Secondhand Smoke from Marijuana: The Return of a Familiar Problem

Matthew L. Springer, Ph.D.
Professor of Medicine, UCSF
8/16/17

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Flight Attendant Medical Research Institute, NIH/NIDA, Elfenworks Foundation, CA Tobacco-Related Disease Research Program
The Bad Ol’ Days
The Bad Ol’ Days
Typical day in 2016
“Partygoers dance and smoke pot April 19, the first of two days of the annual 4/20 marijuana festival in Denver. The 4/20 event was the first one since Colorado legalized recreational marijuana in January.”
Today (well, actually last year): 4/20/16...1/2 mile from UCSF!

(4/20/17)
Already: WA, 2015

...really!

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HIGH ON LEGAL MARIJUANA
RAISED ON BIGGIE AND NIRVANA
WE ARE THE NEW AMERICANA

ELEVATE THE MOMENT
WITH ZOOTS PREMIUM CANNABIS INFUSED EDIBLES

Elevate the moment with Washington’s top selling marijuana infused edibles. You can trust Zoots to blend our proprietary Cypress™ extract with all natural ingredients to assure a controlled, consistent and pleasantly elevated experience every time.

WE ARE THE NEW AMERICANA
HIGH ON LEGAL MARIJUANA
RAISED ON BIGGIE AND NIRVANA
WE ARE THE NEW AMERICANA

Find a local retailer at www.zootology.com/store-finder

Warning: This product has intoxicating effects and may be habit forming. Marijuana can impair concentration, coordination, and judgment. Do not operate a vehicle or machinery under the influence of this drug. There may be health risks associated with consumption of this product. For use only by adults 21 and older. Keep out of the reach of children.
Already: SF, 2017... REALLY!!!

“NOW SERVING CANNABIS FOR BRUNCH
In S.F., gourmet fare infused with artisanal weed offers medicated spreads to new connoisseurs”
– SF Chronicle 1/22/17
Secondhand smoke (SHS)

• Smoking causes over 140,000 cardiovascular deaths in the US per year

• Secondhand smoke is estimated to cause ~50,000 US deaths/year, mostly from cardiovascular disease

• Smoking bans in public places lead to reduction in frequency of heart attacks
Secondhand smoke (SHS)

Long-term secondhand smoke exposure impairs *vascular endothelial function*

“blood vessel function”
Tobacco secondhand smoke exposure impairs ability of arteries to **vasodilate** when they need to pass more blood

**(Vasodilation: Arteries grow in diameter when necessary)**

Important: Impairment is temporary, but repeated exposures lead to **long-term** impairment
Measuring Endothelial Function

- Principle of Flow-Mediated Dilation (FMD) -

Ischemic dilation of downstream vessels

\[ \downarrow \]

Flow in artery \[ \uparrow \]

\[ \downarrow \]

Shear stress on endothelium \[ \uparrow \]

\[ \downarrow \]

Nitric oxide \[ \uparrow \]

\[ \downarrow \]

Flow-mediated vasodilation

Alberts et al., 1995

Springer et al., 2003
Brachial artery FMD gets lower with increasing cardiovascular risk factors

Dilation of coronary arteries in response to increased coronary blood flow gets lower with increasing cardiovascular risk factors (Nabel, Selwyn, and Ganz, 1990)

Improves FMD:
Dark chocolate, green tea, red wine, etc.

Impairs FMD:
Age, smoking, secondhand smoke, etc.
Measuring Endothelial Function
“Flow-Mediated Dilation” (FMD)

Cerelmaer NEJM 1992

FMD = 10%

4.0 mm 4.4 mm
Cigarette smoking is associated with dose-related and potentially reversible impairment of endothelium-dependent dilation in healthy young adults
DS Celermajer, KE Sorensen, D Georgakopoulos, C Bull, O Thomas, J Robinson and JE Deanfield
Circulation 1993;88:2149-2155

...that is, smoking impairs FMD
Several years of secondhand smoke exposure impairs FMD.
Brief Secondhand Smoke Exposure Depresses Endothelial Progenitor Cells Activity and Endothelial Function

Sustained Vascular Injury and Blunted Nitric Oxide Production

Christian Heiss, MD, Dr Med,* Nicolas Amabile, MD,* Andrew C. Lee, MD,* Wendy May Real, BS,* Suzaynn F. Schick, PhD,† David Lao, MD,* Maelene L. Wong, BS,* Sarah Jahn, MB,* Franca S. Angeli, MD,* Petros Minasi, BA,* Matthew L. Springer, PhD,* S. Katharine Hammond, PhD,‡ Stanton A. Glantz, PhD, FACC,* William Grossman, MD, FACC,* John R. Balmes, MD,*† Yerem Yeghiazarians, MD, FACC*

San Francisco and Berkeley, California
30 min SHS exposure impairs FMD
376 ± 43 µg/m³ RSP, constant sidestream smoke

Heiss et al., 2008
Bars = SEM
FMD measured in rat hindlimb using micro-ultrasound
1 minute of secondhand smoke (tobacco) exposure was enough to impair vascular endothelial function

n=8 for all groups

*P<.01 impairment vs. mean of pre-exposure and recovery

Pinnamaneni et al., 2014, Nicotine Tob. Res. 16:584-590
It’s not enough simply to minimize public exposure to secondhand smoke; it’s important to prevent exposure...
Impairment of Endothelial Function by Little Cigar Secondhand Smoke

Jiangtao Liu, MD
Xiaoyin Wang, MD
Shilpa Narayan, BS
Stanton A. Glantz, PhD
Suzaynn F. Schick, PhD
Matthew L. Springer, PhD

*Tobacco Regulatory Science. 2016;2(1):56-63*
“Smokewar” by Rui Zheng, 2013
(the daughter of Xiaoyin Wang in my lab)
Problem: General public avoids tobacco SHS but many think marijuana SHS is ok

“No one said it ISN’T ok”

“Theresa’s no nicotine”

“It’s natural”

“It’s medicinal”
Table 4. Various Analytes Including Tobacco-Specific Compounds and Their Meta-Derivatives Determined in Dried Tobacco Smoke from Tobacco and Marijuana under Two Smoking Conditions

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Tobacco</th>
<th>Marijuana</th>
</tr>
</thead>
<tbody>
<tr>
<td>tar (mg/g)</td>
<td>24.1 ± 1.8</td>
<td>97.5 ± 1.6</td>
</tr>
<tr>
<td>nicotine</td>
<td>6.7 ± 0.26</td>
<td>6.05 ± 0.018</td>
</tr>
<tr>
<td>NO</td>
<td>110.1 ± 4.7</td>
<td>1191.2 ± 5.5</td>
</tr>
<tr>
<td>NNO</td>
<td>1172.4 ± 4</td>
<td>1284.2 ± 2.9</td>
</tr>
<tr>
<td>CO</td>
<td>715.2 ± 2.1</td>
<td>715.2 ± 2.1</td>
</tr>
<tr>
<td>CO2</td>
<td>616.2 ± 0.17</td>
<td>616.2 ± 0.17</td>
</tr>
<tr>
<td>CO2</td>
<td>5136.1 ± 72</td>
<td>5136.1 ± 72</td>
</tr>
<tr>
<td>HCN</td>
<td>24.8 ± 0.2</td>
<td>24.8 ± 0.2</td>
</tr>
<tr>
<td>NNN</td>
<td>1.4 ± 0.1</td>
<td>1.4 ± 0.1</td>
</tr>
<tr>
<td>NNK</td>
<td>1.2 ± 0.1</td>
<td>1.2 ± 0.1</td>
</tr>
<tr>
<td>NO2</td>
<td>1.2 ± 0.1</td>
<td>1.2 ± 0.1</td>
</tr>
<tr>
<td>O3</td>
<td>1.2 ± 0.1</td>
<td>1.2 ± 0.1</td>
</tr>
<tr>
<td>CO2</td>
<td>1.2 ± 0.1</td>
<td>1.2 ± 0.1</td>
</tr>
<tr>
<td>CO2</td>
<td>1.2 ± 0.1</td>
<td>1.2 ± 0.1</td>
</tr>
<tr>
<td>CO2</td>
<td>1.2 ± 0.1</td>
<td>1.2 ± 0.1</td>
</tr>
</tbody>
</table>

Table 5. Miscellaneous Organics Determined in Mainstream and Sidestream Tobacco Smoke from Tobacco and Marijuana under Two Smoking Conditions

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Tobacco</th>
<th>Marijuana</th>
</tr>
</thead>
<tbody>
<tr>
<td>formaldehyde</td>
<td>200.2 ± 28</td>
<td>25.1 ± 2.7</td>
</tr>
<tr>
<td>nitril</td>
<td>157.2 ± 45</td>
<td>157.2 ± 45</td>
</tr>
<tr>
<td>nitril</td>
<td>82.6 ± 22</td>
<td>82.6 ± 22</td>
</tr>
<tr>
<td>nitril</td>
<td>220.2 ± 42</td>
<td>220.2 ± 42</td>
</tr>
<tr>
<td>nitril</td>
<td>403.7 ± 10</td>
<td>403.7 ± 10</td>
</tr>
<tr>
<td>nitril</td>
<td>360.2 ± 30</td>
<td>360.2 ± 30</td>
</tr>
<tr>
<td>nitril</td>
<td>157.2 ± 45</td>
<td>157.2 ± 45</td>
</tr>
<tr>
<td>nitril</td>
<td>220.2 ± 42</td>
<td>220.2 ± 42</td>
</tr>
<tr>
<td>nitril</td>
<td>403.7 ± 10</td>
<td>403.7 ± 10</td>
</tr>
</tbody>
</table>

Table 6. Aromatic Amines Determined in Mainstream Tobacco Smoke and Marijuana under Two Smoking Conditions

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Tobacco</th>
<th>Marijuana</th>
</tr>
</thead>
<tbody>
<tr>
<td>naphthalene</td>
<td>2097.0 ± 159</td>
<td>2097.0 ± 159</td>
</tr>
<tr>
<td>naphthalene</td>
<td>2097.0 ± 159</td>
<td>2097.0 ± 159</td>
</tr>
<tr>
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</tr>
<tr>
<td>naphthalene</td>
<td>2097.0 ± 159</td>
<td>2097.0 ± 159</td>
</tr>
</tbody>
</table>

Table 7. Selected Carbonyl Compounds Determined in Mainstream and Sidestream Tobacco Smoke from Tobacco and Marijuana under Two Smoking Conditions

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Mainstream</th>
<th>Sidestream</th>
</tr>
</thead>
<tbody>
<tr>
<td>formaldehyde</td>
<td>200.2 ± 28</td>
<td>25.1 ± 2.7</td>
</tr>
<tr>
<td>nitril</td>
<td>157.2 ± 45</td>
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</tr>
<tr>
<td>nitril</td>
<td>403.7 ± 10</td>
<td>403.7 ± 10</td>
</tr>
</tbody>
</table>

Table 8. PAPS and Aza-arenes Determined in Mainstream Tobacco Smoke and Marijuana under Two Smoking Conditions

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Tobacco</th>
<th>Marijuana</th>
</tr>
</thead>
<tbody>
<tr>
<td>pyrene</td>
<td>8.8 ± 0.3</td>
<td>45.6 ± 4.4</td>
</tr>
<tr>
<td>pyrene</td>
<td>8.8 ± 0.3</td>
<td>45.6 ± 4.4</td>
</tr>
<tr>
<td>pyrene</td>
<td>8.8 ± 0.3</td>
<td>45.6 ± 4.4</td>
</tr>
<tr>
<td>pyrene</td>
<td>8.8 ± 0.3</td>
<td>45.6 ± 4.4</td>
</tr>
<tr>
<td>pyrene</td>
<td>8.8 ± 0.3</td>
<td>45.6 ± 4.4</td>
</tr>
</tbody>
</table>

Table 9. PAHs and Aza-arenes Determined in Mainstream Tobacco Smoke from Tobacco and Marijuana under Two Smoking Conditions

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Tobacco</th>
<th>Marijuana</th>
</tr>
</thead>
<tbody>
<tr>
<td>bBN</td>
<td>346.9 ± 22.2</td>
<td>346.9 ± 22.2</td>
</tr>
<tr>
<td>bBN</td>
<td>346.9 ± 22.2</td>
<td>346.9 ± 22.2</td>
</tr>
<tr>
<td>bBN</td>
<td>346.9 ± 22.2</td>
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<td>346.9 ± 22.2</td>
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</tr>
<tr>
<td>bBN</td>
<td>346.9 ± 22.2</td>
<td>346.9 ± 22.2</td>
</tr>
</tbody>
</table>

Table 10. PAHs and Aza-arenes Determined in Mainstream Tobacco Smoke and Marijuana under Two Smoking Conditions

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Tobacco</th>
<th>Marijuana</th>
</tr>
</thead>
<tbody>
<tr>
<td>benz(a)anthracene</td>
<td>564.1 ± 48</td>
<td>564.1 ± 48</td>
</tr>
<tr>
<td>benz(a)anthracene</td>
<td>564.1 ± 48</td>
<td>564.1 ± 48</td>
</tr>
<tr>
<td>benz(a)anthracene</td>
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</tr>
<tr>
<td>benz(a)anthracene</td>
<td>564.1 ± 48</td>
<td>564.1 ± 48</td>
</tr>
</tbody>
</table>

Values are provided ± standard deviations; n = 7. Units are ng/g. **P < 0.05 vs. tobacco. Values shown with "=" were below the limit of detection; values shown as a range were above the limit of detection but below the quantification limit.
Dried plant smoke: similar chemicals in varied proportions

Sample comparisons of components of tobacco and marijuana secondhand smoke

From Moir et al., 2008. Subset of 65 components analyzed under standard tobacco smoking conditions

Inhaling a whole chemistry lab...
2. Business Activity/Schedules

Your business activity is: RESEARCHER (I)

Please make any requested changes to your registered schedules below, and select Next to continue.

DRUG SCHEDULES [see schedules]

Select all that apply

☐ Schedule

Is the researcher human? ○ Both ○ Human Only ○ Non-Human Only

☐ Check here if you require order forms to only purchase Schedule I and II from suppliers.

Fields with a (*) are required.

[Previous] [Next]
Marijuana SHS for 30 minutes impaired FMD (American Heart Association, Chicago, Nov. 2014)

Low dose

High dose

THC-free

Chamber air

low dose = ~200 µg/m³ particles;
high dose = ~670 µg/m³ particles
(starting concentrations)
Marijuana SHS for 1 minute lowered FMD

"30 minutes is kind of long, how about shorter times?"

59% drop in FMD
“Could the impairment in FMD be caused by smoke from the burning paper, rather than tobacco and marijuana?”

SHS from marijuana without paper still impairs FMD
“They totally smoke out the rats”

The smoke was invisible in the exposure chamber
Marijuana SHS for 1 minute lowered FMD for at least 90 minutes

“How long does it take for FMD to recover?”

1 minute exposure (THC-free)
"How do marijuana and tobacco compare in impairment of FMD?"

Impairment from one minute of marijuana SHS persists longer than impairment from tobacco SHS.
Summary of marijuana results
Wang et al., 2016, J Am Heart Assoc 5:e003858

Marijuana SHS for one minute substantially impairs vascular endothelial function in rats.

Neither THC nor paper smoke are required for marijuana SHS to impair vascular function.

...nicotine is not required for impairment of vascular function by smoke.

One minute of marijuana SHS exposure impairs vascular function for at least 90 minutes, longer than impairment from tobacco SHS.
commentary by AHA past president, Ralph Sacco, MD, FAHA
Presented at the Pediatric Academic Societies 2016 Meeting (Dr. Karen Wilson):

One in six infants and toddlers admitted to a Colorado hospital with coughing, wheezing and other symptoms of bronchiolitis tested positive for marijuana exposure.
Regulators and lawmakers

How do we protect our kids? [more]

Steering Committee

Gavin Newsom
Lieutenant Governor of California

Who We Are

The Blue Ribbon Commission on Marijuana Policy was formed in light of the likelihood that a marijuana legalization initiative will be placed on the ballot of the State of California in the fall of 2016. The Commission is comprised of leading policymakers, public health experts and policy challenges and offer possible solutions.
Regulators and lawmakers

**Toronto Star 11/25/15:**

Using medical marijuana now OK in public places in Ontario under new regulations

The exemption includes everything from movie theatres to restaurants, offices, stadiums, playgrounds full of children and more.

**Toronto Star 11/26/15:**

Ontario government taking medical marijuana plan back to the drawing board

Associate Health Minister Dipika Damerla quickly reversed course Thursday over concerns about exposure to second-hand cannabis smoke in restaurants, theatres, offices and other public spaces where tobacco smoking is banned.
California State Assembly bill AB 2300 (Jim Woods)

Clarifies that landlords can prohibit smoking of marijuana even with medicinal ID card in properties where tobacco smoking is banned

- Our 2014 report cited as a major reason for the bill
- Passed State Assembly Judiciary Committee 10-0
- Passed State Assembly 77-0 (3 non-votes)
- Died in State Senate Judiciary Committee
City Council tweaks proposal for smoking restrictions at apartments

Medical marijuana smoking, with doctor's note, would be allowed only in designated area at complexes

by Jeremy Walsh / Pleasanton Weekly

The Pleasanton City Council took another step Tuesday toward establishing new stringent...
The Pleasanton City Council took another step Tuesday toward establishing new stringent smoking regulations for rental apartment complexes across the city.

Reviewing a proposed ordinance they gave initial support to two months ago, council members left most of the original proposal intact -- including the ban on tobacco smoking in apartment units and common areas -- but they adjusted course to limit medical marijuana smoking at complexes only to designated outdoor smoking areas.

Vice Mayor Jerry Pentin said he supported that option for medical marijuana smoking "so we're not banning it entirely but we're still keeping it away from people who are inside their own rental units and dealing with secondhand smoke."
Regulators and lawmakers

City staff's recommendation was to allow medical marijuana smoking inside apartment units "if tenant provides landlord written documentation that tenant needs it for medical purposes, no alternative means of delivery or ingestion are available and tenant is unable to smoke outside," assistant city attorney Larissa Seto said.

The council's follow-up discussion Tuesday focused on how to reduce the effects of secondhand smoke on neighbors living in close quarters in apartments while accommodating residents who rely on marijuana for legitimate medical reasons but can only smoke it -- and what about residents physically unable to leave their apartments…

Tamiko Johnson of the Alameda County Public Health Department also voiced support for prohibiting medical marijuana smoking indoors.
"There's no safe level of secondhand smoke exposure," Johnson told the council. "From experience with other cities, gaining compliance with your smoke-free-housing law and having effective enforcement if you're allowing someone to smoke anything inside their apartment is going to be incredibly difficult for you all."

"I don't have problems with people smoking medical marijuana. I have problems with people who smoke it and then the person next door has to suffer from the secondhand smoke," Pentin said.

"When people take medication, it normally doesn't affect anybody else. And in this case, it does affect other people," Mayor Jerry Thorne added. "I just kind of wonder where you draw the line here. It's kind of darned if you do, darned if you don't."
Smoking marijuana is typically thought of as not that bad, especially compared to the hazards of drinking. But is secondhand smoke from marijuana more dangerous than people think? Or does it damage your lungs, heart, and blood vessels in the same ways as cigarette smoke? Find out with John and Sandra!

What do you think of this study? Will it deter you from smoking marijuana, or spending time around those who do? Let us know in the comments!
How Dangerous Is Secondhand Marijuana Smoke?

December 2, 2014 by Aaron Wysocki — Leave a Comment

Smoking marijuana is typically thought of as not that bad, especially compared to the hazards of drinking. But is secondhand smoke from marijuana more dangerous than people think? Or does it damage your lungs, heart, and blood vessels in the same ways as cigarette smoke? Find out with John and Sandra!

What do you think of this study? Will it deter you from smoking marijuana, or spending time around those who do? Let us know in the comments!
Acute and long-term cardiovascular risk is unclear

Risk of MI goes up ~5-fold in the hour after marijuana use (Mittleman, 2001)

No clear correlation between long-term marijuana use and cardiovascular disease later in life (e.g., CARDIA study)

…but, 3-fold increase in risk of death from hypertension reported for marijuana users relative to non-users (Yankey, 2017)
Do Researchers Have the Right Marijuana?

by JEANINE BARONE | OCTOBER 25, 2016

Matt Springer, PhD, is a Professor of Medicine at the University of California, San Francisco, who studies the effects of secondhand marijuana smoke. He spoke with us about the implications of the recent announcement by the federal Drug Enforcement Administration that it will lift restrictions on the growing of marijuana to supply researchers.

How will the DEA’s announcement affect your research?

Not as much as you might think. I still will not be able to study what I’d like to. I’d like to study real-world cannabis used by real people. UCSF used real-world cigarettes, not research-reference cigarettes, for tobacco studies in the past. But that was a very different world.
Health Effects of Cannabis and Cannabinoids

Current State of Evidence and Recommendations for Research

This report will be available to download as a free pdf: Nationalacademies.org/CannabisHealthEffects
Cardiometabolic Risk

- The evidence is unclear as to whether and how cannabis use is associated with heart attack, stroke, and diabetes.
Policy Goals:

Public exposure to secondhand smoke should be avoided whether the source is tobacco or marijuana.
Policy Goals:

Change the perception and the dialogue
Policy Goals:
Change the perception and the dialogue

“There’s tar and chemicals”
“It’s gross!”
“It’s bad for you”
“No one said ‘It ISN’T ok’”
If the FMD impairment by marijuana smoke is caused by the dried plant material combustion smoke, rather than the THC...
Smoking marijuana is typically thought of as not that bad, especially compared to the hazards of drinking. But is secondhand smoke from marijuana more dangerous than people think? Or does it damage your lungs, heart, and blood vessels in the same ways as cigarette smoke? Find out with John and Sandra!

What do you think of this study? Will it deter you from smoking marijuana, or spending time around those who do? Let us know in the comments!
A DIRECT CANCER CONNECTION!!!