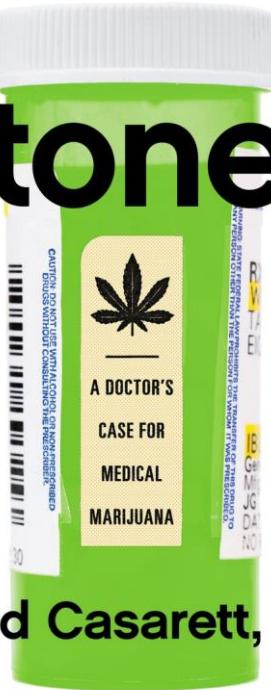


Stoned



David Casarett, M.D.

David Casarett MD MA
Professor of Medicine
Chief of Palliative Care
Duke University



Conflicts of interest

- SAB: Curio Wellness, Gram Research
- Senior advisor: Silver Swan Capital
- Principal: Medicinal Management
- No consulting or speaking for the pharmaceutical industry



David Casarett by Nathan Gelgud, 2015.

Views do not reflect the opinions
of Duke University or Duke Health



Marijuana: Medication or weed?



I wrote Stoned for Judith...



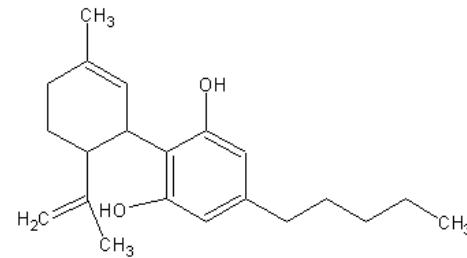
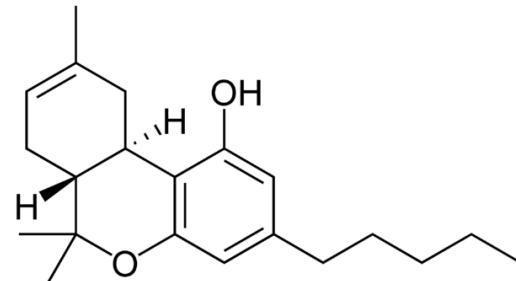
3 Surprises

- There's a science of how cannabis works
- Cannabis has real potential benefits (and risks)
- There's a wide gap between enthusiasm for medical cannabis and the evidence supporting it



Surprise #1: There's a science of how cannabis works

- Tetrahydrocannabinol (THC)
- Cannabidiol (CBD)
- (And many other cannabinoids)



Ms. Sativa: Up close and personal



BENJAMIN RABINOWITZ FOR GQ



Cannabis sativa/indica: what's the difference?



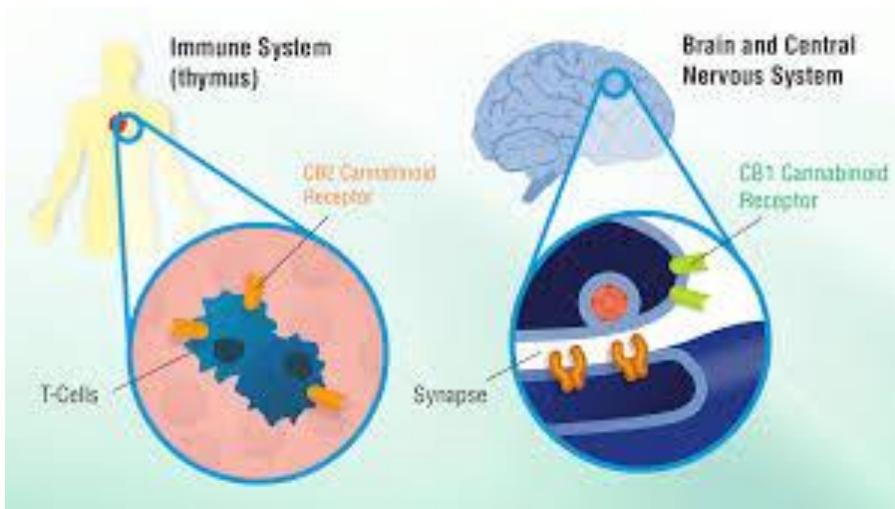
Sativa strains: Often higher THC concentrations

Indica strains: Generally lower THC and higher CBD

BUT: Species don't really predict THC/CBD levels



The science of cannabinoid receptors



THC: CB1 and CB2 receptors, mostly in the brain, plus reproductive system

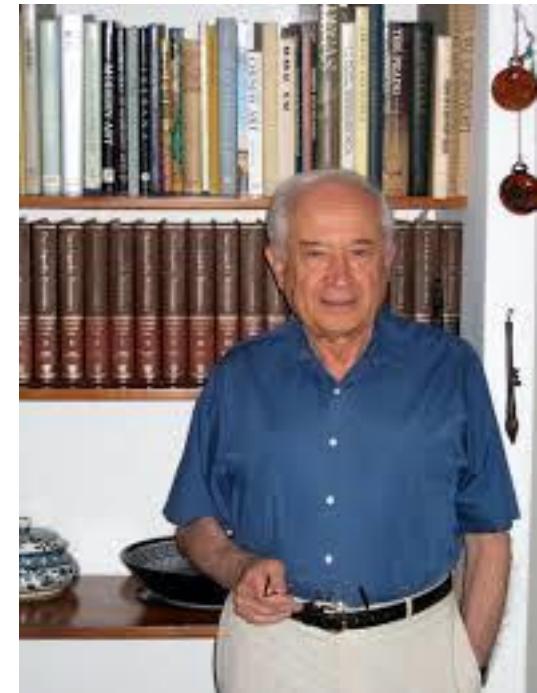
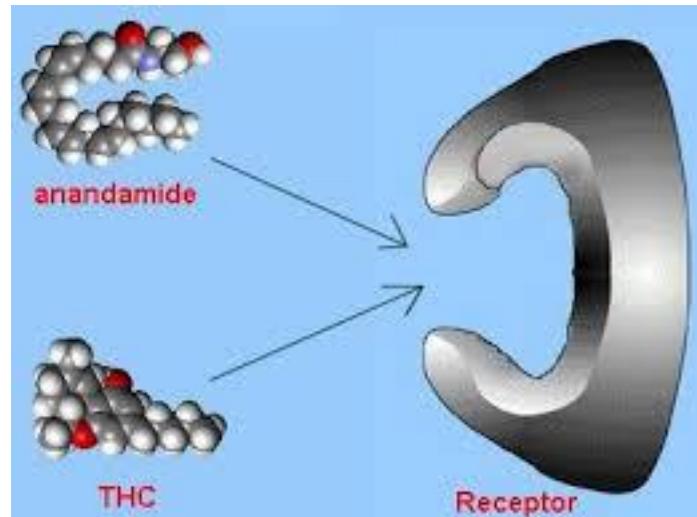
CBD: Other receptors, mostly in the immune system, plus microglial cells in the brain

Other cannabinoids...
Other receptors...



Cannabis is nature's way of hacking the endocannabinoid system

- Anandamide, the “Bliss Molecule”
- 2-AG
- Many more



Surprise #1B

There's a science of how to use marijuana



Absorption and metabolism

- Concentration (THC)
 - flower=2-10%
 - hash>30%
 - shatter>80%
- Bioavailability
 - PO=10-20%; Inhaled=30-50%
 - BUT: Wide (10-fold) inter-individual variability (inhaled)



Advantage of smoking: fast uptake

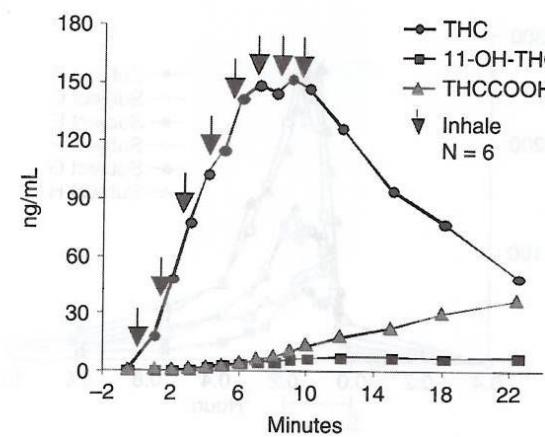


Figure 13-1 Mean Δ^9 -tetrahydrocannabinol (THC), 11-hydroxy-THC (11-OH-THC), and 11-nor-9-carboxy-THC (THCCOOH) concentrations during smoking of a 3.55% THC cigarette. Each arrow indicates a single puff on the cannabis cigarette, demonstrating the rapid increase in THC concentrations. Note that concentrations peak before the end of smoking.



William O'Shaughnessy, goats, and tinctures



Edibles



The science of edibles

- Cannabinoids are soluble in alcohol and lipids:
- Alcohol-based (infused grain EtOH)
- Lipid-based (Brownies)



The future of cannabis delivery systems?



Surprise #2: Cannabis does have real medical benefits (and risks)



“The best medicine the drug companies don’t want you to know about.”

-Dispensary owner in San Diego



Potential uses in state laws:

- Nausea
- Chronic pain
- Anxiety
- PTSD
- Anorexia/weight loss
- Insomnia
- Pediatric epilepsy
- And many more...



How much evidence is there of medical benefit?

Original Investigation

Cannabinoids for Medical Use A Systematic Review and Meta-analysis

Penny E. Whiting, PhD; Robert F. Wolff, MD; Sohan Deshpande, MSc; Marcello Di Nisio, PhD; Steven Duffy, PgD; Adrian V. Hernandez, MD, PhD; J. Christiaan Kuertenjes, MD, PhD; Shona Lang, PhD; Kaiti Misso, MSc; Steve Ryder, MSc; Simona Schmidkofler, MSc; Marie Westwood, PhD; Jos Kleijnen, MD, PhD



Answer: Not as much as we'd like

- Moderate evidence:
 - Neuropathic pain
 - Spasticity
- Weak evidence:
 - Nausea
 - Weight gain in the setting of chronic, serious illness (AIDS, cancer)
 - Sleep



Neuropathic pain

- Good RCT data*
- Evidence of effectiveness as adjuvant to opioids (Abrams, 2011, Clin Pharm Ther)



*Abrams, Neurology, 2007; Lynch, Br J Clin Pharm, 2011 (Systematic review); Wilsey, J Pain, 2008)





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 ELSEVIER

The Journal of Pain, Vol 14, No 2 (February), 2013: pp 136-148
Available online at www.jpain.org and www.sciencedirect.com

Low-Dose Vaporized Cannabis Significantly Improves Neuropathic Pain

Barth Wilsey,* Thomas Marcotte,[†] Reena Deutsch,[†] Ben Gouaux,[†] Staci Sakai,[‡] and Haylee Donaghe[‡]



Low-Dose Vaporized Cannabis Significantly Improves Neuropathic Pain

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- Strengths

- RCT
- Placebo control
- Blinded
- Low- and high-dose groups to examine dose effects

- Weaknesses

- 39 subjects
- Imperfect blinding

❖ Imperfect blinding and small size made this a “low quality” study



Blinding: The Achilles heel of medical cannabis research

Neuropsychopharmacology (2009) **34**, 672–680; doi:10.1038/npp.2008.120; published online 6 August 2008

Smoked Medicinal Cannabis for Neuropathic Pain in HIV: A Randomized, Crossover Clinical Trial

Ronald J Ellis¹, Will Toperoff¹, Florin Vaida², Geoffrey van den Brande³,
James Gonzales⁴, Ben Gouaux⁵, Heather Bentley⁵ and J Hampton Atkinson⁵



- Among patients assigned first to “active” marijuana, 14/15 (93%) guessed correctly



[Cannabis doesn't cure cancer]



“Risks? Marijuana doesn’t have any risks—it’s a flower. Not like morphine.”

-Dispensary owner in Denver



Risks?

Known risks

- Driving impairment****
- Addiction****
- Hyperemesis syndrome****



Possible risks

- Myocardial infarction**
- Stroke*
- Schizophrenia*
- Psychotic episodes****
- Long-term cognitive dysfunction**
- NOT: Cancer, lung disease



(Pulmonary risks)

- Very minor PFT changes
 - Increased FVC
 - Decreased FEV1 and FEV1/FVC for very heavy users
 - No cancer risk
- (Tashkin, Annals ATS, 2013)



Weed and wheels

- Slow reaction times
- Distraction
- Lack of focus
- Poor salience detection
- Field sobriety test not helpful



Contaminants



“Other”

- Infertility
- Gynecomastia
- Recurrent herpes
- Koro
- Pneumothorax
- Etc



Risks

- A few risks are known
- Many are speculative
- Everyone has an axe to grind
- Case reports are common and can be misleading



So...Medication or weed?

- Significant benefits
- Real risks



“What is a weed? A plant whose virtues have never been discovered.”

-Ralph Waldo Emerson



The medical marijuana enthusiasm-evidence gap



How much evidence of benefit and safety is enough?

For patients and physicians:

- One or two small studies
- Ideally a controlled trial
- Anecdote

For researchers and policymakers:

- Multiple large controlled trials
- Placebo controls
- Rigorous blinding
- Large-scale safety studies



What I Learned at the Weed Dispensary

By DAVID CASARETT JULY 28, 2015

If enthusiasm for medical marijuana has outstripped the evidence supporting its use, that's often because people are dissatisfied with the medical care they're receiving.



Thanks

- Zach Klein, Heather Despres,
Nathan Pollack, Bob Melamede,
John Morley, Orrin Devinsky,
Donald Tashkin, Barth Wilsey,
Jonathan Gavrin, Steve Lankenau,
Teri Franklin, Marina Goldman,
Christine Rabinak, Donald Abrams,
Raphael Mechoulam, Clint Werner,
Larry Gidaley...and Sasha the
Wonder Dog

