MARIJUANA TOXICOLOGY

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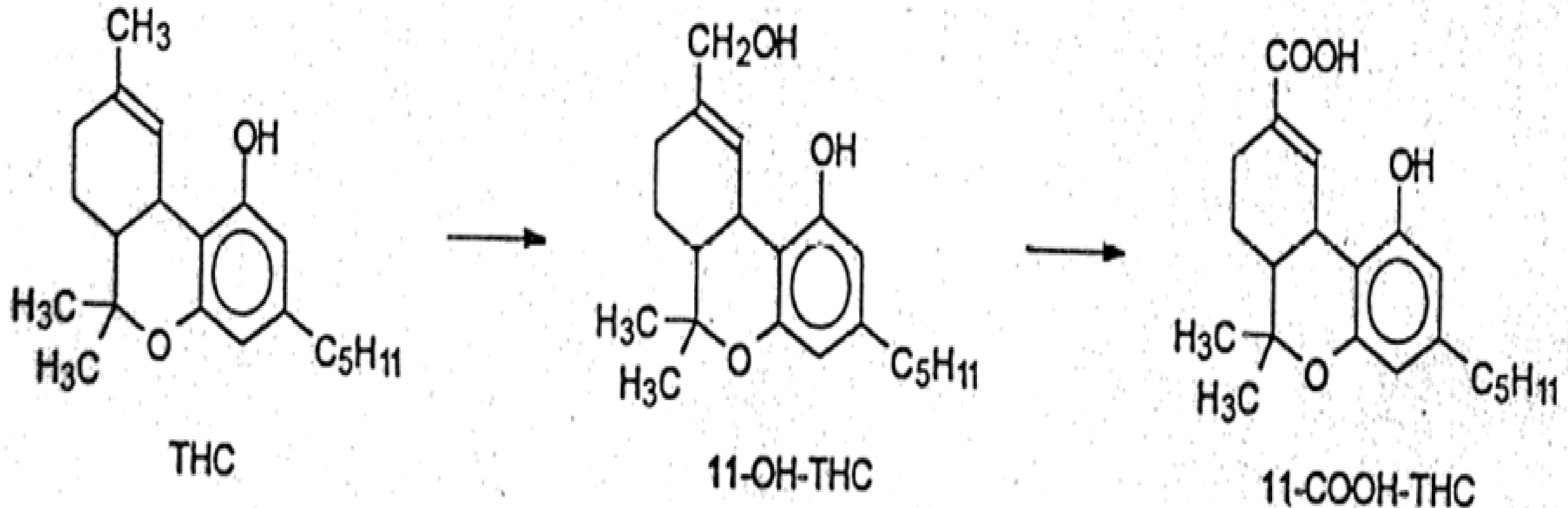
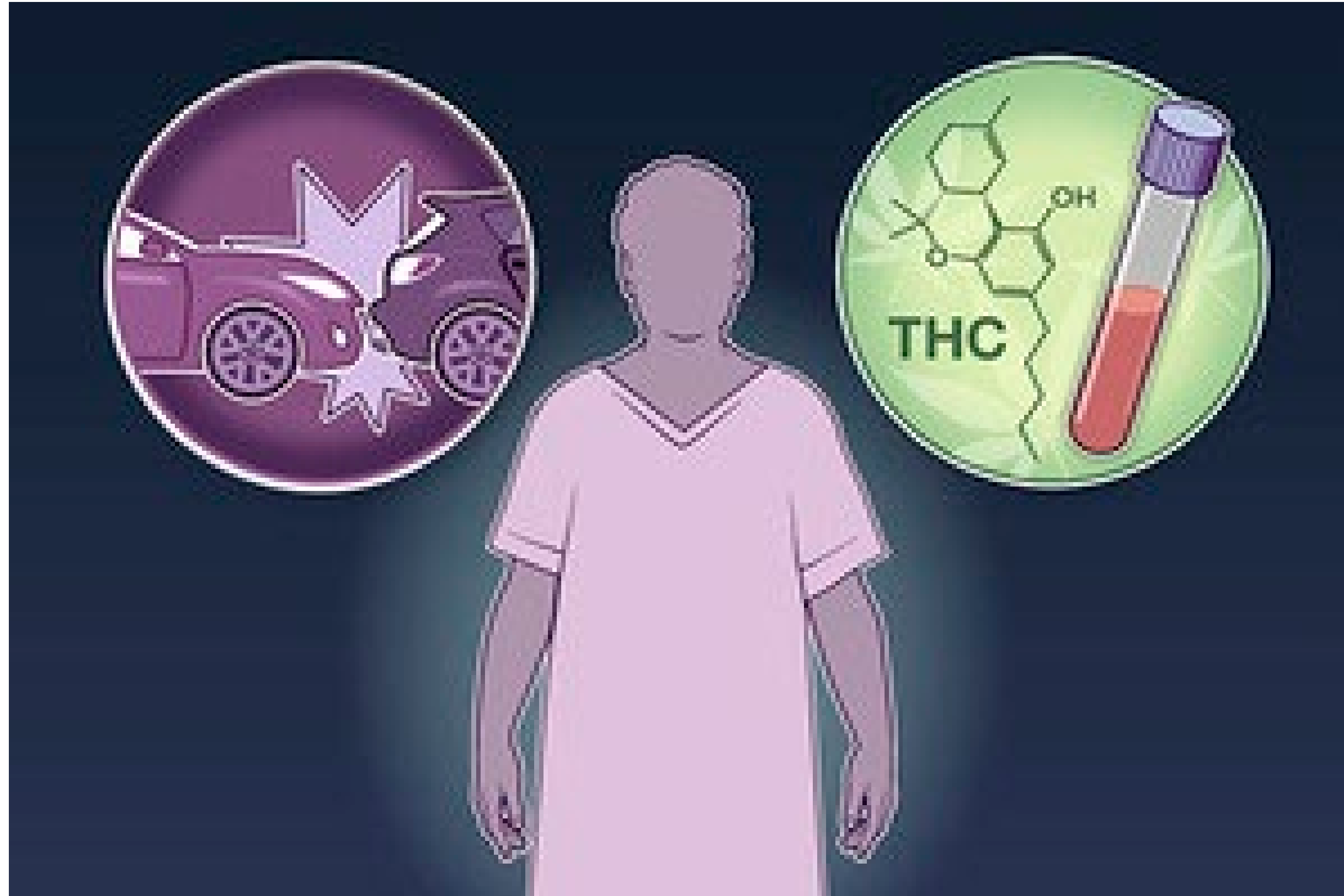
OBJECTIVES – MARIJUANA TOXICOLOGY

- PHARMACOLOGY
- PHARMACOKINETICS
- TOXICOLOGY
- TESTING
- USES MEDICAL AND RECREATIONAL
- EFFECTS
- CASES
- DRE

METABOLISM OF MARIJUANA



MARIJUANA (THC) and DRIVING
N Engl J Med 2022; 386:148-156 01/13/22



NEJM Legalization increases use and auto injuries

- After cannabis legalization, the prevalence of moderately injured drivers with a THC level of at least 2 ng per milliliter in participating British Columbia trauma centers more than doubled. The increase was largest among older drivers and male drivers.
- (same experience in Colorado)

Pa Med Marijuana Law 210 PL Safety Warning required of dispensary

- Pregnancy
- breast feeding
- MIGHT impair the ability to drive or operate heavy machinery
- Keep out of reach of children (deaths)

- MD, RPh, PA, NP on site or video certify clinical conditions met
- (better than 'pot-heads')

3802: DUI ETOH OR Controlled Substance (THC)

- ANY AMOUNT OF CS (THC) OR METABOLITE THEREOF
- UNDER INFLUENCE TO A DEGREE WHICH IMPAIRS ABILITY TO DRIVE SAFELY
- 2-HOUR RULE // EXCEPTIONS
- 10 ng/mL Delta THC (active ingredient)

Who is using marijuana now?
JAMA Int Med Feb 2020

- Teens – increasing; 4% vape THC daily; 35% HS SRS USED/2019
- Young adults 5 – 7% (Colorado highest) (12 MILLION/2018)
- Pregnant Women (20% positive UDS) (JAMA – California) (50% denied use - + UDS)
- 65+ 4.2% (7 x increase since 2006)

- (USE IN TEENS AND YOUNG ADULTS LESS NOW THAN 1974 – G&G)

Marijuana arrests are up!

- An estimated 700,993 arrests were made nationwide for marijuana-related offenses in 2014 — up from 693,058 in 2013 — of which 88.42% were for possession. On average, one person was arrested for a marijuana-related offense in the U.S. approximately every 45 seconds (every 51 seconds for possession).
- Substantial decreases with de-criminalization and legalization (medical and/or recreational)

MARIJUANA ADVERSE EFFECTS RELEVANT TO DRIVING IMPAIRMENT - NHTSA

- ability to concentrate and maintain attention are decreased during marijuana use
- impairment of hand-eye coordination is dose-related over a wide range of dosages.
- Impairment in retention time and tracking, subjective sleepiness,
- distortion of time and distance, vigilance, and loss of coordination in divided
- attention tasks have been reported.
    - (Syllabus)

Sewell RA et al. Effect of THC Compared with Alcohol on Driving. *Am J Addict* 2009:18(3)

- Detrimental effects of THC vary in a dose-related fashion, and are more pronounced with highly automatic driving functions than with more complex tasks that require conscious control, whereas with alcohol produces an opposite pattern of impairment. Because of this and an increased awareness that they are impaired, THC smokers tend to compensate effectively while driving. (abstract in Syllabus)

INSTITUTE OF MEDICINE

- acknowledges potential benefits of marijuana use
  - stimulating appetite, particularly in patients with AIDS and the related wasting syndrome
  - combating chemotherapy-induced nausea and vomiting
  - alleviating severe pain
  - ameliorating some forms of spasticity.

Approved medical conditions – just about anything that hurts!(or can make you feel better)

- Cancer, HIV, ALS, Parkinson, MS, Spinal Cord, Crohns,, Seizures, Glaucoma, Sickle Cell
- Chronic/intractable neuropathic pain
- PTSD
- 2021 addition – Autism

- MEDICAL / SURGICAL COMMUNITY
- DECREASE OPIATE USE FOR PAIN

(Syllabus)

ACUTE EFFECTS OF MARIJUANA NHTSA

- relaxation,
- euphoria,
- relaxed inhibitions,
- Disorientation
- altered time and space/perception lack of concentration impaired learning and memory
- alterations in thought formation and expression
- drowsiness sedation mood changes and paranoia.
- (Syllabus – NHTSA Drug Fact Sheet – THC)

SAFETY – A POLISHED WORD FOR TOXICITY!

- SHORT TERM
  - MEMORY PERCEPTION
  - MOTOR IMPAIRMENTS, DRIVING SKILLS, INJURIES
  - JUDGMENT, RISK TAKING
  - PARANOIA AND PSYCHOSIS – DOSE AND PREDISPOSITION (HIGHER WITH ORAL)
  - CARDIAC TOXICITY – MI, HYPERTENSION
  - ANXIETY, PANIC

SAFETY

- LONG TERM USE
  - DEPENDENCE / ADDICTION > WITHDRAWAL(irritability, sleeping difficulties, dysphoria, craving, and anxiety)

  - ALTERED BRAIN DEVELOPMENT - ADOLESCENTS
  - POOR EDUCATIONAL OUTCOME
  - COGNITIVE IMPAIRMENT – LOWER IQ
  - CHRONIC BRONCHITIS (SMOKERS)
  - LUNG CANCER (?)
  - CHRONIC PSYCHOSIS – PREDISPOSITION
  - (Syllabus : HealthCare Challenges)

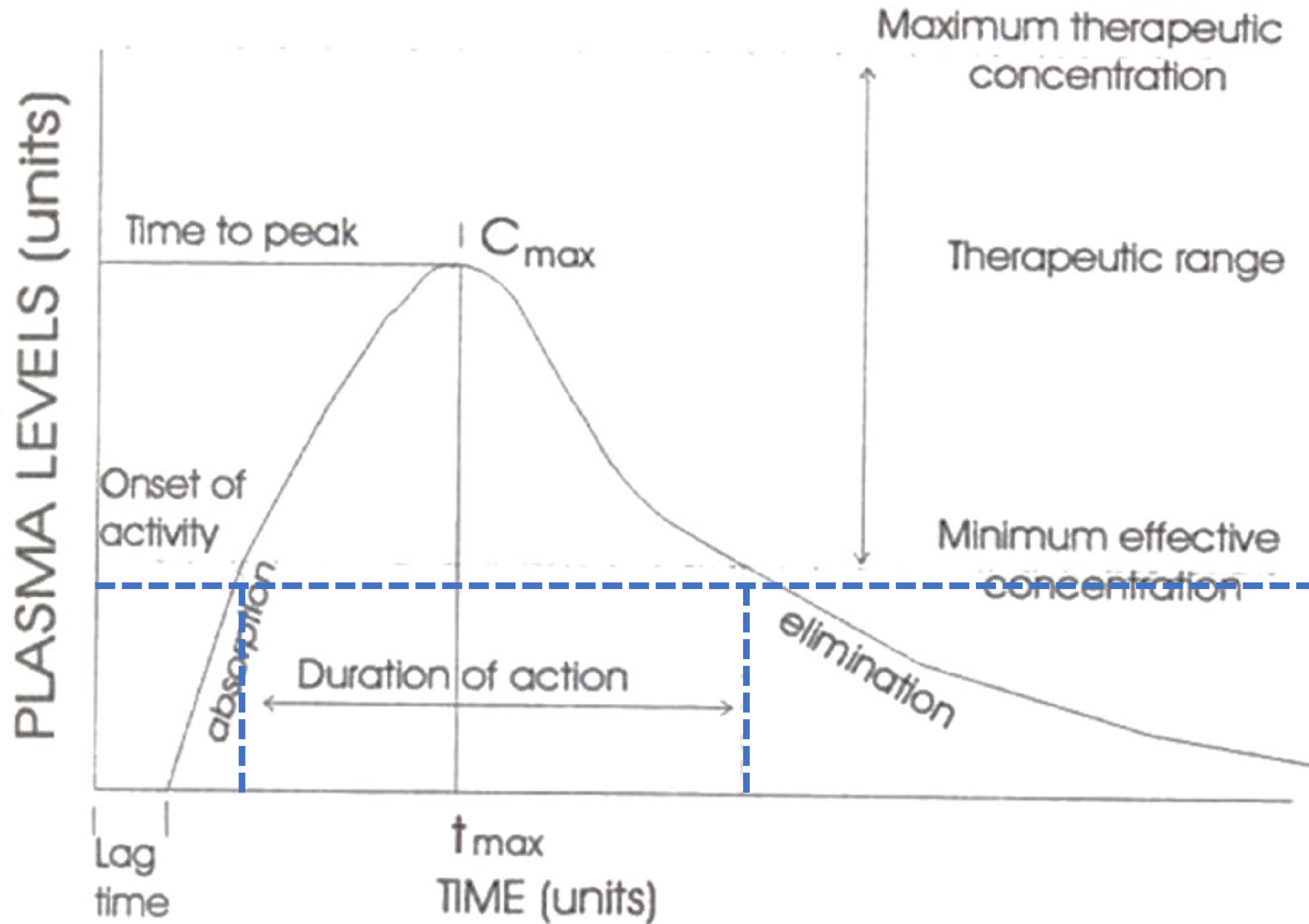
THC NHTSA DEC CRITERIA

- Horizontal gaze nystagmus not present; vertical gaze nystagmus not present;
- lack of convergence present;
- pupil size normal to dilated;
- reaction to light normal to slow;
- pulse rate elevated; blood pressure elevated;
- Body temperature normal to elevated.

PHARMACOKINETICS - TIMING

- A division of the science of pharmacology involving the absorption, distribution, metabolism, and excretion of a drug.
  - A D M E

Terms to Know



ROUTES OF ADMINISTRATION

- SMOKING / PYROLYSIS
- VAPORIZATION
- SUBLINGUAL / BUCCAL UNDER TONGUE/CHEEK
- EDIBLE – ORAL BAKED, CANDY, LIQUIDS

- ROUTE DETERMINES THE ONSET, AND PEAK OF DRUG ACTIONS. INHALED - THE DOSE IS TITRATED BY USER! (‘HIT’, ‘DEPTH’, ’HIGH’) . ROUTE ALSO DETERMINES METABOLISM (USUALLY ‘FIRST PASS EFFECT’). INCREASED PSYCHOACTIVE METABOLITE WITH ORAL

WHY GREATER PSYCH RISK ORAL

- NO TITRATION OF THE 'DOSE' (OD risk greater with oral – no titration)
- orally ingested THC - metabolism in the GUT & LIVER where there is a synthesis of a relatively significant amount of 11-OH-THC that can combine its psychoactive effects with those of THC to produce an additive psychotropic affect in the CNS.
- 11-OH-THC IS A PSYCHO-ACTIVE METABOLITE OF THC

Effect of Blood Collection Time on Measured Δ9-Tetrahydrocannabinol Concentrations: Implications for Driving Interpretation and Drug Policy – Hartmann et al. Clin. Chem 62:2 367-77 (2016)

- Residual blood THC concentrations' fluctuation in this study's participants after placebo cannabis was consistent with gradual extended THC release after chronic frequent smoking
- Serum THC concentrations previously showed poor correlation with magnitude of neurocognitive performance impairment.
- Individual variability around the THC concentration during driving, and the rate of decrease varies on the basis of an individual's intake frequency, metabolism, and elimination rate.

Huestis – foremost THC Scientist: NIDA/NIH

- 1. blood levels don't correlate with impairment // not predictive of time of use. Interpretation controversial
- 2. BAC 0.05 //THC 8.2ng/mL and 0.08 // 13.1 ng/ml lateral positions
- 3. Can't use retrograde extrapolation (Syllabus – expert report)
- 4. Epidemiology studies do not support a statistically significant increase in crash risk
- 5. Limited data exist evaluation THC impaired drivers by DRE
- 6. Eyelid and body tremors – no correlation b/w THC levels
- 7. HGN and VGN and Convergence not typically associated with THC

REAR END COLLISION VICTIM- THC BLOOD TESTS

1. There is insufficient evidence to state with reasonable certainty that EM was impaired and/or intoxicated at the time of the occurrence;
2. Determination of impairment and/or intoxication cannot be based on blood cannabinoids concentrations alone;
3. There is no competent evidence to demonstrate that EM used cannabis on Crash date;
4. Urine cannabinoids test results do not provide competent evidence of impairment and/or intoxication, only past use;
5. Impairment and/or intoxication cannot be reasonably concluded from EM's acts and/or inactions on Crash date;

CRIMINAL SEXUAL ASSAULT DEFENSE
VICTIM INTOXICATED BY THC

1. Ms. C. was severely intoxicated and impaired by marijuana at the time of the alleged sexual assault.
2. She reported visual and perceptual disturbances, consistent with hallucinations. She reported significant central nervous depression signs, consistent with marijuana intoxication.
3. She consumed marijuana as an edible; that is, she swallowed the marijuana in a cookie. The metabolism of marijuana consumed by mouth is quite different than when smoked; an abundance of a psycho-toxic active metabolite (11-OH-THC) is formed by the liver metabolism that it absent in smoking. Psychiatric toxicities are greater with edibles/oral than with smoking.

4. Adolescents, especially naïve users, are subject to greater psychiatric toxicity and effects of marijuana than adults.

5. Marijuana psycho-toxicity causes distorted perceptions of reality, makes memory formation difficult, and alters the thought and deliberation processes of the marijuana intoxicated person.

6. Ms. C. herself describes her symptoms and experiences which are textbook signs of marijuana intoxication. Given this well documented toxicity, based on her description of the effects, her memory and recollections of the events of the evening are highly suspect and subject to substantial doubt.

RECKLESS HOMICIDE//DECEDENTS STONED

- MARIJUANA INTOXICATION OPINION IN DECEDENT, BASED ON AUTOPSY TOXICOLOGY THC LEVELS >> 40NG/ML
- TESTIMONY ON IMPAIRMENT//CONTRIBUTORY TO CRASH
- TRUCK DRIVER FOUND NOT GUILTY
- (REPORT IN SYLLABUS)

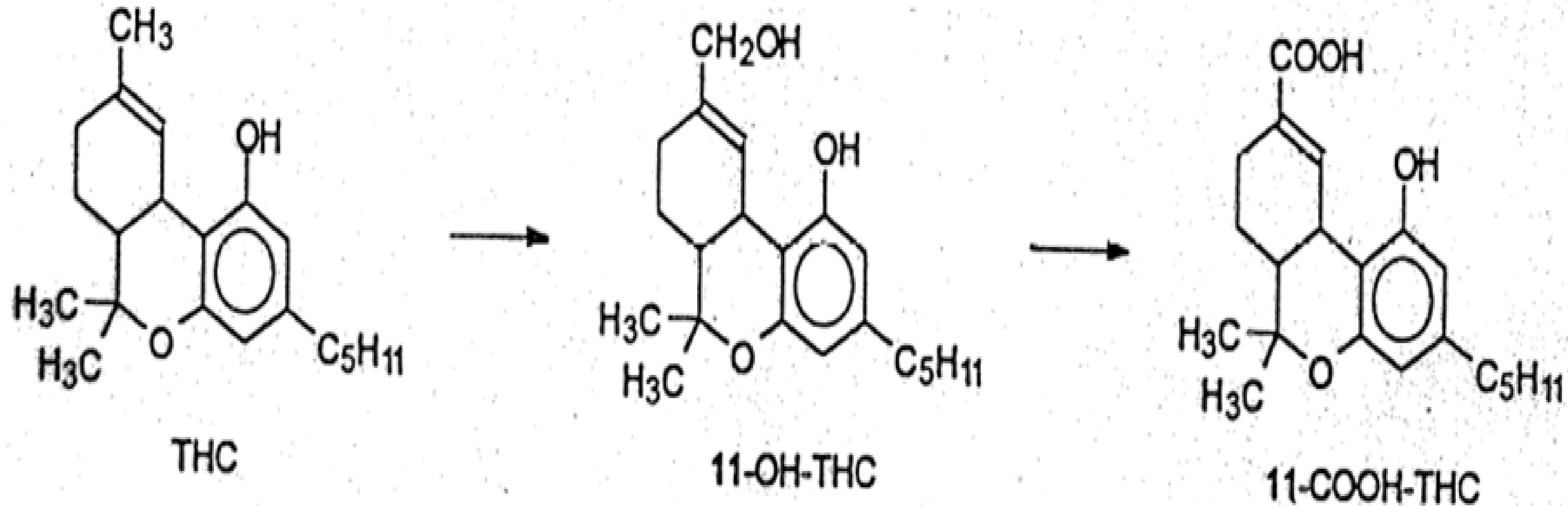
- (Trial Exam outline in Syllabus)

Aggravated dui/owi defense

Mr. K was not impaired by or under the influence of marijuana…. Neither his appearance on the video, the failure of certain FSTs, nor the toxicology tests provide proof of impairment. I disagree with the opinions expressed by DRE Officer.

Indeed, if you compare Mr. K's findings and compare them to NHTSA, there is no substantive evidence of support for DRE OFFICER's impairment opinion. Indeed, this is evidence of a lack of marijuana effects at the time of the Drug Recognition Evaluation.

METABOLISM OF MARIJUANA



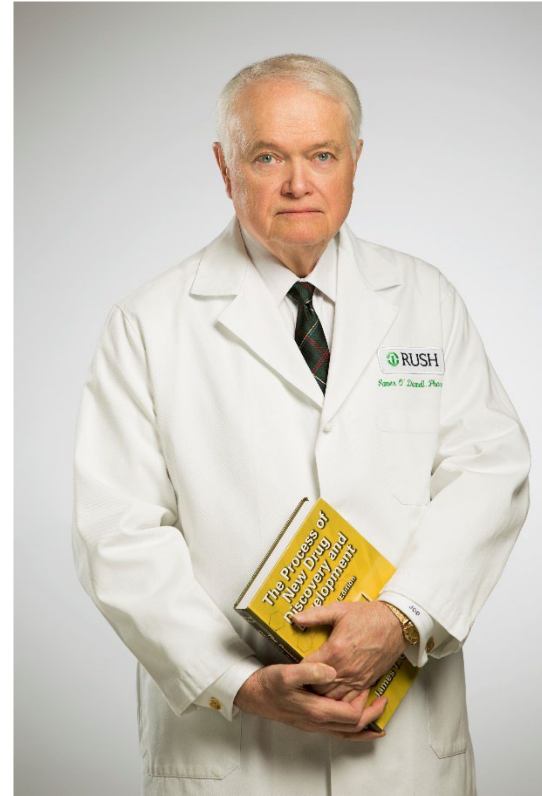
Agg dui; under influence 4 deaths

- https://www.youtube.com/watch?v=jL9z0Twt9MI
- Driver lost control, crossed median, 4 deaths (2 mother/daughter pairs
- Driver blood QUALITATIVE THC, Hydroxy (11-0H) THC, Carboxy THC (COOH)
- Prosecutor stated presence of 11-OH indicated “use within hours, therefore, he was impaired” 11-OH metabolite detectable > 24hr; agg dui charges dropped. (Syllabus – report)

Blood levels may not support Impairment

- 18 y/o crossed center line; other driver died
- Blood level of alprazolam “sub-therapeutic” (Baselt’s Toxicology Book)
- Low blood sugar at scene per EMS + flu supported erratic driving behavior
- Per Se law “any amount Controlled Substance” Pled Guilty
- Expert testimony at Sentencing Hearing
  - Drug present but not enough to have any effect
  - Probation (90 interim incarceration) Sentence
  - (News report in Syllabus)

Uniforms and Authority



DRE v. PHARMACOLOGIST

DRE	PHARMACOLOGIST
High School, some college? Police Academy, DUI training, DRE 7 days, 12 assessments	PhD or PharmD doctoral training in Pharmacology and chemistry 7-8 years Clinical experience,
Authority / Uniform	Clinical appointment, Professor
One drug - Alcohol	100'S OF DRUGS
"Uppers and downers" Learns some facts about classes of drugs	Author/ Scientist/Research Understands how drugs work and interact
Confirmation Bias? "What drugs are you taking?"	Training in physiology and diseases
Relies on Alcohol FST	Medical / Pharmacy records

DRE LACKS SCIENTIFIC FOUNDATION

- DRE is not a reliable, valid, accurate, or generally accepted method in the
- Medical, toxicological, and pharmacologic community.
- DRE's simplistic classification and the erroneous symptoms/signs/effects properties described in the DRE program are inconsistent withcurrent understanding, pharmacologic teaching, pharmacologic literature, and clinical monitoring
- The DRE protocol is new and novel and the science it is based on is not generally accepted within the scientific community.

DRE OPINION - JTOD

- The DRE fails to produce an accurate/reliable determination of whether a suspect is impaired by drugs and by what specific drug
- training police officers receive does not enable DREs to accurately observe the signs and symptoms of drug impairment,
- officers not able to reach accurate and reliable conclusions (medical diagnoses / drug causation assessments) regarding what drug may be causing impairment.

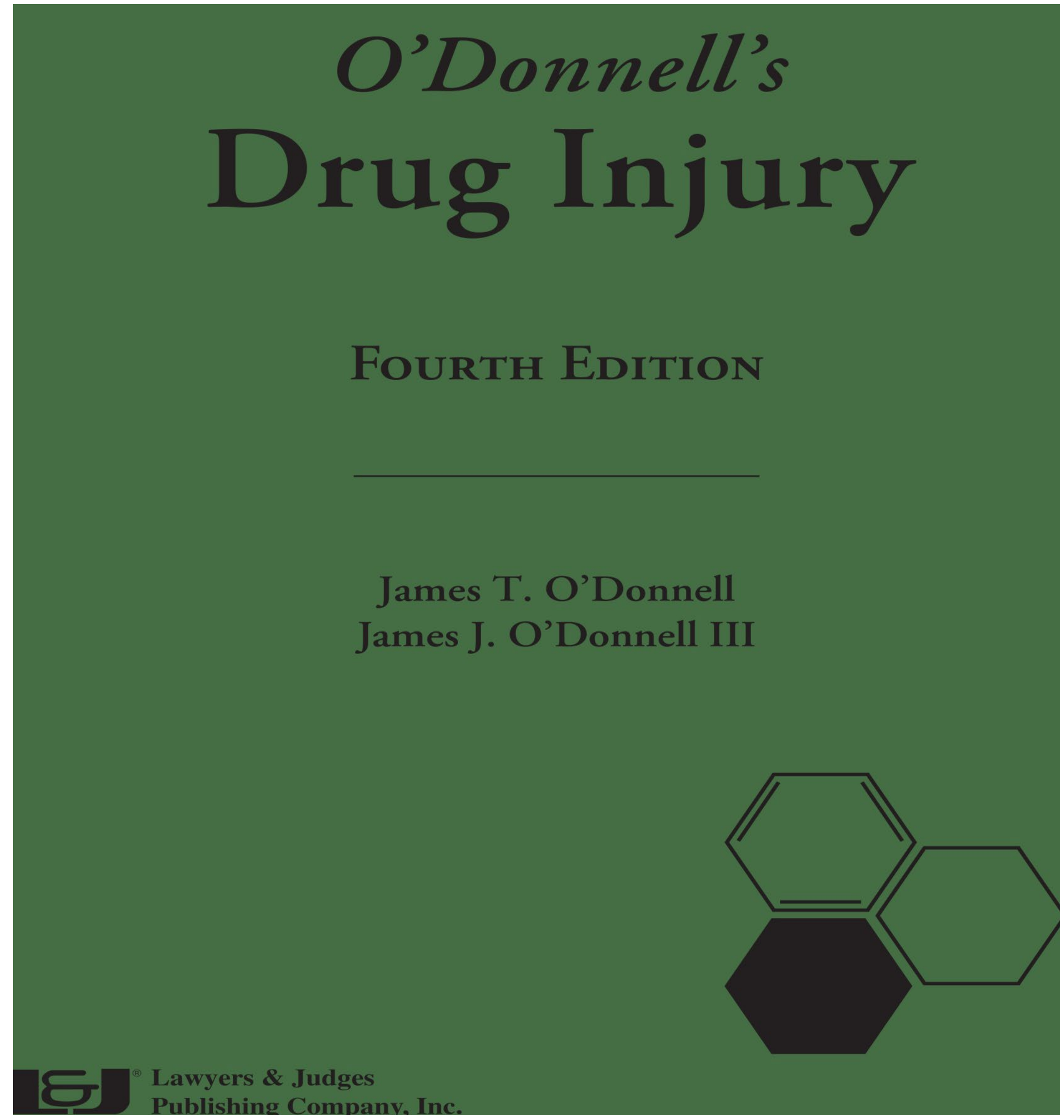
LEGITIMATCY OF DRE

- DRE and the evaluation protocol should be held to a rigorous standard. Significant concerns have been raised regarding the scientific merit of the process by experts in the judicial and medical fields.
- sufficient to warrant dismissal of DRE testimonial and recent evidence (i.e., *State of Maryland vs. David Brightful et al*)

CHALLENGE TO ATTORNEYS

- LEARN, UNDERSTAND, APPLY SCIENCE OF PHARMACOLOGY AND PHARMACOKINETICS TO FACTS OF INDIVUAL CASES
- ‘MEDICAL’ VS ‘RECREATIONAL’ VS ‘ILLEGAL’ DIFFERENT LAWS AND SCIENTIFIC STANDARDS APPLY
- SELECT AN EXPERT TO ASSIST YOU IN ASSESSING THE CASE AND PRESENTING THE SCIENCE TO THE JURY

Reference book



Medicolegal Aspects of Marijuana

Colorado Edition

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REFERENCES

- https://www.fda.gov/news-events/public-health-focus/fda-and-cannabis-research-and-drug-approval-process
- O'Donnell JT and Vogenberg FR. Beyond Medical Cannabis: Considerations for Updates to Hospital Policies and Procedures. *P&T Journal*. July/August 2019. 44(7).
- O'Donnell, J.T., O'Donnell III, J.J., Benjamin, D.M. Marijuana: Pharmacology and Medical-Legal Issues. In: O'Donnell J.T., O'Donnell III, J.J., eds. *O'Donnell's Drug Injury*. 4th ed. Lawyers & Judges Publishing Company, Inc. Tucson, AZ: 2016.
- Bryson EO and Frost EAM. The Perioperative Implications of Tobacco, Marijuana, and Other Inhaled Toxins. Int Anes Clin. Vol 49, (1), 103-118.
- Budney AJ and Hughes JR. The Cannabis Wirthdrawal Syndrome. Curr Opin Psychiatry 19:233-238. 2006.
- Endocannabinoid System_How THC Affects the Brain and the Body_Scholastic_Nida.pdf.

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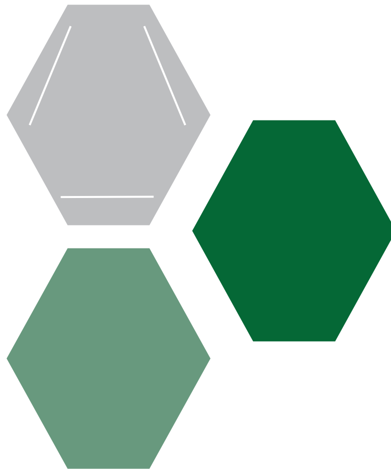

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