Cannabinoid Treatment as Approved by State of Georgia

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Objectives

• Explain pharmacological principles for use of cannabinoids

• Identify appropriate indications for clinical uses of cannabinoids

• Explain Georgia law on medical cannabis
History

- First recorded use of cannabis as medicine by Emperor Shen Neng of China (2,727 B.C.)
- Cultivated in China for food and fiber
- Treatment of rheumatism, pain, and convulsions (around 4,000 B.C.)
Cannabis

- Plant contains more than 421 chemicals (61 are cannabinoids)

- More than 2000 compounds are produced by pyrolysis during smoking of cannabis

- Primary psychoactive component
  Delta 9-tetrahydrocannabinol ($\Delta^9$-THC)
  - Contributes to behavioral toxicity of cannabis
Cannabis Pharmacology

http://www.drugabuse.gov/publications/research-reports/marijuana/how-does-marijuana-produce-its-effects
Targets of Marijuana

**CB1 Receptors**
- Hippocampus
  - Short term memory
- Cerebellum
  - Motor coordination
- Basal ganglia
  - Motor activity
- Hypothalamus and limbic
  - Appetite and sedation
- Neocortex
  - Thinking
- Pertequeductal gray dorsal horn
  - Pain
- Immune cells

**CB2 Receptors**
- Brain
  - Role not established
- Immunologic cells
  - Natural killer cells
  - B lymphocytes

Effect on Brain

Marijuana’s Effects on the Brain

When marijuana is smoked, its active ingredient, THC, travels throughout the body, including the brain, to produce its many effects. THC attaches to sites called cannabinoid receptors on nerve cells in the brain, affecting the way those cells work. Cannabinoid receptors are abundant in parts of the brain that regulate movement, coordination, learning and memory, higher cognitive functions such as judgment, and pleasure.
Behavioral and Physiological Effects

- Feeling of euphoria
- Relaxation
- Altered time perception
- Lack of concentration and impaired learning.
Behavioral and Physiological Effects

- Rapid changes in heart rate and diastolic blood pressure
- Conjunctival suffusion
- Dry mouth and throat
- Increased appetite
- Vasodilatation and decreased respiratory rate
Dependence and Tolerance

- Affect the same reward systems as alcohol, cocaine and opioids.
- Tolerance to occur in relation
  - Mood, psychomotor performance, sleep, arterial pressure, body temperature, and antiemetic properties
- Symptoms during abstinence
  - Irritability, anxiety, craving and disrupted sleep
Psychiatric Conditions Associated with Abuse

- Strong evidence that use may precipitate schizophrenia or exacerbate its symptoms
- Reasonable evidence that use exacerbates symptoms of psychosis
- Heavy cannabis (30-50mg oral and 8-30 mg smoked) use
  - Mania-like psychosis
  - Precipitant for manic relapse in bipolar patients
## Cannabinoid Formulations

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Trade name</th>
<th>Manufacturer</th>
<th>Dosage and components</th>
<th>Study and dosage used of this formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral administration</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cannabis extract</td>
<td>Cannador</td>
<td>IKF, Berlin, Germany</td>
<td>Ratio of $\Delta^8$-THC 2.5 mg: CBD 1.25 mg</td>
<td>Mean 0.146 mg/kg/d up to maximum of 1.25 mg/kg/d (Carroll 2004$^{38}$; mean 1.25 mg/kg/d up to maximum of 25 mg/d; maximum varied by weight (Zajicek 2003$^3$))</td>
</tr>
<tr>
<td>Cannabis extract</td>
<td>None</td>
<td>Not stated</td>
<td>Ratio of $\Delta^8$-THC 2.5 mg: CBD 0.9 mg</td>
<td>Mean 0.146 mg/kg/d up to maximum of 0.25 mg/kg/d (Vaney 2004$^5$)</td>
</tr>
<tr>
<td>Cannabis extract</td>
<td>None</td>
<td>NIH, Bethesda, MD</td>
<td>100 mg CBD</td>
<td>100–300 mg/d (Cunha 1980$^{19}$)</td>
</tr>
<tr>
<td>Cannabis extract</td>
<td>None</td>
<td>NIH, Bethesda, MD</td>
<td>100 mg CBD</td>
<td>10 mg/kg/d (Consroe 1991$^{26}$; Curtis 2009$^{27}$)</td>
</tr>
<tr>
<td>Dronabinol</td>
<td>Marinol</td>
<td>Solvay Pharmaceuticals, Marietta, GA</td>
<td>2.5 mg $\Delta^8$-THC</td>
<td>Maximum of 10 mg/d (Svensen 2004$^{28}$; Müller-Vahl 2003$^{30}$; maximum of 25 mg/d (Freeman 2006$^{29}$; Zajicek 2003$^3$)</td>
</tr>
<tr>
<td>Nabiximola</td>
<td>Cesamet</td>
<td>Meda Pharmaceuticals, Somerset, NJ</td>
<td>100 mg CBD</td>
<td>100 mg (Curtis 2009$^{31}$; 0.03 mg/kg (Fox 2002$^{28}$)</td>
</tr>
<tr>
<td><strong>Oromucosal spray administration</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Nabiximola</td>
<td>Sativex</td>
<td>GW Pharmaceuticals, PLC, London, UK</td>
<td>Ratio of $\Delta^8$-THC 2.7 mg: CBD 2.5 mg/spray</td>
<td>Mean 7.19 mg/d (Kavia 2010$^{28}$)</td>
</tr>
<tr>
<td>Nabiximola</td>
<td>Sativex</td>
<td>GW Pharmaceuticals, PLC, London, UK</td>
<td>Ratio of $\Delta^8$-THC 2.7 mg: CBD 2.5 mg/spray</td>
<td>Dosage varied by study; maximum 65 mg/d (Collin 2010$^{10}$; maximum 120 mg/d (Wade 2004$^6$)</td>
</tr>
<tr>
<td><strong>Smoked (inhaled) marijuana</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marijuana</td>
<td>None</td>
<td>Source not stated</td>
<td>4% THC</td>
<td>4 puffs (hits)/d (Corey-Bloom 2012$^{14}$; 3.5%THC (Abrams 2007$^{13}$; 3.5%–7% (Wilsey 2008a$^{15}$; 1%–8% THC (Ellis 2009a$^{16}$; 0%–9.4% (Ware 2010$^{14}$)</td>
</tr>
</tbody>
</table>

Abbreviations: CBD = cannabidiol, a major less-psychoactive resin extract constituent of the plant Cannabis sativa L (marijuana); THC = $\Delta$-9-tetrahydrocannabinol.
### Key Recommendations

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Formulation</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spasticity</td>
<td>OCE (oral cannabis extract)</td>
<td>Effective effective</td>
</tr>
<tr>
<td></td>
<td>Nabiximols and THC</td>
<td></td>
</tr>
<tr>
<td>Central pain or painful spasms</td>
<td>OCE</td>
<td>effective effective</td>
</tr>
<tr>
<td></td>
<td>Nabiximols and THC</td>
<td></td>
</tr>
<tr>
<td>Urinary dysfunction</td>
<td>Nabiximols THC and OCE</td>
<td>Probably effective</td>
</tr>
<tr>
<td></td>
<td>THC and OCE</td>
<td>Probably ineffective</td>
</tr>
<tr>
<td>Tremor</td>
<td>THC and OCE nabiximols</td>
<td>Probably ineffective</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Possibly ineffective</td>
</tr>
<tr>
<td>PD-dyskinesis</td>
<td>OCE</td>
<td>Probably ineffective</td>
</tr>
<tr>
<td>Huntington disease</td>
<td>OCE</td>
<td>Probably ineffective</td>
</tr>
<tr>
<td>Tourette syndrome, cervical dystonia, epilepsy</td>
<td>OCE</td>
<td>Probably ineffective</td>
</tr>
</tbody>
</table>
Treatment of Epilepsy

- Strong evidence that THC acts via cannabinoid receptor CB$_1$
- Mechanism of action of CBD is less clear
  - Likely polypharmacological
- Scientific data support role of endocannabinoid system
  - Seizure generation, maintenance, and control in animal models of epilepsy

Treatment of Epilepsy (CB1R)

- Cloning of CB1R
  - Confirmation that Δ9-THC binds CB1R
- Discovery of two endogenous ligands which bind CB1R
  - 2-arachidonoylglycerol (2-AG)
  - Anandamide
Treatment of Epilepsy (CB₁R)

- Activation of CB₁R receptors with the use of Δ⁹-THC or synthetic agonists in experimentally induced seizure
  - Studied in various animal models
- CB₁R agonists
  - Most studies reduced seizures,
  - In others no effect was observed
  - In four studies CB₁R activation associated with convulsant effects at some doses
- CB₁R antagonists reduced threshold for seizure in some animals studies

Friedman D, Devinsky O. Cannabinoids in the Treatment of Epilepsy. NEJM. 2015; 373:1048-1058.
FDA Approved Cannabinoid Medications

- **Dronabinol**
  - Schedule III
  - Synthetic version of THC
  - Nausea and vomiting associated with cancer chemotherapy
  - Anorexia-associates weight loss in adult with AIDS

- **Nabilone**
  - Schedule II
  - Synthetic cannabinoid, mimics the effects of THC
  - Nausea and vomiting associated with chemotherapy

Other Cannabinoids NOT FDA Approved

- **Nabiximols**
  - *Cannabis sativa*
  - Oromucosal spray
  - MS; neuropathic pain; cancer pain

- **Phytocannabinoid-dense botanicals**
  - Schedule I medical plants
  - *Cannabis sativa; Cannabis indica; Cannabis ruderalis*
  - University of Mississippi research

No Conflicts of Interest

- Dr. Reece has no conflicts of interest.
Charlotte’s Web

**Charlotte's History**

- First seizure: prolonged status epilepticus at 3 months of age.
- Frequent bouts of febrile and afebrile status epilepticus; tonic, tonic–clonic, and myoclonic seizures
- By 5 years of age “had reached the end of the road”
- Failing many medications and ketogenic diet
  - Levetiracetam, oxcarbazepine, topiramate, zonisamide, valproate, clobazam, clonazepam, and valium
Charlotte’s Web

• **Charlotte’s History**
  - Started low sublingual preparation of the plant extract and slowly increased the extract dose
  - Baseline frequency 300+ convulsions per week
  - Experienced seven consecutive days without a single seizure
  - >90% reduction in GTC seizures
HALEIGH’S HOPE ACT
Approved Conditions

- Cancer: end stage
- Lou Gehrig’s Disease (ALS): severe or end stage
- Seizure disorders
- Multiple sclerosis
- Crohn’s disease
- Mitochondrial disease
- Parkinson’s disease: severe or end stage
- Sickle cell disease: severe or end stage
Provisions

- Persons with any of these diagnosed conditions may possess up to 20 ounces of “low THC oil”
- Low THC oil can contain no more than 5% THC, the psychoactive agent in marijuana
- Possession of more than 20 ounces of low THC oil is a criminal offense
Low THC Oil Registry Page

Welcome to DPH’s Low THC Oil Registry page.

DPH, in close consultation with the Georgia Composite Medical Board, has developed a Low THC Oil Registry for patients and caregivers who qualify to carry an identification card under Georgia House Bill 1.

This page contains information for the general public, physicians and law enforcement. Please take a moment to review all of the resources on this page, especially the Frequently Asked Questions (FAQ) sections.

The basic steps to obtaining a card are as follows:

1. Patients and caregivers of patients who believe they may be eligible should consult with their physician about the possibility of obtaining a card allowing them to possess 20 fluid ounces of low THC oil within the state of Georgia.

2. If approved by the physician, the patient or patient’s caregivers’
Physician Certification

- Must have active MD or DO license in good standing with Georgia Composite Medical Board
- Must have doctor-patient relationship when certifying an individual needing low THC oil
- Must be treating a patient for specific condition requiring such treatment
Physician Certification

• Must conduct a physical exam and review patient history to certify patient has qualifying debilitating medical condition
  – New physical required each year as part of patient’s renewal process
• Must keep copy of physician certification in patient’s medical record
Georgia Low THC Oil Registry

If you have an approved account, please login below. If you would like to request an account, please register here.

It is recommended that you use Google Chrome for this website! Get it here

Please enter your User name: ________
Please enter your Password: ________

Login

(If you have forgotten your password: Please enter your user name above and then click Here)

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Registry Program
Next Steps

- Georgia Commission on Medical Cannabis
- Ongoing challenges for access for patients and caregivers
Questions