TOBACCO and CANNABIS

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Outline

1. Tobacco Basics
2. Tobacco Treatments
3. Cannabis Basics
4. Cannabis Treatments
5. Cannabis Special Topics
6. Conclusions
1 Tobacco Basics
The Molecular Structure
Intoxication

- Serotonin ➔ Mood Elevation, (▼ appetite)
- GABA ➔ Anxiety Relief
- Acetylcholine ➔ Arousal and Cognition
- β-Endorphins ➔ Reduction of Tension
- Glutamate ➔ Learning and Memory
- Norepinephrine ➔ Arousal, (▼ appetite)
- Dopamine ➔ Pleasure, (▼ appetite)

Withdrawal

Serotonin ➞ Depressed Mood
GABA ➞ Anxiety
Acetylcholine ➞ Insomnia
β-Endorphins ➞ Irritability
Glutamate ➞ Difficulty Concentrating
Norepinephrine ➞ Decreased Heart Rate
Dopamine ➞ ▲ Appetite (and Cravings)

Compounds in Tobacco Smoke

An estimated 4,800 compounds in tobacco smoke, including 11 proven human carcinogens

**Gases**
- Carbon monoxide
- Hydrogen cyanide
- Ammonia
- Benzene
- Formaldehyde

**Particles**
- Nicotine
- Nitrosamines
- Lead
- Cadmium
- Polonium-210

Nicotine is the addictive component of tobacco products, but it does NOT cause the ill health effects of tobacco use.

Slide courtesy of Judith J. Prochaska, PhD, MPH - University of California, San Francisco.
Health Consequences

• Cancers
  – Acute myeloid leukemia
  – Bladder and kidney
  – Cervical
  – Esophageal
  – Gastric
  – Laryngeal
  – Lung
  – Oral cavity and pharyngeal
  – Pancreatic

• Pulmonary diseases
  – Acute (e.g., pneumonia)
  – Chronic (e.g., COPD)

• Cardiovascular diseases
  – Abdominal aortic aneurysm
  – Coronary heart disease
  – Cerebrovascular disease
  – Peripheral arterial disease

• Reproductive effects
  – Reduced fertility in women
  – Poor pregnancy outcomes (e.g., low birth weight, preterm delivery)
  – Infant mortality

• Other effects: cataract, osteoporosis, periodontitis, poor surgical outcomes

Slide courtesy of Judith J. Prochaska, PhD, MPH - University of California, San Francisco.
Lung cilia regain normal function
Ability to clear lungs of mucus increases
Coughing, fatigue, shortness of breath decrease
Risk of stroke is reduced to that of people who have never smoked
Risk of CHD decreases to half that of a continuing smoker
Risk of cancer of mouth, throat, esophagus, bladder, kidney, pancreas decrease
Risk of CHD is similar to that of people who have never smoked

Time Since Quit Date
- 2 weeks to 3 months: Circulation improves, walking becomes easier
- 1 to 9 months: Lung function increases up to 30%
- 1 year: Excess risk of CHD decreases to half that of a continuing smoker
- 5 years: Lung cancer death rate drops to half that of a continuing smoker
- After 15 years: Risk of cancer decreases

Slide courtesy of Judith J. Prochaska, PhD, MPH - University of California, San Francisco.
Drugs that may have a decreased effect due to induction of CYP1A2 by tobacco smoke:

- Caffeine
- Clozapine
- Olanzapine
- Haloperidol
- Chlorpromazine
- Fluvoxamine
- Tacrine
- Theophylline

**Smoking cessation may reverse the effect.**
Smokers who use oral combined contraceptives (estrogen and progestin) have an increased risk of serious cardiovascular adverse effects including:

- Stroke
- Myocardial infarction
- Thromboembolism

Experts do not recommend oral contraceptives for women who are:

- Over 35, and
- Heavy (>15 cigarettes per day) smokers
Causes of Annual Deaths in the US

Individuals with mental illness or substance use disorders

Centers for Disease Control and Prevention, NHIS, 2007; slide courtesy of Judith J. Prochaska, PhD, MPH - University of California, San Francisco.
Psychiatric History

- 41.0% Overall

- None: 22.5%
- History: 34.8%
- Active:
  - Panic Disorder
  - PTSD
  - GAD
  - Dysthymia
  - Major Depression
  - Bipolar Disorder
  - Nonaffect Psychosis
  - ASPD
  - Alcohol Abuse/Dep
  - Drug abuse/dep

Tobacco Treatments
Evidence-Based Practices

1. Physician advice
2. Individual counseling
3. Telephone counseling
4. Group programs
5. Aversion therapy
6. Hypnotherapy
7. NRT, bupropion, varenicline, nortriptyline, clonidine
1. SSRIs and SNRI
2. Anxiolytics: benzodiazepines, buspirone
3. Homeopathic treatments
4. Herbal supplements
5. Massage Therapy
6. Acupuncture
7. Nicotine Anonymous
Clinician Interventions

Compared to patients who receive no assistance from a clinician, patients who receive assistance are 1.7–2.2 times as likely to quit successfully for 5 or more months.

Nicotine Replacement Therapy
1. Patients with underlying CVD:
   - Recent MI (within past 2 weeks)
   - Serious arrhythmias
   - Serious or worsening angina

2. Patients under 18 years of age

3. Pregnant women
Advantages

1. Patch provides consistent nicotine levels
2. Patch is easy to use and conceal
3. Gum/lozenge/inhaler/spray can titrate therapy to manage withdrawal and may satisfy oral cravings
4. Inhaler mimics hand-to-mouth ritual of smoking
5. Spray is most rapidly absorbed form of nicotine replacement
Disadvantages

1. Allergic reactions to patch adhesive
2. Vivid or disturbing dreams with nocturnal patch use
3. Gum may be socially unacceptable and difficult to use with dentures
4. Patients with underlying bronchospastic disease must use inhaler with caution
5. Spray may be addictive and patients must wait 5 min before driving
Gum Chewing Technique

- Chew between cheek & gum
- Chew slowly
- Stop chewing at first sign of peppery taste or tingling sensation
- Chew again when peppery taste or tingle fades
- Park between cheek & gum
- Do not eat or drink 15 min before or after use.

Slide courtesy of Judith J. Prochaska, PhD, MPH - University of California, San Francisco.
Bupropion
Advantages

1. Easy to use
2. Can be used with NRT or varenicline
3. May delay cessation-related weight gain
4. May be beneficial in patients with coexisting depression
Disadvantages

1. Common side effects:
   - Dry mouth
   - Anxiety
   - Insomnia (avoid bedtime dosing)

2. Should be avoided in patients with an increased risk for seizures
Varenicline
Advantages

1. Oral formulation with twice-a-day dosing
2. Offers a new mechanism of action for persons who previously failed using other medications
3. Early industry-sponsored trials suggest this agent is superior to bupropion SR
Disadvantages

1. Common side effects:
   - Nausea (in up to 33% of patients)
   - Sleep disturbances (insomnia, abnormal dreams)
   - Constipation
   - Flatulence
   - Vomiting

2. Psychiatric Risks

3. Cardiovascular Risks
“Stimulated Reporting”

> 6 Month Quit Rates

Beyond Gum and Patches
A vaccine would keep nicotine from reaching the brain

NICOTINE ADDICTION
1. Nicotine from inhaled cigarette smoke enters the bloodstream through lung tissue and quickly spreads through body
2. A small molecule, nicotine easily passes over the blood brain barrier
3. The molecules bind to nicotine receptors, releasing dopamine which provides pleasurable sensations

HOW THE VACCINE WORKS
1. Vaccine is administered via injection
2. The vaccine prompts the body to generate antibodies that bind to nicotine molecules
3. The antibodies are too big to cross into the brain, keeping nicotine away from receptors

Sources: Nabi Biopharmaceuticals and Kim Janda

NicVax 2006

NicVax 2013
“Why drink and drive, when you can smoke and fly.”

“If we all had a bong, we’d all get along.”
Pleasurable Effects

• Mild euphoria and relaxation
• The giggles
• Increased sensitivity to external stimuli:
  ▪ Colors seem brighter
  ▪ Smells are more pungent
• Distortion of time perception
The Molecular Structure
The Cannabinoid System

- THC activates the CB₁ and CB₂ cannabinoid receptors:
  - CB₁ has high density in cerebellum, basal ganglia, hippocampus, cerebral cortex
  - CB₁ has low density in the brainstem, hence low risk of respiratory depression
  - CB₂ is found in spleen, hematopoietic cell lines, mast cells.

- Anandamide is the endogenous ligand.
Routes of Administration

• Smoked marijuana:
  ▪ Reaches the brain in minutes
  ▪ Effects last 1 - 3 hours
  ▪ Delivers a lot of THC into the bloodstream

• Eating or drinking marijuana:
  ▪ Takes $\frac{1}{2}$ - 1 hour to have an effect
  ▪ Effects last up to 4 hours
  ▪ Delivers significantly less THC into the bloodstream
Biphasic Distribution

Toxicology Testing

• Casual use:
  ▪ Up to 10 days in urine
  ▪ 50% positive in hair samples

• Heavy use:
  ▪ Up to 30 days in urine
  ▪ 85% positive in hair samples

• Weight loss gives serial UTox spike.

• Dronabinol gives positive test.

• Passive inhalation gives negative test.
Cannabis Potency

MARIJUANA USERS, TREATMENT ADMISSIONS, AND AVERAGE POTENCY: 1986-2010

- Millions of current marijuana users
- 10,000s of primary marijuana treatment admissions
- Average seizure potency

NSDUH, TEDS, National Seizure System.
Cannabis Intoxication

If drunk –
  you run the RED lights

If stoned –
  you stop at the GREEN lights
Cannabis Withdrawal

- Irritability and restlessness
- Aggression
- Insomnia
- Appetite decrease

Withdrawal syndrome is **not**:
- As painful as heroin withdrawal,
- As dangerous as alcohol withdrawal, or
- As long-lasting as cocaine withdrawal

- No indication for treatment
Neurocognitive Decline – 8 IQ points

Meier, PNAS, 2012.
Addictive Potential

- Tobacco 32 %
- Heroin 23 %
- Cocaine 17 %
- Alcohol 15 %
- Sedatives 9 %
- Cannabis 9 %

Cannabis Treatments
Weeks of Continuous Abstinence

- V: 6.9
- CBT: 3.5 (a)
- CBT + V: 5.3
- V: 17%
- CBT: 20%
- CBT + V: 43% (b,c)

(a) V vs. CBT comparison, p < .05
(b) CBT+V vs. CBT comparison, p < .05
(c) CBT+V vs. V comparison, p < .05

Budney, *J Consult Clinical Psychology*, 2006; slide courtesy of Dr. Frances Levin.
Dronabinol

Log Rank Wilcoxon: $P = 0.0249$

Time to drop

Levin, *Drug Alcohol Depend*, 2011; slide courtesy of Dr. Frances Levin.
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Cannabis

Special Topics
The Schizophrenia-Marijuana Link

Adolescence

MonitoringTheFuture.org.
Medical Marijuana

• Therapeutic potential for:
  - Pain (cancer, multiple sclerosis)
  - Nausea (cancer)
  - Loss of appetite (HIV/AIDS)
  - Increased occular pressure (glaucoma)

• Savitex ® (available only in UK and Canada) is a mouth spray:
  - Plant-derived THC – 50%
  - Cannabidiol – 50%
Synthetic Cannabinoids

[Chemical structure image]
Cannabidiol

Summary
1. Smoking rates are 40% to 70% among those with mental illness: 2 to 3 times that of the general population.

2. Marijuana is addictive but not as addictive as tobacco, heroin, cocaine, or alcohol.

3. Psychotherapy works well for both tobacco and cannabis addiction.

4. Pharmacotherapy is proven to be effective for addiction to tobacco, but not cannabis.
Thank you