HOW TO BE A GOOD DOCTOR IN A POLITICAL WORLD

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Disclosure Information

R. Jeffrey Goldsmith, MD, DLFAPA, DFASAM
No Disclosures
Objectives

- This presentation will address:
  - Responding to changing marijuana environments
  - What to tell patients and medical field
  - What to tell patients in states considering reform

- Will not address:
  - Your personal opinion on marijuana reform
ASAM Position

- Public Policy Statement on Marijuana, Cannabinoids and Legalization
  - Adopted September, 2015

- Perspective on medical marijuana
  - FDA approval
  - Policy reform
  - Role of physician
FDA Approval

- Delivery systems subjected to same FDA standards
  - Smoking not safe
- Until FDA approved:
  - Do not market or recommend
  - Reject responsibility to provide cannabis
ASAM Position: Policy Reform

- Need Federal regulatory standards
- States can enact more restrictive limitations
- Discourages state interference in approval process
- Rejects state ballot initiatives by unqualified individuals
Role of Physician

- Adhere to established patient care tenets:
  - History and patient examination
  - Development of treatment plan
  - Provision of informed consent
  - Periodic review of treatment efficacy
  - Consultation
  - Proper-record keeping
Role of Physician (cont.)

- *Bona fide* physician-patient relationship
- Recommendations not disproportionately large/exclusive in practice
- No recommendation unless adequate information of composition and dose
- Able to identify substance abuse and addiction
Use of “medical marijuana” is potentially frustrating for us

Pro-marijuana groups attempting to use “compassion” as manipulation

If frustration takes over, we lose an important opportunity to help

Can turn potential difficulty into “golden moment” for you and patient
Potential Uses

- Medical value of marijuana
  - Specific areas where cannabinoid system is functional
  - Treatment of specific symptoms and diseases
  - Mitigation of side effects from other treatments
Routes of Administration

- **Smoking**
  - Onset takes minutes
  - Lasts 1 to 3 hours
  - Delivers a lot of THC to bloodstream

- **Edible**
  - Onset takes ½ to 1 hour
  - Lasts up to 4 hours
  - Delivers less THC to bloodstream
THC Percentage

- THC percentage increasing in all forms of marijuana
- Average sample ~20% THC
  - 2x higher than 10 years ago
  - 4 - 5 times higher than 1970
- Concentrates (oil, wax, hash) are 80-95% THC
Short-Term Effects

Neurocognitive
- Impairs:
  - Short-term memory
  - Attention
  - Judgement
- Tremors
- Decreased coordination and ataxia

Physiological
- Tachycardia
- Orthostatic hypotension
- Tachypnea
- Conjunctival injection
- Vasoconstriction
- Appetite increase
Long-Term Effects

Persistent Effects
- Memory impairments
- Learning skills impaired
- Drop in IQ with heavy adolescent use

Cumulative Effects
- Bronchitis and chronic cough
- Depression
- Warning for CAD patients

Withdrawal
- Irritable and restless
- Insomnia
- Appetite decrease

Addiction
- 9% users become dependent
- 17% for adolescent users
Driving Under the Influence

- Dangerous:
  - Delayed reaction time
  - Decreased hand-eye coordination
  - Altered time perception
  - Impairs automatic driving functions
  - Combining THC and alcohol cancels out compensation strategies
FDA-Approved Marijuana Products

Two products:
- Dronabinol: synthetic THC
  - appetite stimulation
  - reduces nausea
- Nabilone: synthetic cannabinoid similar to THC
  - treatment of nausea/vomiting in cancer patients
THANK YOU FOR YOUR COMMITMENT TO BEING A GOOD DOCTOR FOR YOUR PATIENTS AND THE MEDICAL FIELD
Current Aspects Of Cannabis Legalization

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NYU School Of Medicine
Immediate Past President Of The New York Society Of Addiction Medicine
President Of The International Society Of Addiction Medicine
ASAM State of the Art Course
October 7, 2016
Disclosure Information

Gregory C. Bunt
No Disclosures
Marijuana is the Most Commonly Used Illicit Drug in the U.S.

- Over 111 million Americans have tried it at least once
- An estimated 2.4 million Americans used it for the first time in 2012

Source: 2012 National Survey on Drug Use and Health, SAMHSA
Marijuana Contains ~100 Cannabinoids Plus Other Chemicals In Varying Concentrations

- delta-9-tetrahydrocannabinol (Δ⁹-THC)
- delta-9-tetrahydrocannabivarin (Δ⁹-THCV)
- cannabigerol (CBG)
- cannabichromene (CBC)
- delta-8-tetrahydrocannabinol (Δ⁸-THC)
- cannabidiol (CBD)
- cannabinol (CBN)
Court Rules That THC Wax, Honey Oil Qualify as Medical Marijuana
Policy Research: The Details Matter

- **Different models of legalization**: advertising, involvement of big business, medical vs. recreational, pricing, taxes, dispensaries, edible products, potency restrictions
- **Economic impact**: revenue generated; illegal markets; costs to public (Alcohol generates ~15B in tax revenue/per year; costs to society are estimated at $235 B)
- **Public Health impact**
  - Other drug use, especially alcohol, tobacco, and opiates
  - New routes of administration; potency/constituents
  - Accidents/ER visits
  - Education outcomes, workforce productivity
  - Opioid Overdoses
  - Minimize harm/use during pregnancy
- **How to minimize to minimize harm, prevent underage use, use during pregnancy…..**
Cannabis Decriminalization/Legalization

- **Legalization/regulated market** - Supply is permitted, possession is allowed.
- **Decriminalization** - Supply is not permitted, possession will still be punished, but with minor penalty.
- **Medicinal use** - under supervision (?!?) of doctor or similar
- **Recreational use** - no supervision

- Definition of decriminalization of marijuana?
- Role of law enforcement with marijuana?
- Extent of marijuana users being criminalized in our current justice system?
Medical Marijuana

Nov 5, 1996: California becomes the first state to legalize medical marijuana.

Approved Conditions: AIDS, anorexia, arthritis, cachexia, cancer, chronic pain, glaucoma, migraine, persistent muscle spasms, seizures, severe nausea, or other chronic or persistent medical symptoms.

Allowed Possession: 8 ounces (1oz += 28 grams)
Fee: $66, unless on Medicaid, then $33.
Note that a typical 1/8th ounce bag of marijuana costs about $50 on the street.
Also note that one ounce of marijuana can be used to make approximately 50 joints

Is there a currently accepted medical use?

- The drug’s chemistry is known and reproducible
- There must be adequate safety studies
- There must be adequate and well-controlled studies proving efficacy
- The drug must be accepted by qualified experts
- Scientific evidence must be widely available
## Cannabis Related Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marional/Dronabinol</td>
<td>Synthetic Delta-9 THC</td>
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<tr>
<td>Sativex</td>
<td>THC (delta-9 tetrahyrocannabinol)</td>
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<tr>
<td></td>
<td>CBD (cannabidiol)</td>
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<tr>
<td>Nabilone/Cesamet</td>
<td>Synthetic cannabinoid similar to THC</td>
</tr>
<tr>
<td>Dexanabinol</td>
<td>Synthetic non-psychotropic cannabinoid that blocks NMDA receptors</td>
</tr>
<tr>
<td>Epidiolex®</td>
<td>Pure plant-derived Cannabidiol (CBD)</td>
</tr>
<tr>
<td>Rimonanbant/Acomplia</td>
<td>Synthetic chemical that blocks endocannabinoids</td>
</tr>
</tbody>
</table>
Harmful Effects Of Marijuana

- as an addictive substance
- as a toxic substance
- as an intoxicating substance
- as a gateway drug

**Addictive Potential**
- Initiate after age 18-9% eventually satisfy DSM criteria of dependence
- Initiate before age 18-17% become addicted within 2 years of use
- With daily use-estimate 35-40% rate of cannabis dependency

**Adolescents**
- impaired neural connectivity fewer fibers
- in hippocampus and prefrontal cortex
- increased sensitivity to drugs (more likely to develop cannabis dependency and use other drugs)
- daily pot for 3 yrs in adolescence-tested in 20’s after abstinent for 2 yrs-had abnormal shape to hippocampus and memory deficits
ASAM Recommendations (2010)

1) Marijuana must be subject to the same standards applicable to prescription medication
2) Clinicians should not provide patient access to marijuana until appropriate FDA approval is present
3) Smoking is inherently unsafe
4) Discourages state interference in the federal medication approval process
5) Rejects state legislative process as a means for which individuals without appropriate qualifications make determinations about medication
6) Physicians ignoring (2) should have a true patient-physician relationship and conduct themselves accordingly.
ASAM Recommendations (2012)

1) Physicians lead efforts to oppose legislative initiatives that would result in legalization of marijuana production, distribution, marketing, possession, and use by the general public.
2) All physicians should incorporate screening and treatment for risky substance use into their routine.
3) Inform the public that marijuana available today is of far higher potency than that which was available in the 1960s. Further inform the public about potential development and progression of psychotic conditions related to use of high-potency marijuana among adolescents.
APA Guidelines (2012)

- By sanctioning patients’ consumption, psychiatrists may contribute to the adverse community impact of the culture surrounding marijuana dispensaries, including criminal behavior.
- They advise that physicians assume their role of educating patients about risks and benefits, particularly when responding to requests for a nonbeneficial treatment.
ASAM supports the decriminalization of marijuana, which would reduce penalties for marijuana possession for personal use to civil offenses linked to contingencies, such as mandated referral to clinical assessment, educational activities, and, when indicated, formal treatment for addiction or other substance-related disorders

ASAM does not support the legalization of marijuana and recommends that jurisdictions that have not acted to legalize marijuana be most cautious and not adopt a policy of legalization until more can be learned from the natural experiments now underway in jurisdictions that have legalized marijuana.
Uruguay

- Government initiative, law passed 12/2013
- Policy goals: No increase in consumption; decline in organized crime
- Non-commercial, regulated market with 3 methods of supply: licensed pharmacy retail, at home and cannabis clubs.
- Access for citizens and residents 18 and older who are inscribed in registry.
- Bans all forms of promotion.
- Limited access of up to 40 grams/month per person.
- Currently operational: at home cultivation and cannabis clubs.
- Pharmacy retail faces regulatory challenges. Currently not implemented.
- Creation of federal regulatory entity (IRCCA).
- Public opinion remains opposed (only 37% support).
### Comparison of Colorado & Uruguay Models

<table>
<thead>
<tr>
<th></th>
<th>Colorado</th>
<th>Uruguay</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Level of Law</strong></td>
<td>State constitution, laws, &amp; regulations (federal conflict)</td>
<td>National laws &amp; regulations</td>
</tr>
<tr>
<td><strong>Authors of Law</strong></td>
<td>Industry</td>
<td>Civil society/government</td>
</tr>
<tr>
<td><strong>Edibles</strong></td>
<td>Permitted: child oriented</td>
<td>Prohibited</td>
</tr>
<tr>
<td><strong>Prevention Programs</strong></td>
<td>Industry veto</td>
<td>Prospective-no industry role</td>
</tr>
<tr>
<td><strong>Labeling</strong></td>
<td>Law to nonexistent (industry veto)</td>
<td>Strict</td>
</tr>
<tr>
<td><strong>Advertising</strong></td>
<td>Flourising</td>
<td>Prohibited</td>
</tr>
<tr>
<td><strong>Public Consumption</strong></td>
<td>Not permitted</td>
<td>Tolerated</td>
</tr>
<tr>
<td><strong>Taxes</strong></td>
<td>40%</td>
<td>None</td>
</tr>
<tr>
<td><strong>Monthly Quota</strong></td>
<td>None (unlimited)</td>
<td>40 G (registration)</td>
</tr>
<tr>
<td><strong>Drug Tourism (sales to out of state visitors)</strong></td>
<td>Permitted</td>
<td>Prohibited</td>
</tr>
</tbody>
</table>
Do You Believe That Crude Marijuana (Whole Plant) May Be A Legitimate Medication To Be Prescribed By Physicians?

A. Strongly agree
B. Agree
C. Not Sure
D. Disagree
E. Strongly Disagree
Do You Believe That The Unrestricted Legalization Of Marijuana (Colorado Model) Is Harmful To Society?

A. Strongly agree  
B. Agree  
C. Not Sure  
D. Disagree  
E. Strongly Disagree
Do You Believe That The Restricted Legalization Of Marijuana (Dutch Model) Is A Good Public Policy?

A. Strongly agree
B. Agree
C. Not Sure
D. Disagree
E. Strongly Disagree
Do You Believe That The Less Regulated Legalization Of “Medical Marijuana” (California Model) Is Good Public Policy?

A. Strongly agree
B. Agree
C. Not Sure
D. Disagree
E. Strongly Disagree
Do You Believe That The More Regulated Legalization Of “Medical Marijuana” (New York Model) Is Good Policy?

A. Strongly agree
B. Agree
C. Not Sure
D. Disagree
E. Strongly Disagree
The Evolving Synthetic Cannabis Epidemic: Lessons For Physicians

Robert L. DuPont, MD, DFASAM
Robert L. DuPont, MD, FASAM

Prescription Drug Research Center (BDA subsidiary) – Salary – Chairman (2003-2015)
RiverMend LLC – Consulting Fee – Member, Scientific Advisory Board (2014-Present)
The Cannabis Legalization Dilemma

- Legalizing cannabis is not simple

- Cannabis comes in many forms
  - From plant products to THC concentrates for “dabbing,” vaping and edibles

- So does “legalization”
What is sold as “Legal Cannabis”? 

- The answer: **whatever sells**

- Bad medicine and bad public health
Synthetic Cannabis

- Synthetic cannabis (SC) – a New Psychoactive Substance (NPS) or “designer drug”

- All fly under the cannabis flag as “legal marijuana”

- Common names include Spice and K2
How It Happened

- Development of endless new synthetic chemicals to activate the cannabis receptors
- Described in widely-available scientific literature
- Hijacked receptor-focused chemistry used for many medicines
A Golden Criminal Business Opportunity

- Rogue chemists in China and beyond
  - Examples: JWH-018, JWH-122, JWH-210, AM2201, XLR11, FDU-PB-22, FDU-NNEI, AB-CHMINACA, NNEI

- No study – many negative consequences for users

- An unintended consequence of proud brain science
Big Business + Dangerous Outcomes

- Designed to evade the law and drug tests
- New drug distribution system – Internet, direct delivery, convenience stores, gas stations
- Sold as potpourri or incense – labeled “not for human consumption”
- The drug users do the health research
A Focus on Synthetic Cannabis

- Why “synthetic cannabis”?
  1. Cannabis is the most widely used drug of abuse (other than alcohol)
  2. There is a determined effort to portray cannabis as harmless
  3. Not illegal
Synthetic Cannabis

- Mixture of herbs or spices that is sprayed with synthetic compound
- SC is packaged in small bags of dried leaves
- Typically smoked in joints or pipes
- Acts on the same brain receptors as marijuana but much more varied side effects --
SC Effects

- NIDA reports some effects similar to cannabis:
  - Elevated mood
  - Relaxation
  - Altered perception
  - Symptoms of psychosis

With **psychotic effects** that include:
- Extreme anxiety
- Confusion
- Paranoia
- Hallucinations

Other negative health effects:
- Fast, racing heartbeat and higher blood pressure
- Reduced blood supply to heart
- Nausea and vomiting
- Muscle spasms, seizures, and tremors
- Suicidal and other harmful thoughts and/or actions
Emergency Department Visits

- Synthetic Cannabinoids Only: 59%
- In Combination with Marijuana: 17%
- In Combination with Pharmaceuticals: 17%
- In Combination with Alcohol: 13%

*Because multiple drugs may be involved in each visit, percentages add to more than 100 percent.
Source: 2010 SAMHSA Drug Abuse Warning Network (DAWN).
Emergency Department Visits

![Chart showing the age distribution of SC and Marijuana-related emergency department visits in 2010.](chart.png)

* Estimates for ED visits involving synthetic cannabinoids for patients aged 30 or older were suppressed due to low statistical precision.

Note: ED visits in which the patient age was unknown are excluded.

Source: 2010 SAMHSA Drug Abuse Warning Network (DAWN).

SAMHSA CBHSQ, 2012
SC Cases Reported in ToxIC Registry

- From 2010-2015, the ToxIC Case Registry of the American College of Medical Toxicology reported 456 cases of SC intoxication (out of 42,138 cases of toxic exposure in 101 hospitals and clinics)
- In 61% (277) of these cases, SC was the only intoxicant
- 3 deaths: 1 with SC as the sole agent and 2 with multiple agent exposures
- Synthetic cannabinoid poisonings increased in all US Census regions
Monitoring the Future

- In 2011 SC was the most widely used illicit drug other than cannabis
- In March 2011 DEA scheduled some of the most widely used chemicals
- Good news: recent declines in youth SC use
The Market for SC is Strong

- Dominates the global NPS market

- Of the 32 tons of SC seized worldwide in 2014, 26.5 tons or nearly 83% were seized in the US
Current Approach to SC

- Focus on suppliers, including crackdown on gas stations, smoke shops, convenience stores

- Harm reduction – not addressing the use itself

- Cost $1/cigarette, not much more than a tobacco cigarette
Consequences of Continued Demand

The New York Times

K2 Overdoses Surge in New York: At Least 130 Cases This Week Alone

By SARAH MASLIN NIR  JULY 14, 2016

K2’s Sudden Surge Tests New York Authorities

By ELI ROSENBERG  JULY 15, 2016
National Drug Early Warning System (NDEWS)

- Tests urine samples from criminal justice populations
- Specific focus on NPS and their metabolites, including 12 synthetic cannabis metabolites
- Sign up for latest updates at www.ndews.org
Pilot Community Drug Early Warning System (CDEWS) Findings

- SC metabolites detected vary considerably by city/site
- In Washington, DC, between one quarter and one third of young male offenders tested positive for SC
- Unlike prescription drugs, SC found in the urine that passed drug screens
Final Thoughts

- SC message on the legalization of cannabis – be careful what you wish for

- Legalize SC to end illegal market?

- What does SC popularity tell us about the drug market?
Thank you!
References + Resources

- Center for Substance Abuse Research. (2013, September 30). CESAR pilots new Community Drug Early Warning System in criminal justice system; finds synthetic cannabinoids in all populations studied. CESAR Fax, 22(39).
References + Resources

Role of Cannabinoids in Medicine: Clinical Evidence

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Types of Cannabis

Sativa generally has a higher THC to CBD ratio as compared with Indica.
Components 2

~100+ cannabinoids, each with their own—often complementary—pharmacology, e.g., CBDV, THCV, CBG, CBN, CBC, etc., have been promoted for different medical conditions

- Only THC is psychoactive
- Multiple extracts can be blended to form new products
- Likely research targets: cancer, epilepsy, inflammation, metabolic disorder/diabetes, psychiatric disorders, substance abuse, etc.
- Plus non-cannabinoid active components, e.g., terpenes, flavonoids
- Can plant extracts be adequately characterized and standardized?
- GW have shown that they can and have been!
MEDICINAL MARIJUANA

Active chemical constituents of Cannabis:

- **Delta-9 THC (Tetrahydrocannabinol):** Active psychoactive component
- **CBD (Cannabidiol):** increases some of the effects of THC and decreases other effects of THC.
- **THCV (Tetrahydrocannabivarin):** found primarily in strains of African and Asian cannabis.
  - THCV increases the speed and intensity of THC effects, but also causes the subjective experience to end.
- **CBC (Cannabichromene):** is probably not psychoactive in pure form but is thought to interact with THC to enhance the subjective experience.
- **CBL (Cannabicyclol):** is a degradative product like CBN. Light converts CBC to CBL.
Cannabinoids

Δ⁹-tetrahydrocannabinol (THC)  Cannabidiol (CBD)
Components of Cannabis Plant

- Cannabis plant is the unique source of cannabinoids
- Cannabis used centuries ago possessed a 1:1 CBD:THC ratio
  - analgesic, anti-spasmodic, anti-tremor, anti-inflammatory, appetite stimulant, anti-emetic
  - anti-inflammatory, analgesic, anti-convulsant, anti-psychotic, anti-oxidant, neuroprotective;
  - does not bind to cannabinoid receptors
  - does bind to other receptors in the body
  - reduces the negative effects of THC
  - has been bred out of modern herbal cannabis!

Both compounds are in Sativex, unlike other licensed cannabinoid medicines (e.g. dronabinol, nabilone)

Single product polypharmacology
Cannabinoid Pharmaceuticals

- **Sativex (GW)** - Mouth spray; contains natural extract of the cannabis plant; THC+CBD (1:1 ratio); [20 countries but not US]

- **Dronabinol / Marinol** (Unimed)/Solvay; Synthetic Delta-9-THC – Approved for appetite stimulation and reducing nausea

- **Nabilone / Cesamet** (Valeant); Synthetic cannabinoid similar to THC. For Treatment of nausea and vomiting in patients undergoing cancer treatment.
Medicinal Marijuana: Clinical Evidence
Medicinal Marijuana: Anti-emetic Effects

- **Nabilone (Cesamet)** approved; dose: 2-6 mg/day; approximately 15 controlled studies with ~600 patients with cancer, drug was effective (superior to other known drugs such as prochlorperazine, domperidone etc.) for treating chemotherapy-associated nausea/vomiting.

- **Dronabinol (Marinol)** (5-15 mg/m2/day) was found to be effective in 14 controlled studies involving 681 patients with cancer for treating chemotherapy-associated nausea and vomiting. However, there are significant side effects (dizziness, drowsiness, hallucinations, euphoria etc.) that have reduced their use.
Medicinal Marijuana: Anti-emetic Effects cont’d

- **Smoked marijuana**: Three Canadian studies, 2 by Chang et al. 1979 and 1981; and one by Levitt et al. 1984 used smoked marijuana for anti-emetic effects.

- Was effective in 25% patients; of 20 study patients, 20% preferred smoked Mj, 30% preferred oral nabilone and 45% did not express any preference.

- The newer agents such as 5HT3 receptor antagonists are much better than cannabinoids.
Medicinal Marijuana: Appetite Stimulant Effects

- [741 patients; 5 controlled studies] Oral THC (dronabinol [Marinol]), 2.5-20 mg/day; --
- As a stimulant of appetite-(FDA-for treating AIDS-anorexia); and by Canada.
- Smoked marijuana (2.5 mg, tid) was effective in stimulating appetite in 67 HIV-infected patients without affecting viral load or immune function (CD4 counts) (Abrams et al. 2003).

(References for appetite stimulant effects: Iversen 2000; Beal et al. 1995 [139 pts]; Regelson et al. 1976 [54 pts]; Struwe et al. 1993 [12 pts]; Jatoi et al. 2002 [469 pts]; and Abrams et al. 2003 [67 pts]).
Medicinal Marijuana: Analgesic Effect

- 14 studies [353 pts]; oral THC, sublingual spray, or iv THC, have been tested.
- Oral THC at 10, 15 and 20 mg doses was effective, but with significant ADRs (e.g., drowsiness, confusion). The 5mg THC was ineffective as an analgesic.
- Most current data from Ware et al. (2010), although in a small sample (n=23), show positive effects on neuropathic pain with smoked Mj with 9.5%THC. No significant effects at lower doses.

Medicinal Marijuana: Multiple Sclerosis

- 13 controlled studies [total 939 pts]; smoked marijuana, hashish, oral THC in capsule, oral extracts of C. sativa in oral and sublingual spray forms containing THC, cannabidiol, or a combination of the two and oral nabilone.

- Two clinical trials are worthy of note: Zajicek et al. 2003 [630 pts-14 wks]; Wade et al. 2004; 160 pts). Data from most studies showed some effect on mobility and muscle spasticity compared to placebo.
Medicinal Marijuana: Multiple Sclerosis cont’d

- Zajicek et al: [double blind randomized placebo controlled trial]: 206 SS on oral THC in capsule, 211 SS on oral cannabis extract [2.5 mg THC+ 1.25 mg cannabidiol, + <5% other cannabinoids/capsule], and 213 SS on placebo, for 14 wks.

- No objective effects on spasticity but subjective improvement in spasticity was observed; there was objective improvement in mobility and decreased hospitalizations with oral THC. ADRs were mild and tolerable. Overall, one year f/u showed positive effects on spasticity.
Medicinal Marijuana: Multiple Sclerosis cont’d

- Wade et al (2004) study [160 pts]; (Sativex capsules; cannabis extract [oral THC 2.5 mg + cannabidiol 2.7 mg]; total doses: 2.5-120 mg/d; 6 wks].

- Results showed significant reduction in spasticity, sleep quality and mobility with Sativex compared to placebo.

- ADRs were mild and well-tolerated.
Another small randomized, double-blind, parallel groups, placebo controlled study of 4 wks [n=32/group] (Rog et al. 2005) showed similar beneficial effects of Sativex [THC+CBD by oromucosal spray] on pain and sleep disturbance (spasticity).

ADRs (dizziness, dry mouth, and somnolence] were mild]; cognitive effects were limited to long term memory storage.
Medicinal Marijuana: Spinal Cord Injuries

- Only 3 studies in the literature;
- (i)-5 patients, (ii) 1 patient, (iii) 4 patients;
- oral THC or *C. sativa* extracts (THC, cannabidiol or a combination) in sublingual spray, may lead to an improvement in spasticity, muscle spasm, pain, vesicle dysfunction and sleep quality.

(References for Spinal cord injuries: Hanigan et al. 1986 [5 pts]; Wade et al. 2003 [4 pts]; Maurer et al. 1990 [1 pt]).
Medicinal Marijuana: Gilles de la Tourette’s Syndrome

- Two randomized, double-blind, placebo controlled studies (12 and 24 patients), oral THC (up to 10 mg/d for 6 wks) significantly reduced the frequency of tics.
- ADRs – no serious ADRs (one patient dropped out due to anxiety and agitation).

(References for Gilles de la Tourette’s syndrome: Muller-Vahl et al. 2002a [12 pts], 2003a [24 pts])
Medicinal Marijuana: Epilepsy

- Several anecdotal observations suggest positive effects of cannabidiol on grand mal epilepsy.
- Only one controlled clinical study of 15 patients exists.
- These patients while inadequately controlled on their conventional anti-epileptic regimen, were subjected to a randomized, double-blind, parallel group study to 2 groups:
  - Group 1: 8 patients, in addition to their conventional med, received oral cannabidiol at 200-300 mg/d for 8-18 weeks;
  - Group 2: 7 on placebo.
Of the 8 pts on cannabidiol, 4 remained convulsion-free for the duration; 3 showed clinical improvement.

Six of the 7 placebo patients remained unchanged. Drowsiness was seen in 4 of the treated patients. These results have not been confirmed in any other study.

(References for Epilepsy: Cunha et al. 1980 [15 pts])
Medicinal Marijuana: Glaucoma

- Anecdotal reports of cannabis on intraocular pressure but only two controlled studies in the literature.
- Merritt et al. (1980), in a RDBPC study showed that one Mj cigarette containing 2% THC significantly reduced IOP.
- In another RDBPC study, Merritt et al. (1981) showed that eye drops containing 0.01, 0.05, and 0.1% THC, significantly reduced the IOP. ADRs were significant: tachycardia, palpitations, and postural hypotension.

(References for glaucoma: Merritt et al. 1980 [18 pts], 1981 [8 pts])
Medicinal Marijuana: Parkinson Disease

- Only two controlled clinical trials have studied the effect of cannabinoids on Parkinson disease.
- Both clinical trials (one of 7 and another of 19 pts) did not show any beneficial effect of oral THC (nabilone) on the disease.

(References for Parkinson Disease: Sieradzan et al. 2001 [7 pts]; Carroll et al. 2004 [19 pts])
Medicinal Marijuana: Dystonia

- Only one RDB cross-over PC-controlled study (Fox et al. 2002) of 15 patients showed no beneficial effects of oral THC (nabilone) on generalized and segmental dystonia.

- (References for dystonia: Fox et al. 2002 [15 pts])
PTSD & Nabilone

- The use of a synthetic cannabinoid in the management of treatment-resistant nightmares in posttraumatic stress disorder (PTSD). *(Fraser, GA CNS Neurosci Ther. 2009)*

- Use of a Synthetic Cannabinoid in a Correctional Population for PTSD-Related Insomnia and Nightmares, Chronic Pain, Harm Reduction, and Other Indications: A Retrospective Evaluation > Generally positive results but uncontrolled. *(Colin Cameron, MDCM, FRCPC, Diane Watson, MD, FRCPC, and Jeffrey Robinson, MA J Clin Psychopharm, 2104)*

- Marijuana use did not improve PTSD symptom severity, violent behavior, alcohol problems *(AAAP December 6, 2014: Samuel Wilkinson, MD Yale School of Medicine)*
Medicinal Marijuana: Efficacy Summary

- Limited data from small clinical studies or trials show the following:
  - **Nausea/Vomiting**: Oral THC (FDA-approved nabilone or dronabinol) for treating chemotherapy-associated nausea/vomiting.
  - Oral THC shows some appetite stimulant activity in HIV-infected patients, but large clinical trials with oral THC or smoked marijuana are needed for FDA approval.
  - **Neuropathic pain**: Sativex approved in Canada and other countries;
  - For inflammation, MS, dystonia, Tourette’s syndrome, Parkinson disease, or glaucoma:
    - No good evidence from large clinical trial(s) that would support the use of either oral THC or smoked marijuana in clinical practice.
  - **PTSD**: Insufficient evidence to treat with cannabis
- Well-designed RDB-placebo controlled trials are needed to obtain the FDA approval to use smoked marijuana or cannabinoids for the treatment of any of the above mentioned conditions.
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