH-122, JWH-210, AM-2201, AM-2232, MAM-2201</td>
</tr>
<tr>
<td>Phenylacetylindole</td>
<td>JWH-167, JWH-250, JWH-316</td>
</tr>
<tr>
<td>Indazolecarboxamide</td>
<td>ADB-PINCACA, ADB-FUBINACA, AB-FUBINACA, AB-PINACA, 5F-APINACA, AKB48 (APINACA), MAB-CHMINACA</td>
</tr>
<tr>
<td>Cyclohexylphenyl</td>
<td>CP-55, 940, CP-47, 497, 497-C8 homologue</td>
</tr>
<tr>
<td>Naphthylmethylindole</td>
<td>JWH-175</td>
</tr>
<tr>
<td>Naphthylpyrrole</td>
<td>JWH-145, JWH-307, JWH-370</td>
</tr>
<tr>
<td>Naphthylmethylindene</td>
<td>JWH-176, JWH-220</td>
</tr>
<tr>
<td>Aminoalkylindole</td>
<td>WIN-55, 212-2</td>
</tr>
<tr>
<td>Adamantoylindoles</td>
<td>AB-001</td>
</tr>
<tr>
<td>Tetramethylcyclopropylketone indole</td>
<td>UR-144, XLR-11</td>
</tr>
<tr>
<td>Quinolinyl ester indole</td>
<td>5F-PB-22, PB-22</td>
</tr>
<tr>
<td>Ibenzopyran</td>
<td>HU-210, JWH-133</td>
</tr>
</tbody>
</table>
Cannabinoid CB1 Receptors

- Mostly in **brain** (*cerebellum, cerebral cortex, basal ganglia*), spine, GI tract, liver, pancreas, skeletal muscle combined with **GABAergic & dopaminergic & serotoninergic receptors**; to affect appetite, pain sensation, memory, mood

- In the **hippocampus** and **amygdala**, areas associated with partial seizures

- In **liver**, activation of CB1 receptor increases *de novo* lipogenesis (expression of cannabinoid receptors in normal liver tissue is low)

- **Tolerance** and **down regulation of CB1 receptors** occur with repeated marijuana exposure
CB2 Receptors

- Activation causes inhibition of proinflammatory cytokine production, cytokine, and chemokine release, and blockade of neutrophil and macrophage migration (anti-inflammatory)

- In peripheral immune system T-cells, B cells, spleen, macrophages (immunosuppression), kidneys, lungs

- In peripheral nerve terminals with a role in anti-nociception
Main Phytocannabinoids

- **Psychoactive**: THC (Δ-9-THC, Δ-8-THC, 11-hydroxy-THC [active metabolite]). Binds to CB1 & CB2 receptors as a partial agonist.

- **Not Psychoactive**: THCV (tetrahydrocannabivarin) – analogue of THC

- **Not Psychoactive**: CBD (cannabidiol), CBN (cannabinot) – degradation product of THC, CBC (cannabinichromene) – sedative and analgesic, CBG (cannabigerol) – precursor of other cannabinoids

- **Synthesized** in glandular trichomes of leaves and flowers; first appear in their acidic forms (THCA, CBDA), then decarboxylate to neutral counterparts (THC, CBD) due to oxidation, heat, light
Cannabidiol Pharmacology

- Low affinity for CB1 and CB2 receptors (compared to THC - partial agonist for both)
- Agonist at serotonin (5-HT1A) receptors (pain, migraines, anxiolytic & adapts to stress)
- Agonist at Transient Receptor Potential Vaniloid Type I (TRPV1) receptor (anti-nociception)
- Enhances adenosine receptor signaling by inhibiting adenosine inactivation (pain, inflammation, BP modification)
- Anti-inflammatory via CB2 receptors (different from COX-2 system)
- Anti-fibrotic – pulmonary (Zurier. FASEBJ 2016)
- Neuroprotective via CB1 receptors (epilepsy, multiple sclerosis)
- MOA of CBD is not fully understood
- Anxiolytic and antipsychotic MOA mediated by endocannabinoid system or by activation of 5HT1A receptors
- Low affinity for cannabinoid receptors, but blocks the reuptake of anandamide
- 5HT1A receptors are located pre-synaptically in raphe nuclei of brain stem and post-synaptically in hippocampus and hypothalamus – areas related to stress and anxiety
- Unclear whether anxiolytic effects from 5HT1A agonists are due to activation of pre- or the –post synaptic receptors
- Depending on where post-synaptic receptors are, activation -> anxiolytic or anxiogenic
CANNABIS

Side effects
Common Adverse Effects

- Anxiety
  - Changes in visual perceptions
  - Decreased sperm count
  - Reduced tear flow
  - Altered sense of time
    - Decreased eye blink rate
    - Bronchitis
  - Dizziness
    - Reddened eyes

- Dry mouth
  - (and possibly associated caries and periodontitis)

- Sedation
  - Slowed pupillary response to light
  - Reduced coordination
  - Ataxia
  - Cough

- Dysphoria

References: Ashton 1999, Hall and Solowij 1998
Respiratory Effects
Vaporization

- A survey of 6,883 cannabis users found that vaporizing, compared with smoking, causes fewer respiratory symptoms (coughing, wheezing, shortness of breath, mucus production) (Earlywine and Barnwell 2007).

- Analysis of vapor from a vaporizer recovered 89.1% THC and 9.5% smoke toxins; in contrast, cannabis smoke from a pipe recovered 10.8% THC and about 87% smoke toxins (Chemic Laboratories 2003).

- Vaporization, compared to smoking, generates less carbon monoxide (Abrams et al 2007).
Respiratory Effects
Smoked Cannabis

- Smoked cannabis is clearly associated with symptoms of bronchitis, which resolve after cessation of use (Tashkin 2013, Tashkin 2014).

- At least 200 compounds occur in cannabis smoke (Sparacino et al 1990): these include carbon monoxide, acetaldehyde, ammonia, nitrosamines, and polycyclic aromatic hydrocarbons (“tars”).

- Combining tobacco and cannabis appears to have synergistic adverse effects, increasing respiratory symptoms over tobacco use alone (MacLeod et al 2015, Bloom et al 1987).
Cannabis

Respiratory Effects

Lung Cancer

- Cannabis does not appear to increase lung cancer risk.

- A pooled meta-analysis of 6 case-control studies in the US, Canada, UK, and New Zealand that included data on 2,159 lung cancer cases and 2,985 controls found “little evidence for an increased risk of lung cancer among habitual or long-term cannabis smokers, although the possibility of potential adverse effects for heavy consumption cannot be excluded” (Zhang et al 2015).
Cardiovascular Effects

- THC can cause tachycardia; chronic users may develop bradycardia.
- Cannabis can cause changes in blood pressure.
  - High doses can cause orthostatic hypotension and syncope (Handbook on Cannabis 2015).
  - Cannabis can cause an acute increase in blood pressure (Frost et al 2013).
- Cannabis can increase the risk of angina (Frost et al 2013).
- Rarely marijuana can trigger an acute myocardial infarction (Mittleman et al 2001).
- In patients who have had a myocardial infarction, an 18-year follow up study showed no conclusive evidence that smoking marijuana increased mortality (Frost et al 2013).
- Case reports have associated cannabis use with acute coronary syndrome, arrhythmias, sudden cardiac death, cardiomyopathy, transient ischemic attack, stroke (Thomas et al 2014, Jouanju 2014).
Aditi Kalla MD, Cardiology Fellow at Einstein Medical Center in Philly

Study involved 1000 hospitals

Researchers found that MJ use was associated with a significantly increased risk for stroke (26% increase), heart failure (10% increase), CAD, and sudden cardiac death

Cardiac muscle cells have cannabis receptors relevant to contractility
Neuropsychiatric Effects

Cognitive Function

- Long-term cannabis users exhibit deficits in prospective memory and executive function (Montgomery 2012).

- In depressed and non-depressed regular marijuana users, there was an inverse association between marijuana use and verbal learning function.
  - The effect was not moderated by depression (Roebke 2014).

Adolescent marijuana users demonstrated significantly smaller medial orbitofrontal and inferior parietal volumes (regions of the brain associated with higher order cognition); smaller medial orbitofrontal volumes were associated with poorer complex attention.

(Price et al 2015)
Psychiatric Effects

Psychosis/Schizophrenia

- Whether or not cannabis can cause psychosis is debated.
- Studies suggest that people at risk for schizophrenia run a higher risk of psychosis outcomes after cannabis use (Morrison et al 2015).
- A study of cannabis use in 1237 people with schizophrenia, who had ever used cannabis, found no additive effect of cannabis use on cognitive dysfunction (Power 2015).
- Smoking cannabis with a significant proportion of CBD may produce fewer psychotic symptoms (Morgan and Curran 2008, Schubart et al 2011).
- It has been suggested that cannabis has antipsychotic effects, but a Cochrane systematic review of cannabis and schizophrenia noted that studies were limited, and that “currently evidence is insufficient to show cannabidiol has an antipsychotic effect” (McLoughlin 2014).
Cannabinoid Hyperemesis Syndrome

- Chronic cannabis use may be associated with Cannabinoid Hyperemesis Syndrome (also called Cyclic Vomiting Syndrome).
- It is characterized by episodes of nausea and vomiting, abdominal pain, and sometimes polydipsia.
- Obsessive hot-water bathing may be observed, as it alleviates symptoms.
- The syndrome can lead to weight loss or acute renal failure from dehydration.
- The etiology of CHS is thought to be activation of CB₁ receptors that can reduce gastric emptying.

Cannabinoid Hyperemesis Syndrome (CHS)

- Paradoxical, diagnosis of exclusion, due to chronic long-term use
- Does it accumulate over time due to large Vd?
- THC may activate CB1 receptors in enteric nervous system and reduce gastric motility, increasing risk of N&V
- THC may activate CB1 receptors in hypothalamus to induce emesis by impairing thermoregulation, leading to the potential relief through hot bathing
- Cyclic; unrelied by anti-emetics
- Relieved by compulsive bathing in hot water and abstinence
- In Colorado, rates of CHS have doubled since 2009 when cannabis was legalized there
Reproductive Effects
Lactation and Fertility

Cannabis use during lactation is not recommended.

- THC and its metabolites are excreted in breast milk.
- Infants exposed to marijuana during lactation had lower scores on the Psychomotor Developmental Index compared to non-exposed infants (effects could not be separated from prenatal exposure).

Fertility effects in men

- Some studies indicate that chronic use of marijuana may decrease plasma testosterone and decreases sperm count, concentration, and motility.

(Reprotox.org, Metz and Stickrath 2015)
CANNABIS

Reproductive Effects
Exposure During Pregnancy

Cannabis use during pregnancy is not recommended.

- Heavy use of cannabis during pregnancy may cause adverse effects on early neurodevelopment, including subtle cognitive impairment and decrements in executive functioning later in life.
- Cannabis use has not been shown to increase the risk of congenital anomalies.
- Some but not all studies have shown a decrease in fetal growth.
- There is a possible increased risk of preterm birth.

(Fried et al 2003, Goldschmidt et al 2012)
Clinical Aspects

Contraindications

- **Absolute contraindications**
  - Acute psychosis and other unstable psychiatric conditions

- **Relative contraindications**
  - Severe cardiovascular, immunological, liver, or kidney disease, especially in acute illness
  - Cannabis may exacerbate arrhythmia or a history of arrhythmias

(Handbook on Cannabis 2015)
Lethal dose at which 50% of population is killed in a given time period

At present it is estimated that marijuana’s LD-50 is 1:20,000 - 1:40,000. Active dose is far below lethal dose (Gable 2006)

In order to induce death a marijuana smoker would have to consume 20,000 - 40,000 times as much marijuana as is continued in one marijuana cigarette

NIDA-supplied marijuana cigarettes weight 0.9 grams

A smoker would have to consume nearly 1,500 pounds of marijuana within about 15 minutes to induce a lethal response
Psychiatric Effects

Dependence

- Cannabis dependence may occur: the estimated global prevalence is 0.23% in males and 0.14% in females (Degenhardt et al 2013).

- Prevalence peaks in the 20-24 years age group, and decreases steadily with age.

- In a survey of 6,917 marijuana users, 15% met the criteria for a marijuana use disorder. People who met the criteria for marijuana use disorder also were correlated with weekly marijuana use, early marijuana use, other substance use disorders, substance abuse treatment, and serious psychological distress (Wu et al 2012).

- Marijuana usage goes up in states that pass medical marijuana laws. However, the dependence rate among marijuana users does not differ between states with or without medical marijuana laws (Cerda et al 2012).
Marijuana Use Disorder

Physiologic withdrawal, psychological dependence

Chronic low doses not associated with significant physical withdrawal on abrupt discontinuation

Chronic users exhibit compulsive drug-seeking behaviors characteristic of dependence

Gateway drug?
Diagnostic Criteria for Substance Use Disorder

1. Use of substance in larger amounts or for longer durations than intended
2. Personal desire to cut down or stop use of substance but unable to do so
3. Excessive time spent in the acquisition, use, or recovery of substance
4. Craving substance in question
5. Failure to honor personal commitments because of use
6. Ongoing use of substance despite problems in relationships
7. Discontinuing important activities because of use of substance
8. Continued use of substance despite known harm or danger
9. Continued use of substance despite worsening physical or psychological problems
10. Increased tolerance to substance
11. Experiencing withdrawal symptoms without ongoing use of substance

< 2 SXS (no disorder), 2-3 SXS (mild disorder) 4-5 SXS (moderate disorder) >6 SXS (severe disorder) Pharmacy Today April 2017
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addiction</td>
<td>A neurobiologic disease characterized by impairment, cravings, withdrawal syndrome, and negative social, professional and spiritual sequelae as well as inability to abstain from continued used of the substance</td>
<td>Addiction has been replaced by substance use disorder in DSM-V</td>
</tr>
<tr>
<td>Aberrant Drug-Taking Behavior</td>
<td>Departure from strict adherence to prescription instructions or indication for use</td>
<td></td>
</tr>
<tr>
<td>Misuse</td>
<td>Departure from adherence to prescribed instructions while maintaining therapeutic intent (taking more than Rx’ed for what the drug was prescribed for)</td>
<td></td>
</tr>
<tr>
<td>Abuse</td>
<td>Departure from adherence to prescribed instructions and use for nontherapeutic intent (taking more than prescribed for euphoria vs pain control)</td>
<td>Previously used interchangeably with substance dependence as a diagnostic term and is being phased out</td>
</tr>
<tr>
<td>Tolerance</td>
<td>Decreased responsiveness to substance requiring higher doses or amounts to produce the same effect achieved during initial dose</td>
<td></td>
</tr>
<tr>
<td>Withdrawal</td>
<td>Cluster of SXS experienced upon cessation or inability to reduce a substance characterized by stress, anxiety, depression, NV</td>
<td>SXS may be experienced by person possessing no signs of substance misuse or substance use disorder if drug is abruptly DC’d</td>
</tr>
</tbody>
</table>
FDA FOI FAERS Marijuana Analysis 2011-2016

- Search terms: marijuana, Cannabis sativa seed, seed extract, seed oil, Cannabis indica flowering top and whole plant

- Limitations: doses used were largely unknown; FAERS contains observational data from real world use of marijuana and related products and does not include data from well designed, controlled RCTs

- Results: Potential for serious cardiac, respiratory, CNS effects from marijuana abuse, misuse, overdose have been reported
Cincinnati Poison Control Center THC TESS Report Analysis 2010-2016

- Search terms: THC, marijuana, Cannabis sativa, THC homologs (Spice, K2, JWH-018, JWH-073 AB-Fubinaca)
- Scope: Southwest and northeast Ohio regions
- Limitations: Doses were largely unknown; large % involved intentional overdose or abuse; not possible to determine if other drugs were being concomitantly abused/misused
- Results: 2330 reports involving children, teens, adults ad 1242 reports involving K2, Spice, THC homologs. 7 deaths. Main body systems involved – neurological, cardiovascular (drowsiness, irritability, confusion, hallucinations, tachycardia, hypertension)
CANNABIS

Summary

- Cannabis is generally well-tolerated, and serious adverse effects, including increased risk of cardiovascular events, are rare.
- Adverse changes in cognitive function, especially executive function, may occur, especially with fetal or adolescent exposure.
- Cannabis should be avoided by adolescents, pregnant women, and nursing mothers.
- Cannabis should be avoided in those at risk of psychosis.
- Many studies show driving impairment, but on a much lower scale than alcohol.
- Drug interactions are a concern.
  - Cannabis enhances CNS depressant effects when combined with alcohol, barbiturates and benzodiazepines, but probably not opioids
  - THC induces CYP1A2, and can reduce levels of drugs metabolized by CYP1A2.
  - CBD inhibits CYP3A4 and CYP2D6, and can increase levels of drugs metabolized by these isoenzymes. CPY3A4 metabolizes about a quarter of all drugs.
Drug Interactions
Cytochrome P450 Enzymes

- THC and CBD are metabolized by CYP3A4 and CYP2C9 (Yamaori et al 2012, Watanabe et al 2007).
  - CYP3A4 inhibitors slightly increase THC levels.
  - CYP3A4 inducers slightly decrease THC and CBD levels.

- CBD, but not THC, is metabolized by CYP2C19 (Stout and Cimino 2014).
Drug Interactions
Cytochrome P450 Enzymes

- THC is a CYP1A2 inducer.
  - Theoretically, THC can decrease serum concentrations of clozapine, duloxetine, naproxen, cyclobenzaprine, olanzapine, haloperidol, and chlorpromazine (Flockhart 2007, Watanabe et al 2007).

- CBD is a potent inhibitor of CYP3A4 and CYP2D6.
  - As CYP3A4 metabolizes about a quarter of all drugs, CBD may increase serum concentrations of macrolides, calcium channel blockers, benzodiazepines, cyclosporine, sildenafil (and other PDE5 inhibitors), antihistamines, haloperidol, antiretrovirals, and some statins (atorvastatin and simvastatin, but not pravastatin or rosuvastatin).
  - CYP2D6 metabolizes many antidepressants, so CBD may increase serum concentrations of SSRIs, tricyclic antidepressants, antipsychotics, beta blockers and opioids (including codeine and oxycodone).
Cannabis/Drug Interactions

- May interact with warfarin (THC and CBD increase warfarin levels) (Yamaori et al 2012)

- Alcohol may increase THC levels (Hartman 2015)
Case

62 yo male stage IV B-cell lymphoma

Overnight admission to oncology service

**PMHx:** COPD, atrial fibrillation, viral hepatitis C, chronic low back pain, B-cell lymphoma

**CC:** severe back pain, lethargy

**Meds PTA:**
- Amiodarone 200 mg daily
- Acyclovir 400 mg TID
- Entecavir (Baraclude) 0.5 mg daily
- Fentanyl Patch 50 mcg TD q72h
- Metoprolol succinate ER 50 mg daily
- Olanzapine ODT (Zyprexa) 5 mg BID
- Oxycodone 5 mg q6h PRN severe pain
- Naproxen 500 mg BID PRN arthritis pain
- Medical Marijuana (THC:CBD 20:1) 10 mg vaped PRN breakthrough cancer pain

**Interactions/Medication Issues?**

**Plan?**

- 28 randomized clinical trials reviewed
- Per authors: use of MJ for chronic pain, neuropathic pain, and spasticity due to multiple sclerosis is supported by high quality research.
- Six trials that included 325 patients examined chronic pain, 6 trials that included 396 patients investigated neuropathic pain, and 12 trials that included 1600 patients focused on MS.
- Several of these trials had positive results, indicating that MJ or oral cannabinoids may be efficacious for these indications

- 13 studies rated
- Cannabinoids provide effective non-inferior analgesic in chronic neuropathic pain conditions refractory to other treatments
- Very few side effects
- Further high quality studies needed to assess impact of treatment duration (1-6 weeks) as well as best form (smoking versus Sativex-nabixmols: THC:CBD oromucosal spray)
RCT, 5 week trial in 360 patients found that adjunctive use of low (1-4 sprays/day) and medium (6010 sprays/day) doses of nabiximols (Sativex, THC & CBD extract) was significantly more effective than placebo in relieving intractable cancer pain and comparable to placebo in adverse effects.

There are no well designed studies on the effectiveness of cannabis for this indication

The Medical Letter August 1, 2016
Of 79 trials reviewed, 4 were judged at low risk of bias.

Most trials showed symptom improvement associated with cannabinoids but these associations did not reach statistical significance in all trials.

Compared with placebo, cannabinoids were associated with a greater average number of patient showing a complete N&V response in 3 trials (47% vs 20%, OR, 3.82 [95% CI, 1.55-9.42].

Reduction in pain in 8 trials (37% vs 31%, OR, 1.41 [95% CI, 0.99-2.00]

Average reduction in Ashworth spasticity scale in 5 trials (Weighted Mean Difference -0.12 95% [CI, -0.24 to 0.01])

Increased risk of short term AEs with cannabinoid (dizziness, dry mouth, N &V, fatigue, somnolence, euphoria, drowsiness, confusion, loss of balance, hallucination).
Several studies found that cannabinoids are effective in treating some MS symptoms.

**American Academy of Neurology** recommends use of an oral cannabis extract containing a mix of THC and CBD (Cannador 2:1, Germany) or (THC) dronabinol (Marinol) for treatment of spasticity and pain and **nabiximols (Sativex) (THC & CBD extract)** for treatment of pain, spasticity, and urinary dysfunction.

The Medical Letter August 1, 2016
Open label, 12 week study in patients 1-30 years with severe childhood-onset treatment-resistant epilepsy, addition of Epidiolex (investigational purified cannabis extract with 99% CBD) reduced median monthly frequency of seizures by 36%.

Randomized clinical trials of Epidiolex are in progress in US (2-50 mg/kg/day).

Data not adequate to recommend use of cannabinoids for treatment of patients with more common types of epilepsy.

The Medical Letter August 1, 2016
Migraine Studies

- Reduced frequency of migraines with medical marijuana use; THC Anti-Inflammatory MOA by inhibiting prostaglandin E2 synthesis (20x potency of ASA, 2x potency of HC) (Rhyne. Pharmacotherapy 2016;36(5):505-510)


- CBD interacts with serotonergic system to inhibit serotonin reuptake. Reduced use of opioids for migraines with medical marijuana. (Bradford. Health Aff 2016;35(7):1230-1236)
Summary of Randomized Controlled Trials Examining Marijuana’s Effect on Various Symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>RCTs</th>
<th>Patients</th>
<th>Findings</th>
<th>Lead Author Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy-induced nausea</td>
<td>3</td>
<td>43</td>
<td>Smoked cannabis has a modest anti-nausea effect greater than placebo but less effective than ondansetron</td>
<td>Chang 1979</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Chang 1981</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Levitt 1984</td>
</tr>
<tr>
<td>HIV-related anorexia</td>
<td>3</td>
<td>97</td>
<td>Smoked cannabis and oral THC produced comparable but small increases in caloric intake and weight; viral load was unaffected</td>
<td>Abrams 2003</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Haney 2005</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Haney 2007</td>
</tr>
<tr>
<td>HIV-related neuropathic pain</td>
<td>2</td>
<td>89</td>
<td>Half of the patients experienced a 30% reduction in pain ratings</td>
<td>Wilsey 2008</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ellis 2009</td>
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<tr>
<td>Capsaicin-induced pain</td>
<td>1</td>
<td>15</td>
<td>Half of the patients experienced a 30% reduction in pain ratings</td>
<td>Wallace 2007</td>
</tr>
<tr>
<td>Spasticity from multiple sclerosis</td>
<td>2</td>
<td>40</td>
<td>Reduced scores for pain (50%) and spasticity (30%) were observed using high potency cannabis cigarettes</td>
<td>Greenberg 1994</td>
</tr>
<tr>
<td>Intraocular pressure</td>
<td>1</td>
<td>18</td>
<td>Smoked cannabis (one 2% THC cannabis cigarette) caused a significant reduction in intraocular pressure</td>
<td>Merritt 1990</td>
</tr>
</tbody>
</table>
The Health Effects of Cannabis and Cannabinoids

The Current State of Evidence and Recommendations for Research
Process of Obtaining Medical Marijuana Recommendation

- Doctors must be certified to recommend medical marijuana by the Medical Board.
- Patients then visit a doctor who is certified and can be “recommended” medical marijuana if the patient has been diagnosed with a qualifying medical condition and there is a bona fide physician-patient relationship that has been established through all of the following:
  - An in-person physical examination;
  - A review of the patient's medical history by the physician; and
  - An expectation of providing and receiving care on an ongoing basis.
- An application then may be submitted to the Board of Pharmacy on behalf of the patient by the physician to become a registered medical marijuana patient.
- Patients would then be able to obtain medical marijuana from a dispensary that has been licensed and is regulated by the Board of Pharmacy.
- Marijuana cannot be “prescribed” or distributed through a pharmacy due to the fact that it is still illegal under federal law.
Patient Education

- Ohio certified patients register with state to receive a medical marijuana ID card that they bring to a dispensary for products (some states allow home grown)
- Patient will be dispensed MJ in unmarked outer wrap
- Patients should not to share any of their cannabis with others
- Take care with driving under the influence
- May be some paranoia and disorientation in novice users
Patient Counseling Tips

- Go slow (2-5 mg THC to start)! No consistency in dosing.
- Patients of all ages should not drive for 6 hours after taking 35 mg THC or less, and longer if they take more.
- Cannabinoids are very sensitive to light and heat, so patients should store their cannabis in the refrigerator or freezer.
Ohio Dispensary Clinical Directors

Each dispensary will have to hire a clinical director who is either a licensed pharmacist, or one of the following licensed professionals authorized to prescribe drugs: a clinical nurse specialist or certified nurse practitioner, a physician, or physician assistant.

The clinical director will be responsible for implementing a variety of employee trainings and overseeing the dispensary’s operations.

The key dispensary employee is different from the clinical director.

*May 1, 2017 update – rescinded this requirement (too expensive!)*
Dispensaries & Product Labeling

- Dispensaries requiring pharmacists on staff – CT, MN, NY (Maryland has a PharmD Clinical Director but is not required to have a pharmacist)
- Dispensary certified for a maximum allowable amount set by the state

Dispensed MMJ labels have strict requirements
<table>
<thead>
<tr>
<th>THC</th>
<th>CBD</th>
<th>Flower</th>
<th>THC</th>
<th>CBD</th>
<th>Flower</th>
<th>THC</th>
<th>CBD</th>
<th>Flower</th>
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</thead>
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<tr>
<td>25.72</td>
<td>0</td>
<td>Fioraden C T26</td>
<td>CT Pharm</td>
<td>3.5g</td>
<td>$55</td>
<td>7g</td>
<td>$105</td>
<td>$200 $390</td>
</tr>
<tr>
<td>25.73</td>
<td>0</td>
<td>Indicol Y 25.73</td>
<td>AGL</td>
<td>7g</td>
<td>$105</td>
<td>14g</td>
<td>$200</td>
<td>$390</td>
</tr>
<tr>
<td>28.79</td>
<td>0.1</td>
<td>Indicol B 28.79</td>
<td>AGL</td>
<td>14g</td>
<td>$200</td>
<td>28g</td>
<td>$390</td>
<td></td>
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<td>24.5</td>
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<td>Indicol C 24.5</td>
<td>AGL</td>
<td>28g</td>
<td>$390</td>
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<tr>
<td>27.6</td>
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<td>Sativarin A 27.6</td>
<td>AGL</td>
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<td></td>
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<td></td>
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<tr>
<td>31.02</td>
<td>0</td>
<td>Lexikan T31</td>
<td>CT Pharm</td>
<td>3.5g</td>
<td>$55</td>
<td>7g</td>
<td>$105</td>
<td>$200 $390</td>
</tr>
<tr>
<td>28.63</td>
<td>0.1</td>
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<td>AGL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The current "menu" of medicinal marijuana available at Blueprint Wellness of Connecticut, a dispensary in Branford, Conn.
ASHP policy opposes procurement, storage, preparation, distribution of medical marijuana by licensed pharmacies or health care facilities for purposes other than research.

Information about medical marijuana for use during patient counseling and a systematic method for obtaining patient medical histories that ensures the confidentiality of patient health data (HIPAA).
2014 - 2015 APhA Policy Committee Report Recommendations

Support

- Resolution of federal and state conflicts re. legal status
- Establish USP monograph
- Regulatory change to increase research on safety and efficacy
- HCP education
- Pharmacists to collect and document information in patient profile about patient use & provide counseling
- Clinical judgment of pharmacists to decide whether to furnish medical cannabis

Oppose

- Pharmacist participation in furnishing cannabis until scientific data support legitimate medical use and delivery mechanisms and federal, state laws permit pharmacists to furnish them
- Furnishing medical cannabis unless performed by licensed HCPs whose scope of practice includes dispensing of Rx meds and who comply with state/federal laws
- Pharmacist involvement in furnishing cannabis for recreational use
Nursing Issues

- Accidental pediatric ingestion of edibles
- Marijuana is highly protein bound so crosses the placenta, found in breast milk. Triaging mothers-to-be?
- Novice users may experience increase in heart rate and decrease in blood pressure after initial consumption. Monitoring?
Physician Roles & Responsibilities

- Medication reconciliation process/Epic documentation (social history vs medication history?)
- Closer clinical monitoring of cardiac and neuro patients
- Monitoring for potential drug/marijuana interactions
- Research protocol, clinical trial, IND application (Ohio physicians exempted from certificate to recommend requirement)
- Annual submission to Ohio Medical Board a report that describes the MD’s observations regarding effectiveness of MMJ in treating his/her patients
- Request & review Ohio OARRS report covering at least 12 months preceding the date of the report
- Patient education
## Summary of Position Statements by Medical Organizations on Medical Marijuana (Cannabis)

<table>
<thead>
<tr>
<th>Organization</th>
<th>Approval of smoked?</th>
<th>Support of More Research?</th>
<th>Comments</th>
<th>Lead Authors &amp; Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Institute of Medicine</td>
<td>Yes, conditionally</td>
<td>Yes</td>
<td>Calls for more safety data on smoked cannabis. Urges development of safe and reliable delivery systems</td>
<td>Joy 1999</td>
</tr>
<tr>
<td>American College of Physicians</td>
<td>No</td>
<td>Yes</td>
<td>Encourages use of non smoked THC with proven benefit. Calls for review to reclassify CSA Class I status. Recommends clinical exemption for prescribing physicians.</td>
<td>ACP 2008</td>
</tr>
<tr>
<td>American Medical Association</td>
<td>No</td>
<td>Yes</td>
<td>Calls for special CSA schedule to encourage cannabis research</td>
<td>CSAPH</td>
</tr>
<tr>
<td>American Society of Addiction</td>
<td>No</td>
<td>Yes, conditionally</td>
<td>Calls for applying established research standards to cannabis. Discourages cannabis prescribing until research confirms safety and efficacy</td>
<td>Barthwell 2919</td>
</tr>
</tbody>
</table>
The current pattern of physician-authorized medical MJ use in the U.S. is far from the standard established for medicine.

Inconsistencies in how medical conditions are qualified for medical marijuana use within each state.

Inconsistencies in evaluating research, variable product composition/dose (dose conversion from product to product).

Ohio’s reciprocity with Michigan for MMJ possession?

How will hospitals handle admission medication reconciliation?
Associations/Resources

- American Herbal Products Association Cannabis Committee
- Foundation of Cannabis United Standards Creations Committee
- National Association of Specialty Pharmacy Task Force on Medical Marijuana 2014 – established National Association of Cannabis Based Medicine (NACBM) to help pharmacists obtain required coaching to make the most of cannabis as a therapy in the retail channel
- Cannabis Training Institute – online certification resource for cannabis businesses, entrepreneurs, clinicians, policymakers, and certification & CEUs for pharmacists that will be recognized by ACPE
- American Association of Colleges of Pharmacy Medical Cannabis Toolkit (goo.gl/ZqyFSx)
Heartache for healthcare professionals as medical marijuana programs are implemented across the country (Mind)

Patient’s physical heart – monitoring cannabis CV side effects & interactions (Body)

Compassionate heart (Spirit)
Closing on a High Note

THANK YOU
Thank you
Dabbing

- Flash vaporizing butane hash oil based concentrate
- More intoxicating than smoking or vaping
Queen City Hemp is a full spectrum hemp extract suspended in MCT oil. It is a product for current hemp/CBD users seeking an all-natural alternative to big products.

- All Natural
- Non Psychoactive
- No Preservatives
- 100% USA Grown & Extracted Hemp
- Lab Tested for Quality & Potency
- Just 5 Calories per Serving
- 250 total cannabinoids - ~4mg/serving
- 500 total cannabinoids - ~8mg/serving
- 750 total cannabinoids - ~12mg/serving

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