CANNABIS AND ARRHYTHMIAS

Ricardo Samson, MD

Director of Electrophysiology

Children's Heart Center of Nevada

Clinical Professor of Pediatrics

UNLV School of Medicine

Childrens Heart Center Nevada

continuous care for the fetus, child & adult with congenital heart disease

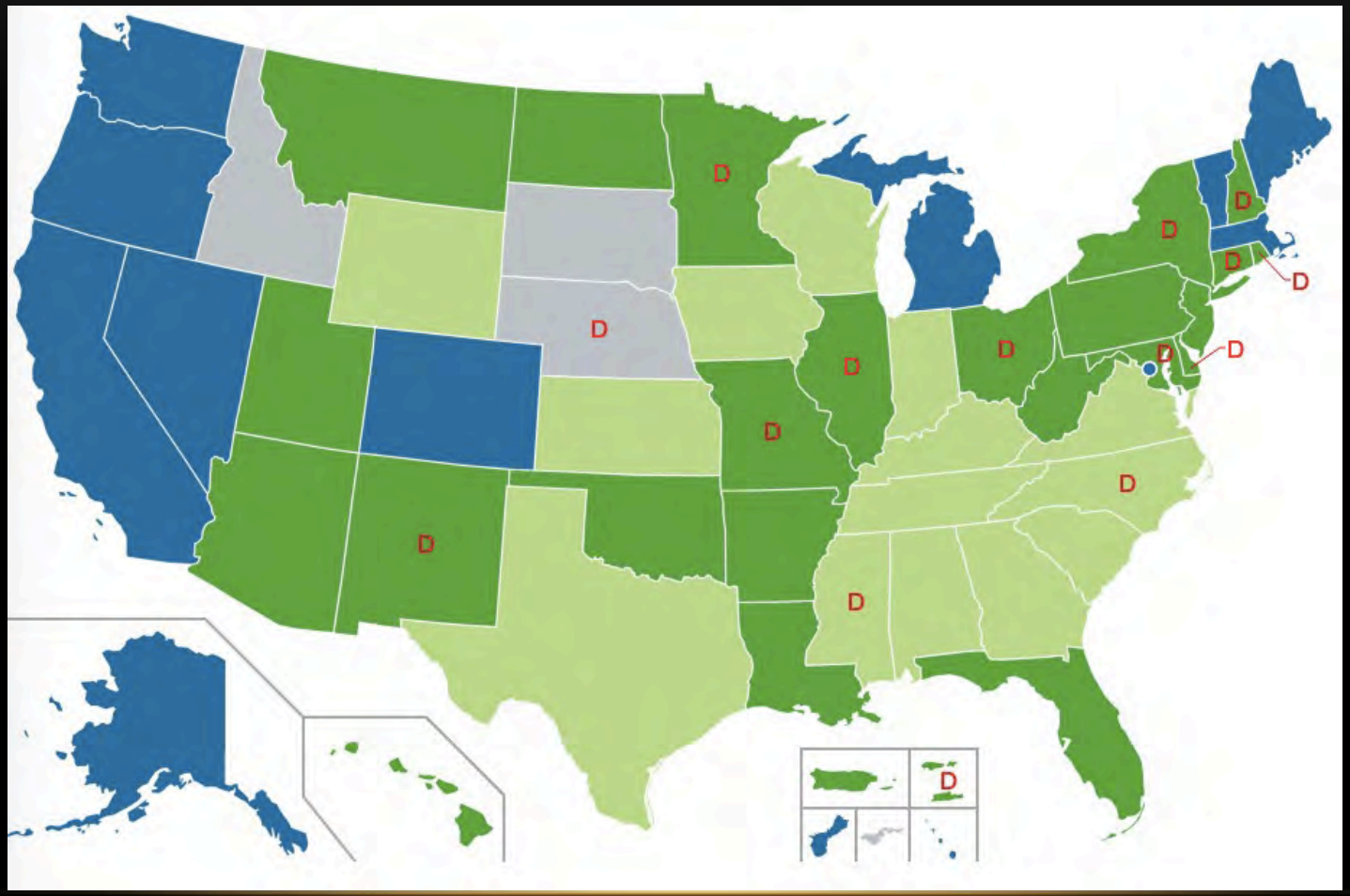
- No conflicts to declare


WELCOME
to Fabulous
LAS VEGAS
NEVADA


MARIJUANA
Restaurant
OVER 8 MILLION ROLLED DUDE


LEGAL
MARIJUANA
21+

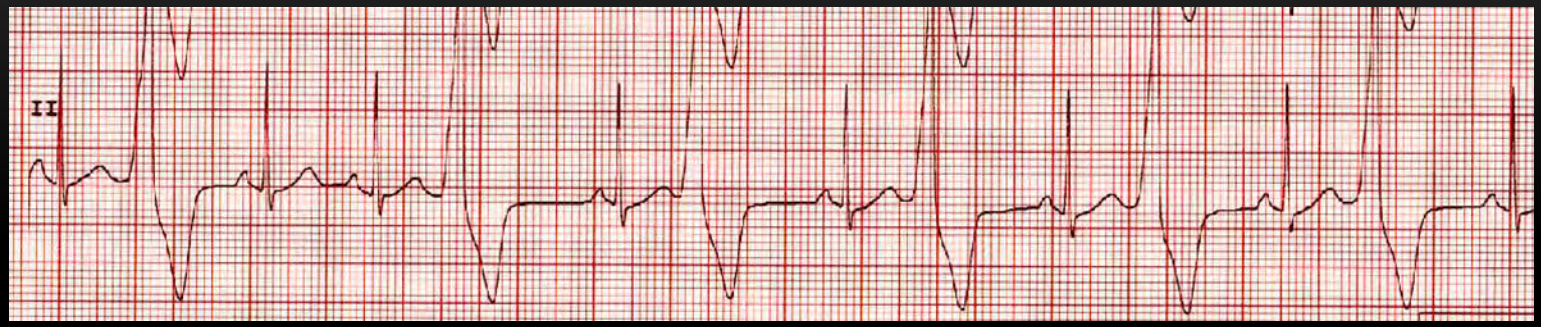
STATES WHERE MARIJUANA IS LEGAL



CASE SCENARIO

- 16 yo male presents to the Emergency Department with palpitations and syncope
  - Passed out while “partying with friends”, LOC x 2 minutes
  - Habitual marijuana user (5-7 days of the week)
  - c/o palpitations, sometimes while smoking
  - Irregular HR on exam, other VS normal
  - Urine tox screen (+) for cannabis, benzodiazapines

CASE SCENARIO (2)



- Based on this, which of the following would be appropriate?
  - Admit to ICU for IV anti-arrhythmic treatment
  - Admit and monitor for worsening arrhythmias (or resolution)
  - Draw and trend serum troponin levels
  - Send home on beta-blockers
  - Send home with outpatient cardiology follow-up

CANNABIS FACTS

- Δ9-tetrahydocannabinol (THC) – active ingredient
- Cannabidiol (CBD) – different psychoactivity than THC
- Effects mediated by cannabinoid receptors, type 1 and 2
  - CB_1 receptors – central and peripheral nervous system
  - CB_2 receptors – non-nervous tissue
- Medical use: chronic pain, muscle spasms, nausea
  - alternative treatment for anorexia, tic disorder, glaucoma
- Recreational use in North America
  - prevalence among population 15-64 yo = 11.6%
  - 2016 survey: 51% of US population had tried it

THE (INEXACT) SCIENCE OF CANNABIS

- Few controlled studies examining biological effects
- Gateway phenomenon: recreational use frequently accompanied by other substance intake
  - Tobacco, alcohol
  - Cocaine, metamphetamines
  - Opiates
- Large population studies
  - Surveys
  - Associations
- Anecdotal reports

PHYSIOLOGIC EFFECTS OF CANNABIS

The New England
Journal of Medicine

Volume 287 AUGUST 3, 1972 Number 5

MARIHUANA SMOKING

Cardiovascular Effects in Man and Possible Mechanisms

PETER BEACONSFIELD, M.D., PH.D., JEAN GINSBURG, M.A., D.M., AND REBECCA RAINSBURY, M.D.

PHYSIOLOGIC CARDIAC EFFECTS OF CANNABIS

- Increase in resting HR
  - Mean 66 bpm to 92. After 1 hr, HR still elevated (89)
  - Blocked by pre-treatment with propranolol
- Mild increase in SBP - not clinically relevant, <5 mmHg
- Increase flow to forearm, calf. No change in intestinal flow

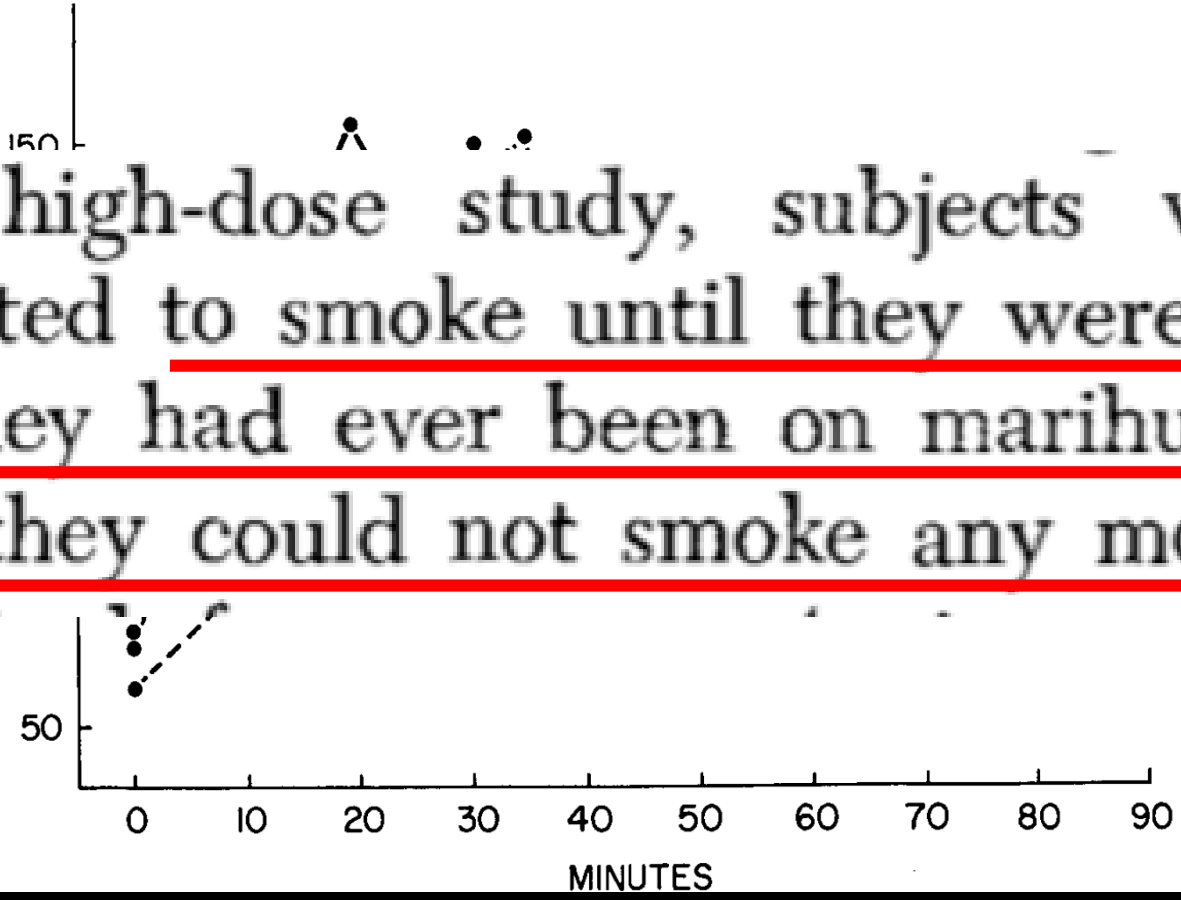
and cardiac activity on an electrocardiogram. Skin and rectosigmoid temperatures were measured by standard thermocouples (Light Laboratories), the skin thermocouple being applied to the nail bed of the great toe and the rectosigmoid probe passed after suitable preparation of the subject. Each figure

Some cardiovascular effects of marihuana smoking in normal volunteers

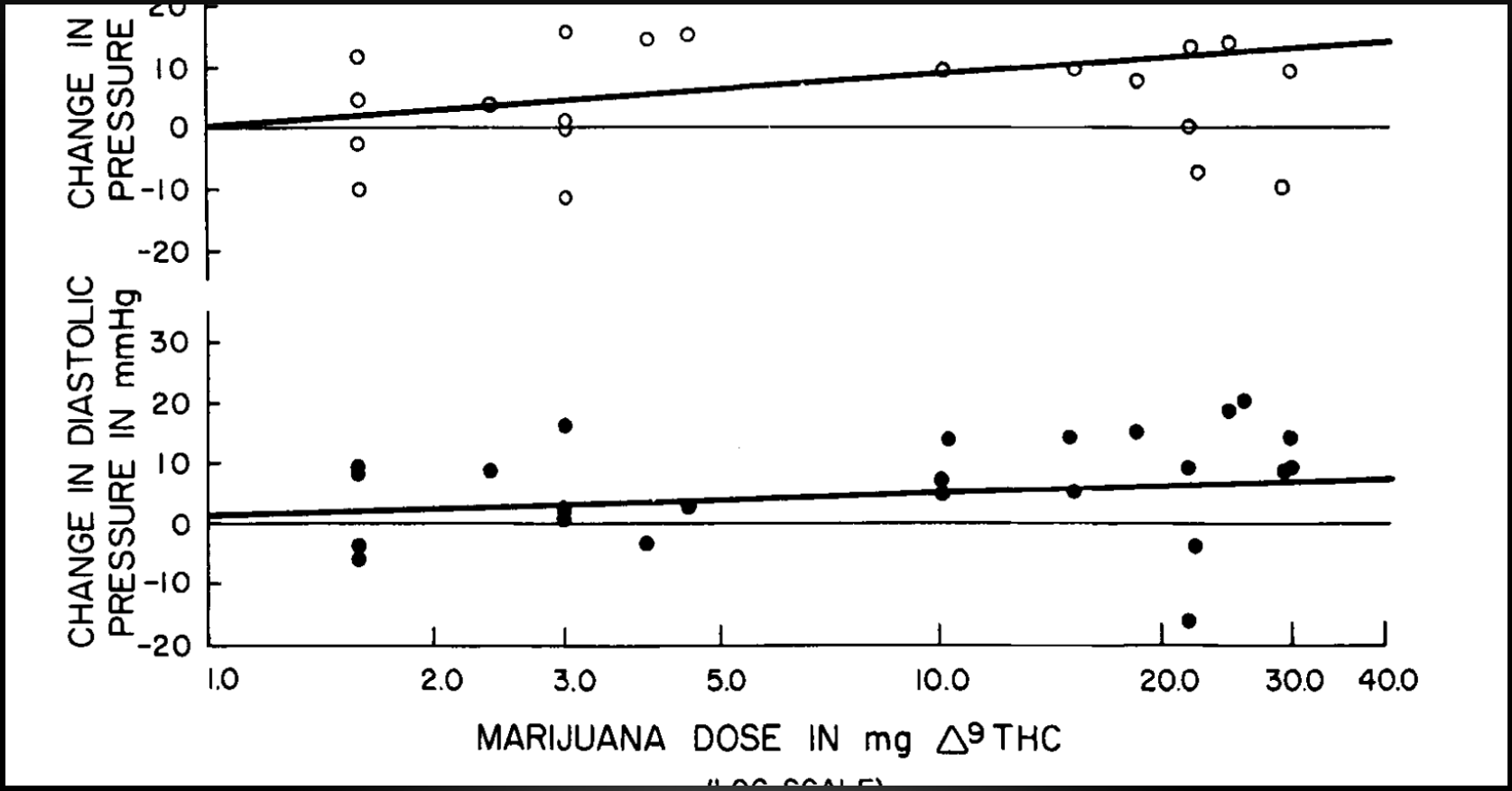
Clin Pharm Ther 1971;12(5)762-8

Stephen Johnson, M.D.,* and Edward F. Domino, M.S., M.D.
Ann Arbor and Detroit, Mich.
Department of Pharmacology, University of Michigan, Ann Arbor, and Lafayette Clinic, Detroit

the high-dose study, subjects were instructed to smoke until they were as high as they had ever been on marihuana and felt they could not smoke any more. This



JOHNSON & DOMINO, CLIN PHARM THER 1971



JOHNSON & DOMINO, CLIN PHARM THER 1971

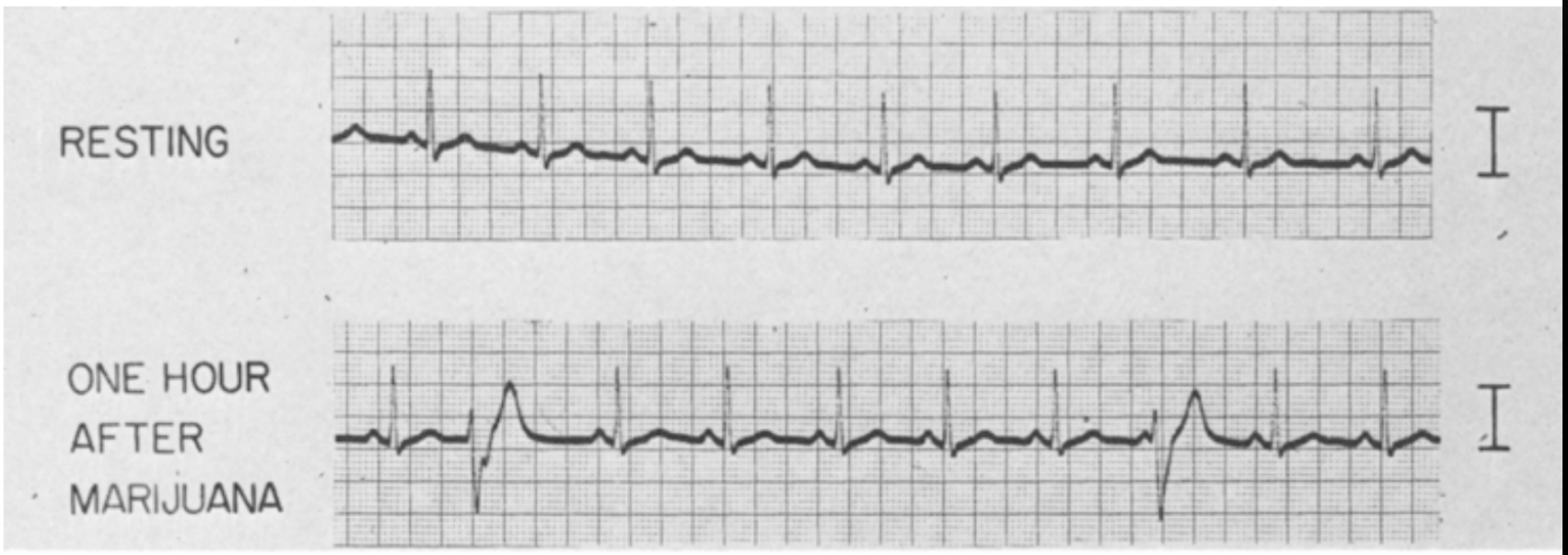


Fig. 5. Premature ventricular contractions after marihuana smoking. During the control ses sions (10 min. tracing) the subject never showed PVC's but did after taking 18.9 mg. o 2.9 per cent Δ-9-THC marihuana cigarettes. This particular record was taken one hour afte smoking but the PVC's were seen on a polygraph record shortly after smoking as well.

(GENERALLY) ACCEPTED CARDIOVASCULAR EFFECTS

- Vasculitis - “cannabis arteritis”: seen in chronic users; segmental narrowing of distal arteries in the extremities without collateral development
- Reduced oxygenation – production of carboxyhemoglobin from smoking
- Sympathomimetic effects: increased HR, BP
- Recipe for myocardial ischemia!

Research Paper

Examining the relationship between medical cannabis laws and cardiovascular deaths in the US

Rahi Abouk[a], Scott Adams[b,*]

[a] Department of Economics, Finance and Global Business, William Paterson University, United States
[b] Department of Economics, University of Wisconsin-Milwaukee, United States

Int J Drug Policy 2018

In states with MCL, cardiac deaths have increased:
1.3% for females and 2.3% for males since legalization

Table 1
MCL effective dates as of December 2014.

State	Effective date	State	Effective date
Alaska	March 1999	Michigan*	December 2008
Arizona*	April 2011	Minnesota	June 2014
California*	November 1996	Montana*	November 2004
Colorado*	June 2001	Nevada*	October 2001
Connecticut	October 2012	New Hampshire	July 2013
Delaware	May 2011	New Jersey	October 2010
District of Columbia	June 2010	New Mexico	July 2007
Hawaii	December 2000	New York	July 2014
Illinois	January 2014	Oregon*	December 1998
Maine	December 1999	Rhode Island	January 2006
Maryland	June 2014	Vermont	July 2004
Massachusetts	January 2013	Washington*	November 1998

Cannabis use predicts risks of heart failure and cerebrovascular accidents: results from the National Inpatient Sample

Aditi Kalla[a,*], Parasuram M. Krishnamoorthy[a,*], Akshaya Gopalakrishnan[b] and Vincent M. Figueredo[a,c]

J Cardiovasc Med 2018

- Query of NIS/HCUP (national inpatient database) 2009-10
  - ICD 9 codes for hospitalized MJ users (304.3) 18-55 yo
    - 316,397 pts (1.3%)
      - MJ users: male, older (33 vs 26 yo), obese, HTN, EtOH, tobacco; less DM. Hyperlipidemia similar
  - Heart failure and CVA higher in MJ users
    - Odds ratio (1.1 [95%CI 1.02-1.18], 1.26 [1.16-1.36])

Circ, 2001

Triggering Myocardial Infarction by Marijuana

Murray A. Mittleman, MD, DrPH; Rebecca A. Lewis; Malcolm Maclure, ScD;
Jane B. Sherwood, RN; James E. Muller, MD

- 3,884 patients with documented MI, surveyed with 4 days of dx
  - 124 patients (3%) MJ users; 3,758 non MJ users (97%)
  - MJ users:
    - younger (44±7 vs 62±12 yrs), more obese, use tobacco
    - less likely to have history of angina, HTN, diabetes
- Risk of MI was higher in the 60 minutes following MJ use
  - Odds ratio 4.8 (95% CI 2.8 – 9.5)

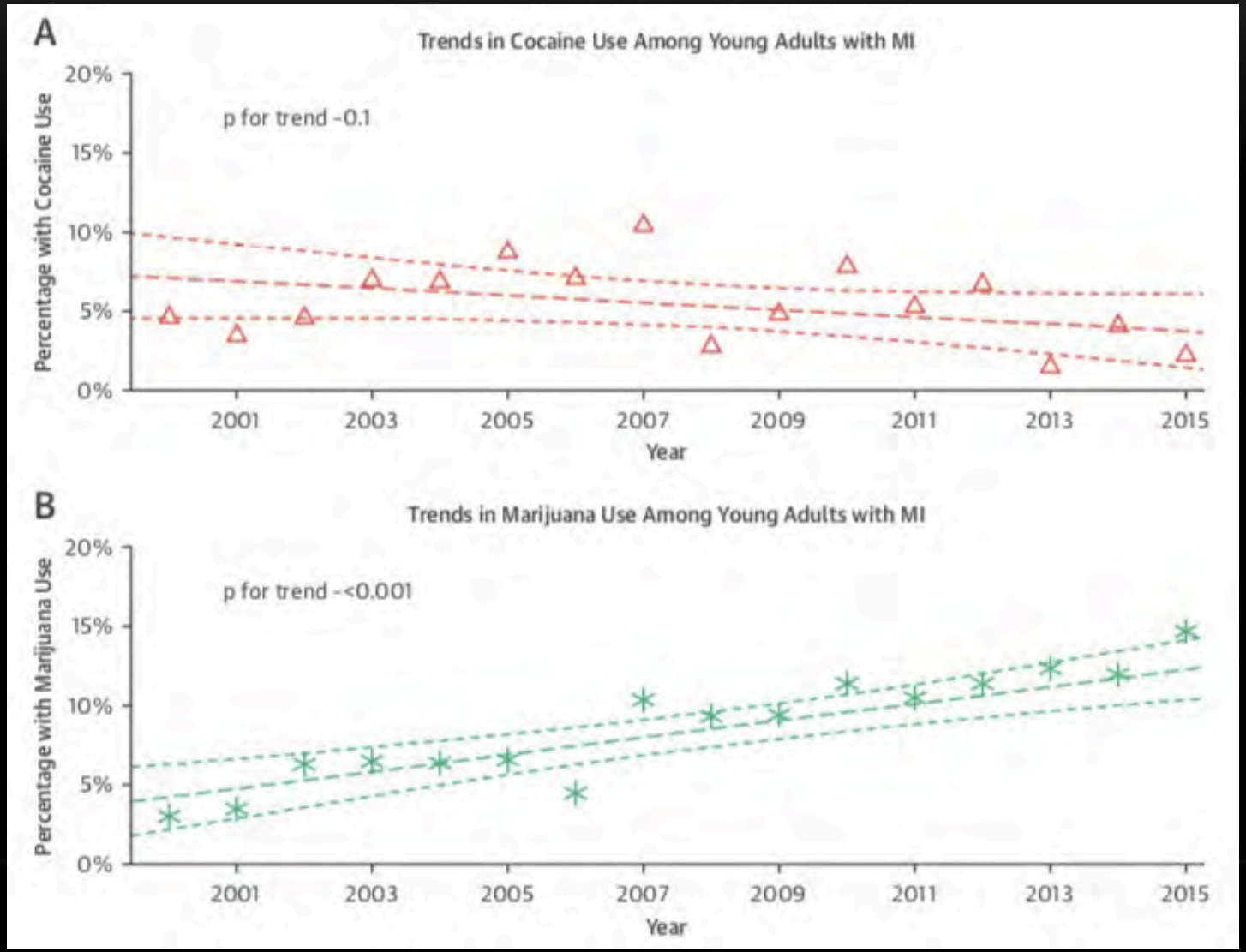
J Am Coll Cardiol 2018; 71(22):2540

Cocaine and Marijuana Use Among Young Adults With Myocardial Infarction

Ersilia M. DeFilippis, MD,[a] Avinainder Singh, MBBS,[a] Sanjay Divakaran, MD,[a] Ankur Gupta, MD, PhD,[a] Bradley L. Collins, BA,[a] David Biery, BS,[a] Arman Qamar, MD,[a] Amber Fatima, MBBS,[b] Mattheus Ramsis, MD,[a] Daniel Pipilas, MD,[a] Roxanna Rajabi, BS,[c] Monica Eng, BS,[c] Jon Hainer, BS,[c] Josh Klein, BS,[c] James L. Januzzi, MD,[d] Khurram Nasir, MD, MPH,[e] Marcelo F. Di Carli, MD,[a,c] Deepak L. Bhatt, MD, MPH,[a] Ron Blankstein, MD[a,c]

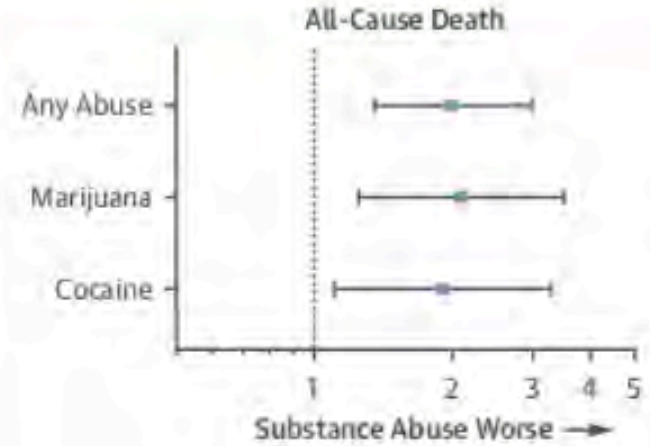
- Documented MI in patients < 50 yo
  - Cocaine use 5%, MJ use 6%
    - Cocaine/MJ users younger, lower rates of DM, dyslipidemia, higher rate of tobacco use
  - Cocaine/MJ use associated with higher rate of
    - CV mortality: hazard ratio 2.2 [95% CI 1.27 – 9.9]
    - All-cause mortality : 1.99 [1.35 – 2.97]

DEFILLIPIS ET AL, JACC 2018

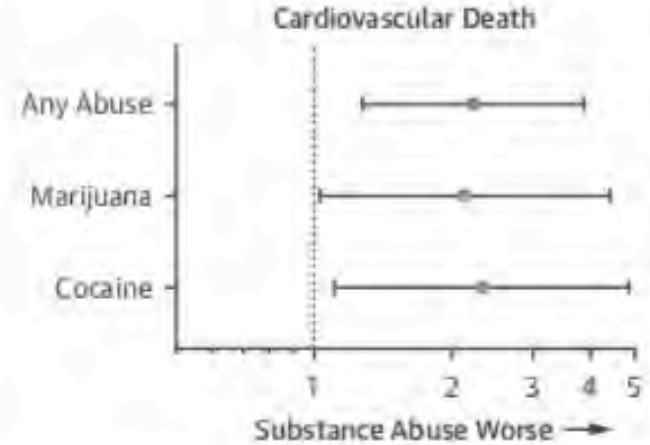


DEFILLIPIS ET AL, JACC 2018

FIGURE 5 Adjusted Cardiovascular Mortality and All-Cause Death



	Total (N)	Death (n)	Adj. HR and 95% CI
Cocaine or marijuana	224	42	1.99 (1.35-2.97)
Marijuana	125	18	2.09 (1.25-3.50)
Cocaine	99	24	1.91 (1.11-3.29)



	Total (N)	CV Death (n)	Adj. HR and 95% CI
Cocaine or marijuana	224	21	2.22 (1.28-3.87)
Marijuana	125	9	2.13 (1.03-4.42)
Cocaine	99	12	2.32 (1.11-4.85)

ARRHYTHMIAS AND CANNABIS

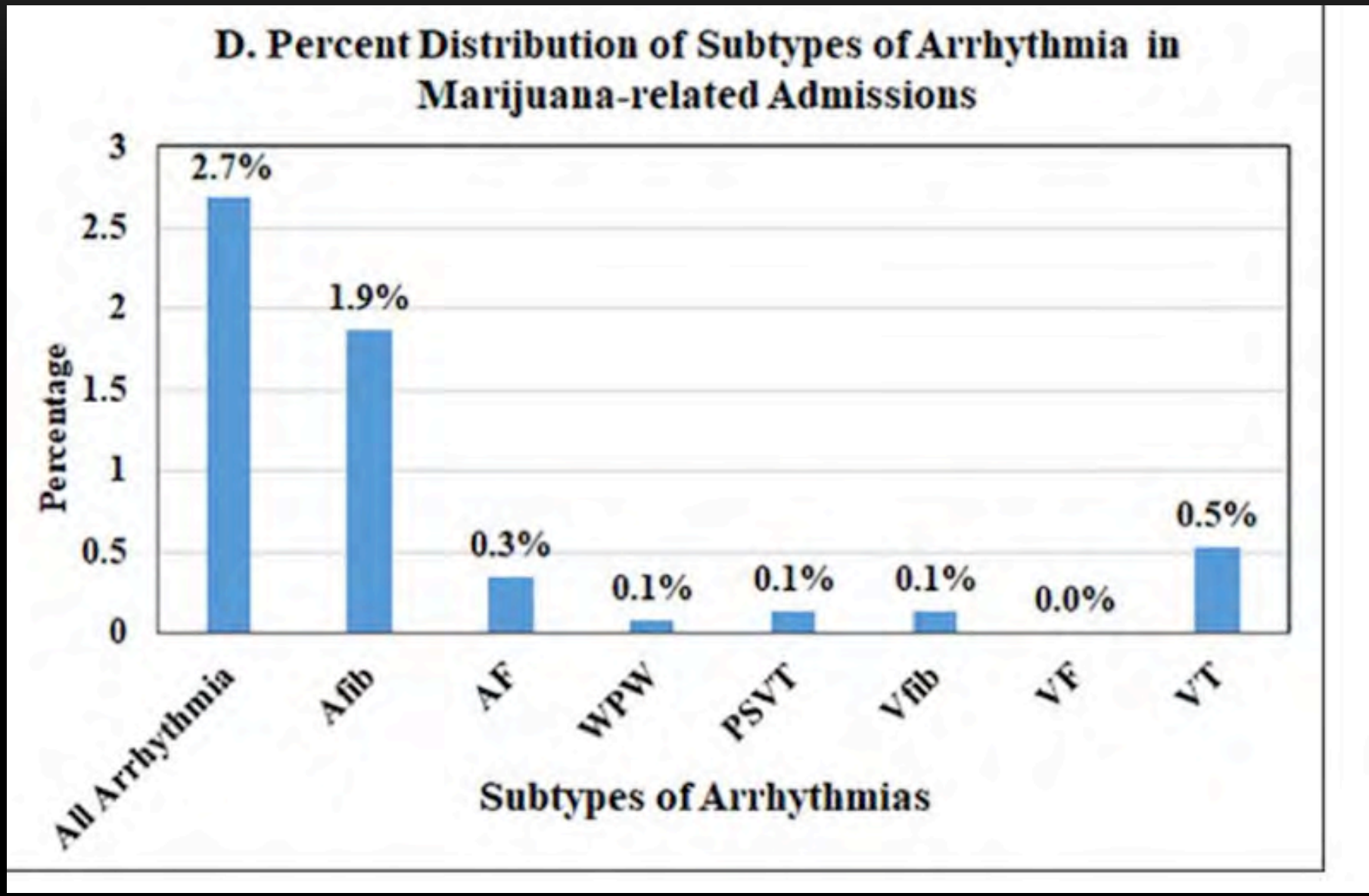
Burden of arrhythmia in recreational marijuana users

Int J Cardiol, 2018

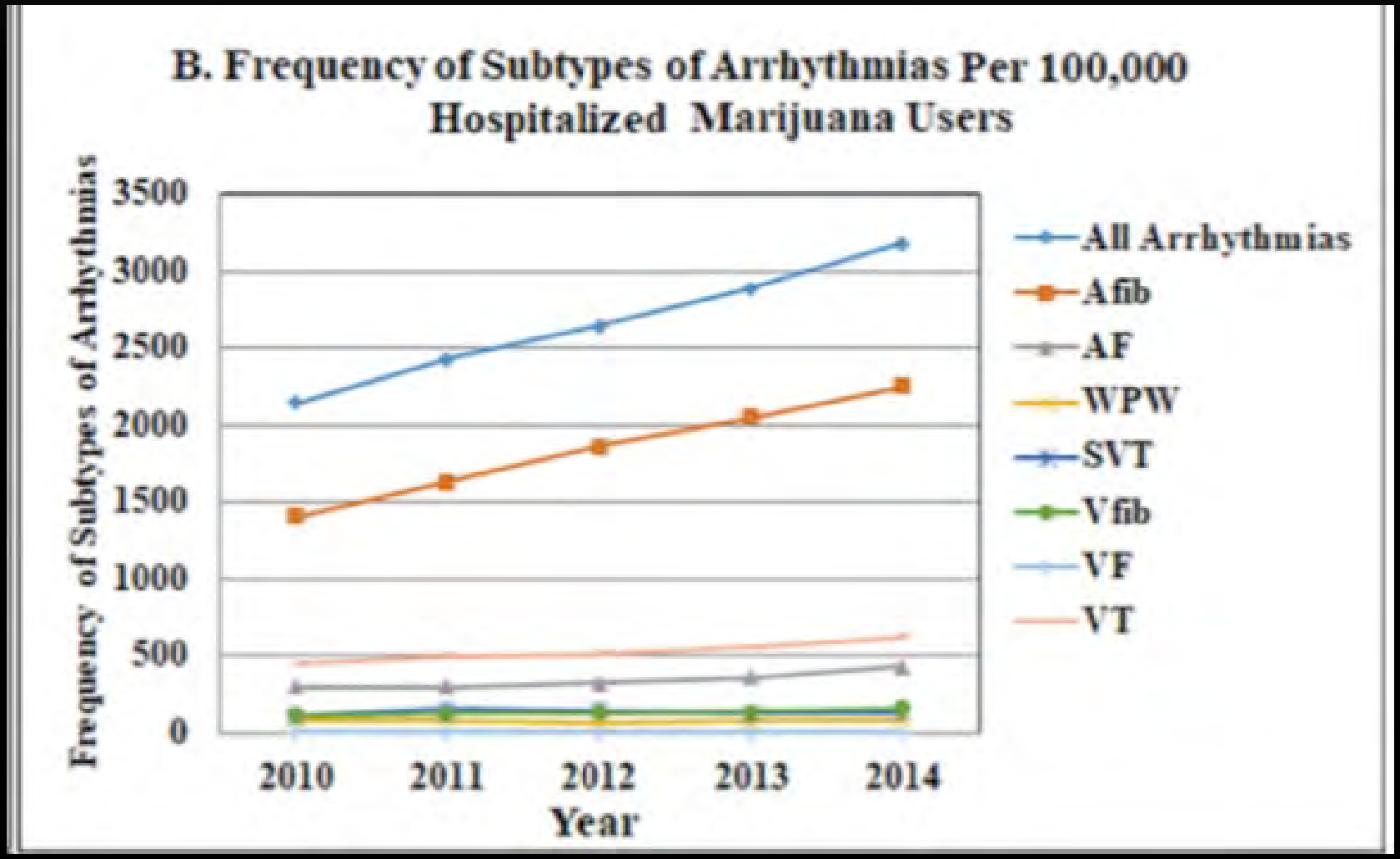
Rupak Desai [a,*], Upenkumar Patel [b], Abhishek Deshmukh [c], Rajesh Sachdeva [d,e], Gautam Kumar

- Query of NIS/HCUP (national inpatient database) 2010-14
  - ICD 9 codes for hospitalized MJ users (304.30-2, 305.20-2)
  - ICD 9 codes for atrial fibrillation, atrial flutter, SVT, WPW, ventricular tachycardia, ventricular fibrillation
  - 2,459,856 admissions
    - 66,176 had arrhythmias (2.7%)

DESAI ET AL, INT J CARDIOL 2018



DESAI ET AL, INT J CARDIOL, 2018



Pediatr Cardiol 21:284, 2000
DOI: 10.1007/s002460010063

Atrial Fibrillation Associated with Marijuana Use

G.K. Singh

Pediatric Cardiology

- 14 yo male presented with palpitations and dizziness, fall but no LOC
  - Had smoked cannabis 1 hour prior to onset of symptoms
  - Toxicology screen (+) only for cannabis
  - Complete W/U unremarkable
  - Converted to NSR 12 h later after first oral digitalization dose
  - No recurrence 1 year after abstinence from cannabis

Paroxysmal atrial fibrillation following marijuana intoxication: a two-case report of possible association

Int J Cardiol, 2000

- Kosior et al describe 2 patients diagnosed with atrial fibrillation
  - 32 yo physician presents with paroxysmal palpitations and tachycardia for several months. Exam and testing including Holter were unremarkable
    - Placed empirically on propranolol but palpitations persist
    - Ubeknownst to his caretakers, he performs provocative testing, smoking marijuana while wearing holters
    - Diagnosis: a-fib
  - 24 yo female presents in a-fib minutes after smoking MJ

The American Journal of Cardiology
Volume 113, Issue 6, 15 March 2014, Pages 1085-1086

Readers' Comments

Marijuana Smoking is Associated With Atrial Fibrillation

Panagiotis Korantzopoulos MD, PhD

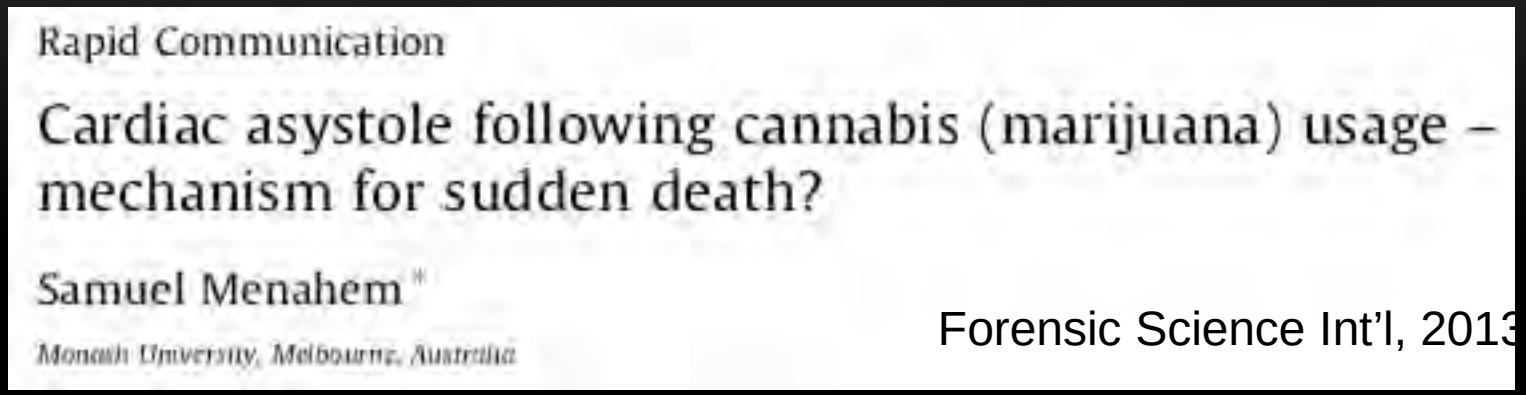
- 6 consecutive patients < 45 yo with “lone a-fib”
  - No structural heart disease, 1 with HTN
  - Onset associated with marijuana smoking
  - All resolved without recurrence with cessation of MJ use

Am J Cardiol, 2018

Relation of Cannabis Use and Atrial Fibrillation Among Patients Hospitalized for Heart Failure

- Query of NIS/HCUP (national inpatient database) 2014
  - Patients admitted with dx of heart failure
    - Subset of cannabis users identified, n = 3,548
      - those with coexisting opioid, amphetamine, pyschostimulants, cocaine, sedative, antidepressants were eliminated
    - Control population: age-matched non-cannabis users
    - Atrial fibrillation was less likely (OR 0.85 [0.75 – 0.9]) among cannabis users!

CANNABIS AND BRADYCARDIA (AND CHD)



Rapid Communication

Cardiac asystole following cannabis (marijuana) usage – mechanism for sudden death?

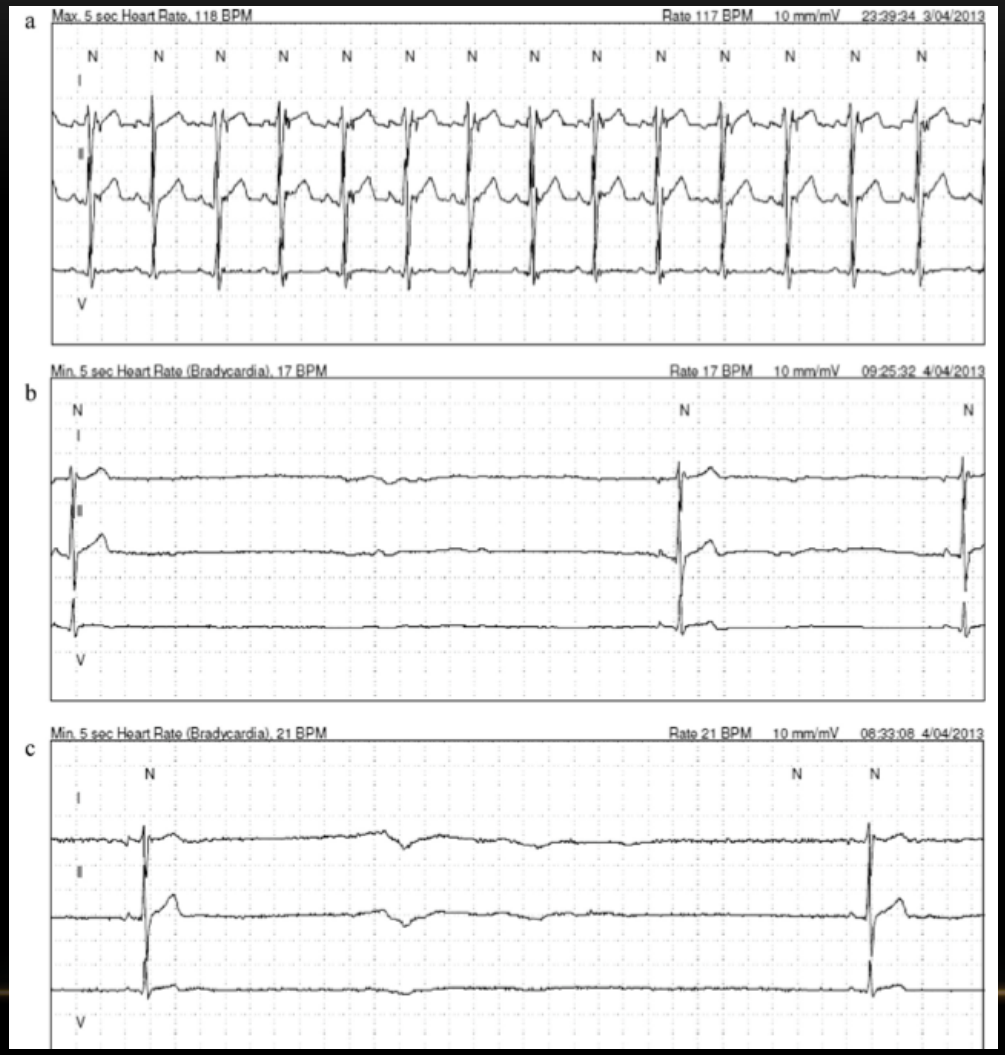
Samuel Menahem *

Monash University, Melbourne, Australia

Forensic Science Int'l, 2013

- 21 yo male with h/o supracardiac TAPVR
  - Presented and repaired at 11 weeks of age
  - Had regular follow-up with no obstruction at LA anastomosis
  - Occasional EtOH, regular MJ use (daily)
  - Normal exercise test after c/o dyspnea on exertion
  - 24 hour holter: multiple sinus pauses > 2 sec

MENAHAIM, FOR SCI INT'L 2013



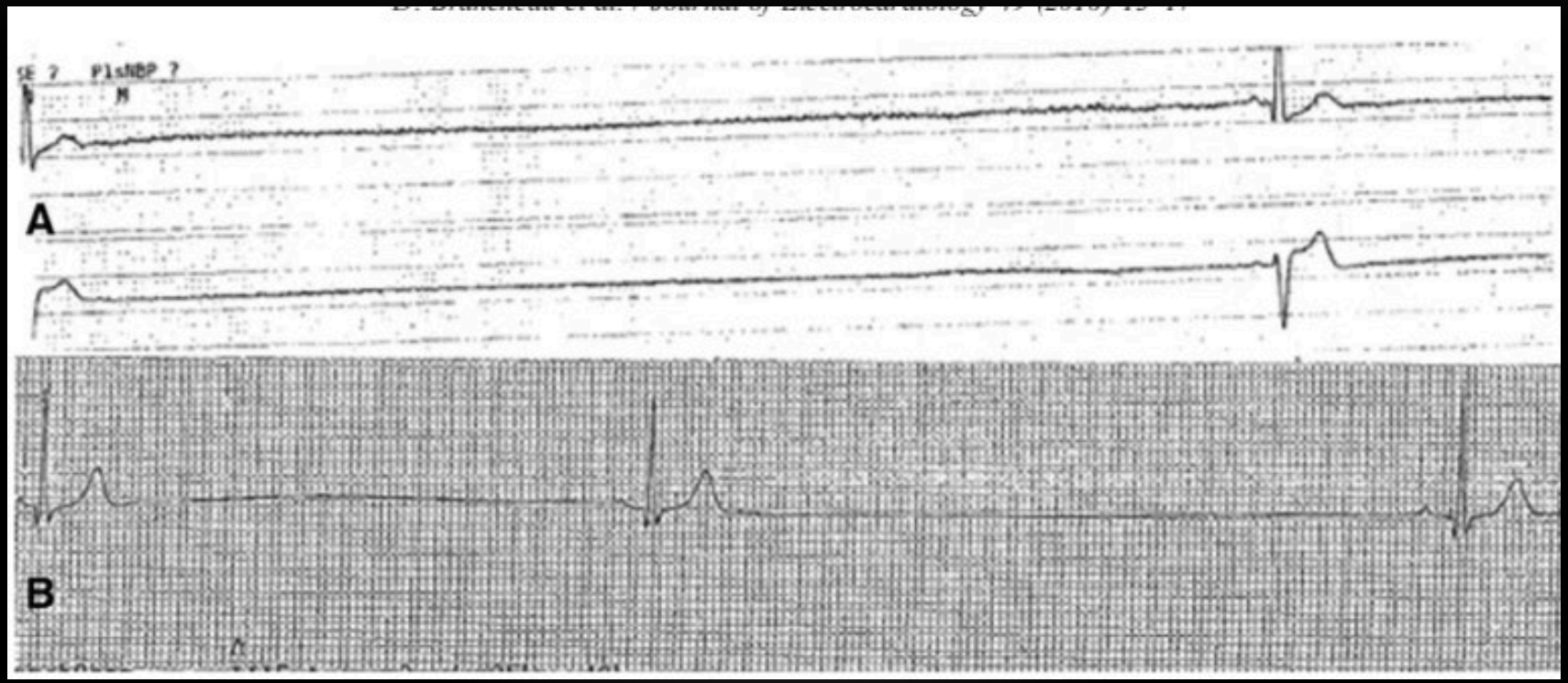
MENAHAIM, FOR SCI INT'L 2013

- Times of pauses coincided with smoking cannabis
- Felt "rather dizzy" but no LOC
- Always recumbent while smoking
- Patient quit smoking marijuana and subsequent holters all normal

Cannabis induced asystole

Journal of Electrocardiology 49 (2016) 15 – 17

JOURNAL OF
Electrocardiology



BRANCHEAU ET AL, J ELECTROCARDIOL 2016

- 28 yo male passes out while driving
- Previous syncopal episodes after smoking MJ
  - Urine tox screen (+) for cannabis
- Bradycardia and sinus pause in ED, spontaneous recovery
- Intracardiac EPS – normal SNRT
- Tilt table test negative (MJ use ceased while in hospital)
- VVI pacemaker placed (lower rate 30, hysteresis @ 50)

BRANCHEAU ET AL, J ELECTROCARDIOL 2016

- Tilt table test repeated as outpatient
  - Patient smoked MJ 4 hrs prior

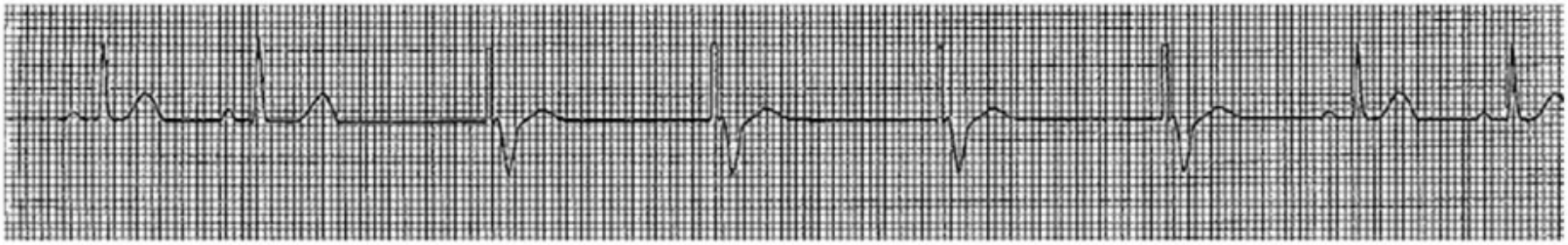


Fig. 2. Paced during tilt-table: Rhythm strip demonstrating paced rhythm with tilt-table testing after recent cannabis consumption.

THE MANY ARRHYTHMIAS OF CANNABIS

Complete Heart Block From Chronic Marijuana Use

Priyam Mithawala, PharmD[1], Priyank Shah, MD, MPH[2,3] and Edward Koomson, MD[4]

[1] Department of Pharmacy Practice, Presbyterian College School of Pharmacy, Clinton, South Carolina; [2] Department of Internal Medicine, Medical College of Georgia – Southwest Clinical Campus, Albany, Georgia; [3] Department of Cardiology, and [4] Department of Electrophysiology, Phoebe Putney Memorial Hospital, Albany, Georgia

Key Indexing Terms: Conduction system abnormalities; Heart block; Marijuana. **[Am J Med Sci 2018;■(■):1–3.]**

Minerva Cardioangiologica 2011 February;59(1):119-20

language: English

Ectopic atrial rhythm associated with cannabis use

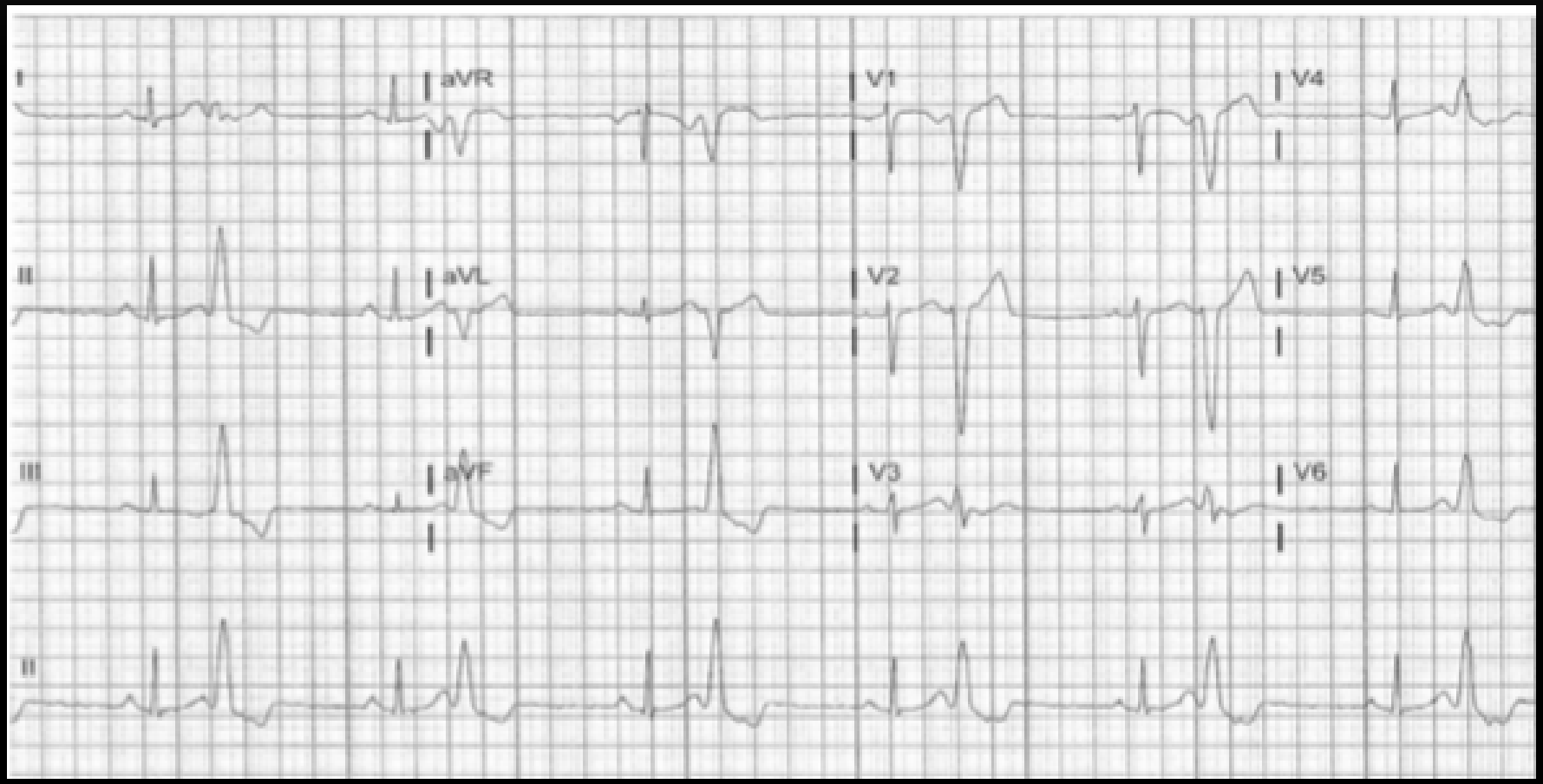
Fernández-Fernández F. J. [1], Cainzos-Romero T. [1], Mesías Prego A. [2], Sesma P. [1] ✉

[1] Department of Internal Medicine, Hospital Arquitecto Marcide, Ferrol, Spain; [2] Section of Cardiology, Hospital Arquitecto Marcide, Ferrol, Spain

Case Report

Marijuana, bigeminal premature ventricular contractions and sluggish coronary flow: Are they related?

J Cardiol Cases, 2013



KHOUZAM ET AL, J CARD CASES 2013

- 37 yo female with h/o MR, HTN, syncope presents with chest pain, dizziness, headache, SOB, worsening palpitations x 2 weeks
- Electrolytes normal, troponin (-). Tox screen (+) cannabis, opiates. ECG shows ventricular bigeminy
- Exercise treadmill – non-sustained VT @ 300 bpm
- Echo diastolic dysnfunction, mild MR, EF 55%
- CXR, CT normal. Nuc med stress test – no perfusion defects
- Cath – no CAD. Slow coronary flow noted in LAD, RCA

KHOUZAM ET AL, J CARD CASES 2013

- Authors conceded that PVCs and slow coronary flow phenomenon (SCFP) could be unrelated
- SCFP - a multifactorial process with several contributing factors including
  - Microvascular perturbations (recurrent)
  - Endothelial cell damage
  - Fibromuscular hyperplasia
  - Myofibrillar disarray
- Speculate that repeated cannabis use could cause SCFP

Annals of Emergency Medicine
Volume 42, Issue 3, September 2003, Pages 365-369

Toxicology

Coronary no-flow and ventricular tachycardia associated with habitual marijuana use ☆

Shereif H Rezkalla MD [a] ... Robert A Kloner MD, PhD [b]

Forensic Science International
Volume 237, April 2014, Pages e11-e13

Case Report

Sudden unexpected death under acute influence of cannabis

Benno Hartung [a], Silke Kauferstein [b], Stefanie Ritz-Timme [a], Thomas Daldrup [a]

Irish Journal of Medical Science
December 2012, Volume 181, Issue 4, pp 479–482 | Cite as

Cannabis, possible cardiac deaths and the coroner in Ireland

Authors Authors and affiliations

W. P. Tormey

MECHANISMS OF ARRHYTHMOGENESIS

- Reentry – classic, paroxysmal, “start-stop” arrhythmias
  - SVT, atrial flutter, incisional atrial tachycardia, scar-related VT
- Automaticity – abnormal spontaneous depolarization
  - Ectopic atrial tachycardia, JET, most PVC foci
- Triggered activity – intracellular phenomena
  - “R on T”, digitalis toxicity arrhythmias, reperfusion injury
  - Ion channelopathies

FOOL ME ONCE…FOOL ME TWICE…BUT 5 TIMES?

FOOL ME ONCE…FOOL ME TWICE…

Acute cannabis intoxication mimicking brugada-like ST segment abnormalities

Int J Cardiol, 2007

Rev Esp Cardiol, 2012

Brugada Electrocardiogram Pattern Induced by Cannabis

Patrón electrocardiográfico de Brugada inducido por cannabis

Am J Emerg Med, 2016

Brugada electrocardiogram pattern induced by cannabis; is cannabis safe?

Brugada Phenocopy Induced by Recreational Drug Use

Case Reports in Cardiol, 201

Marijuana Induced Type I Brugada Pattern: A Case Report

Am J Med Case Rep, 2018

DACCARET ET AL, INT J CARDIOL 2007

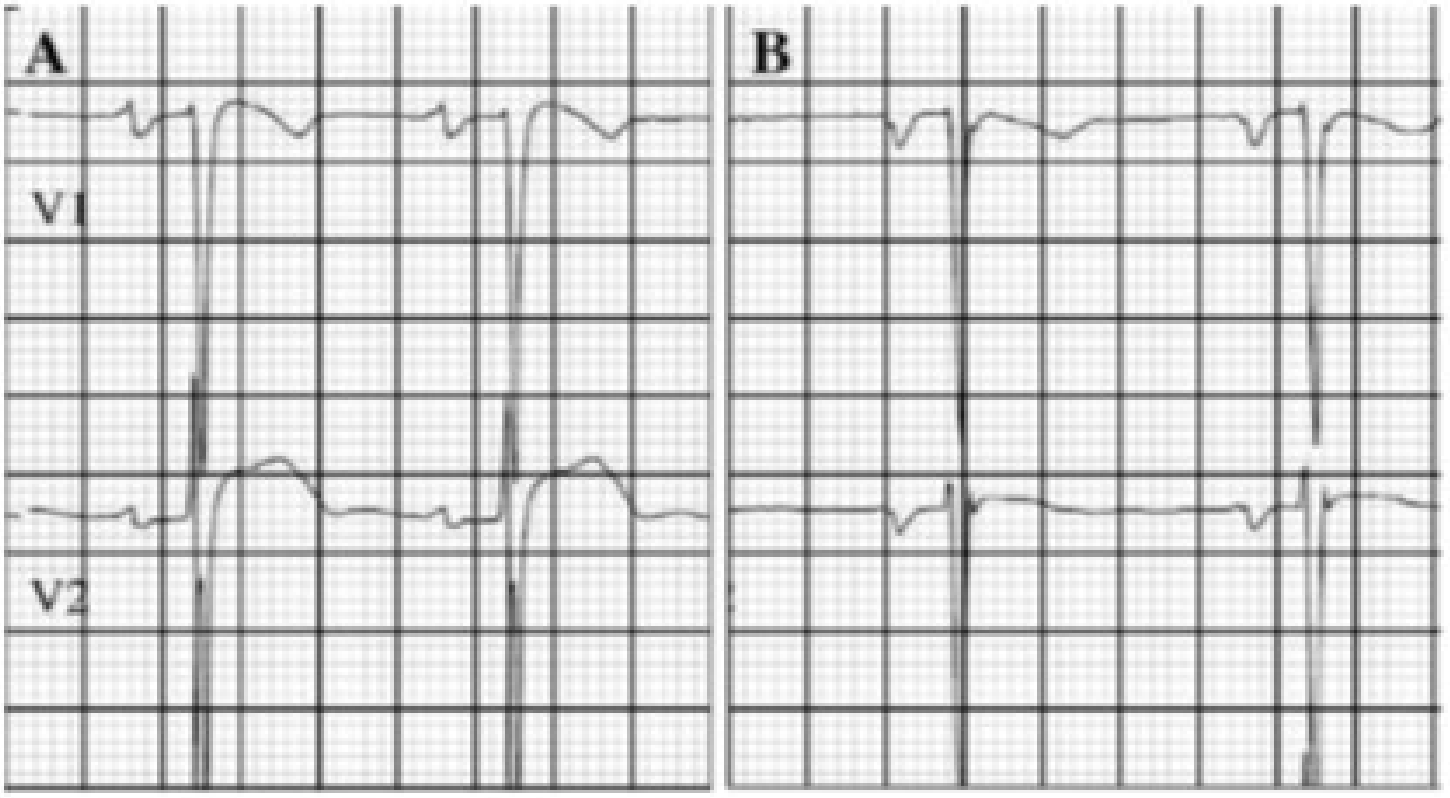


Fig. 1. (A) ECG on admission demonstrating a 2 mm coved ST segment elevation in leads V1 and V2. (B) After ST segment abnormalities resolution a Procainamide stimulation test failed to elicit ST-T wave changes.

ROMERO-PUCHE ET AL, REV ESP CARDIOL, 2012

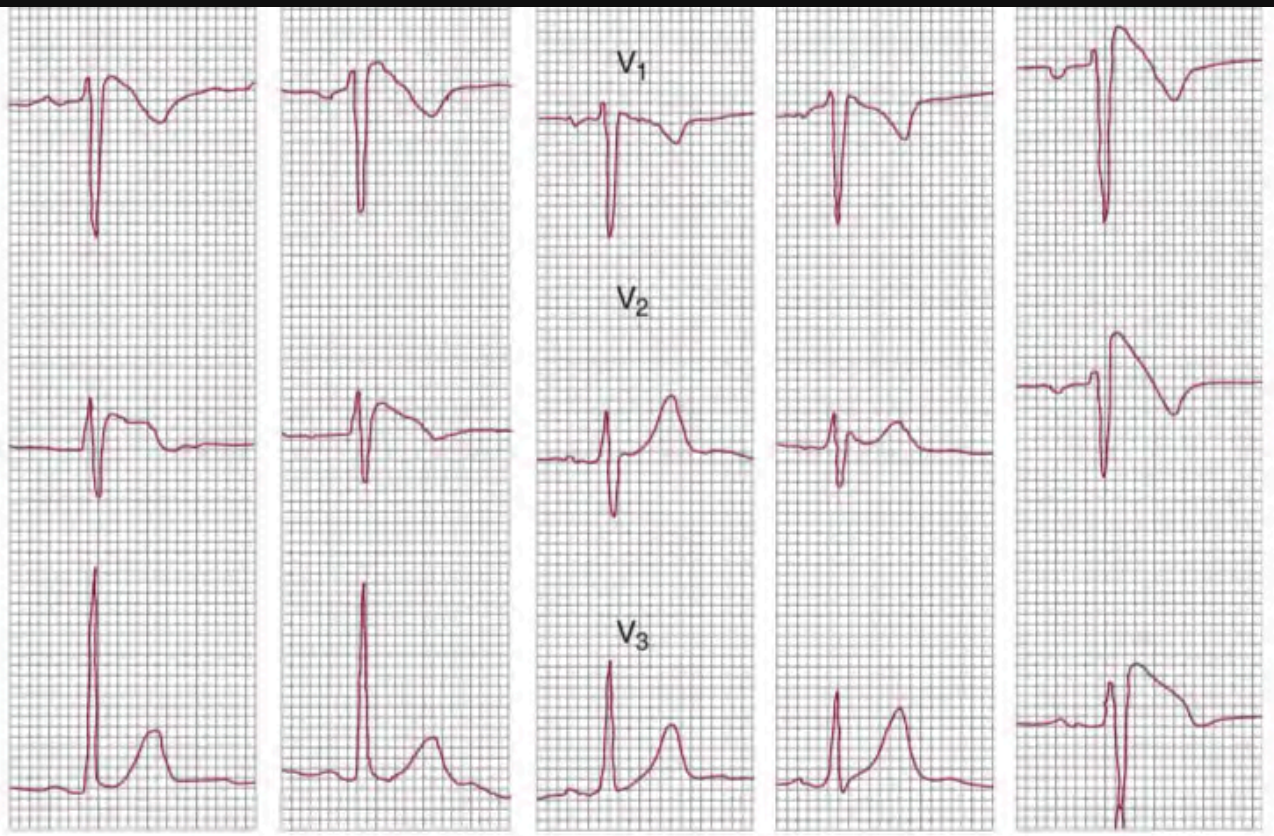
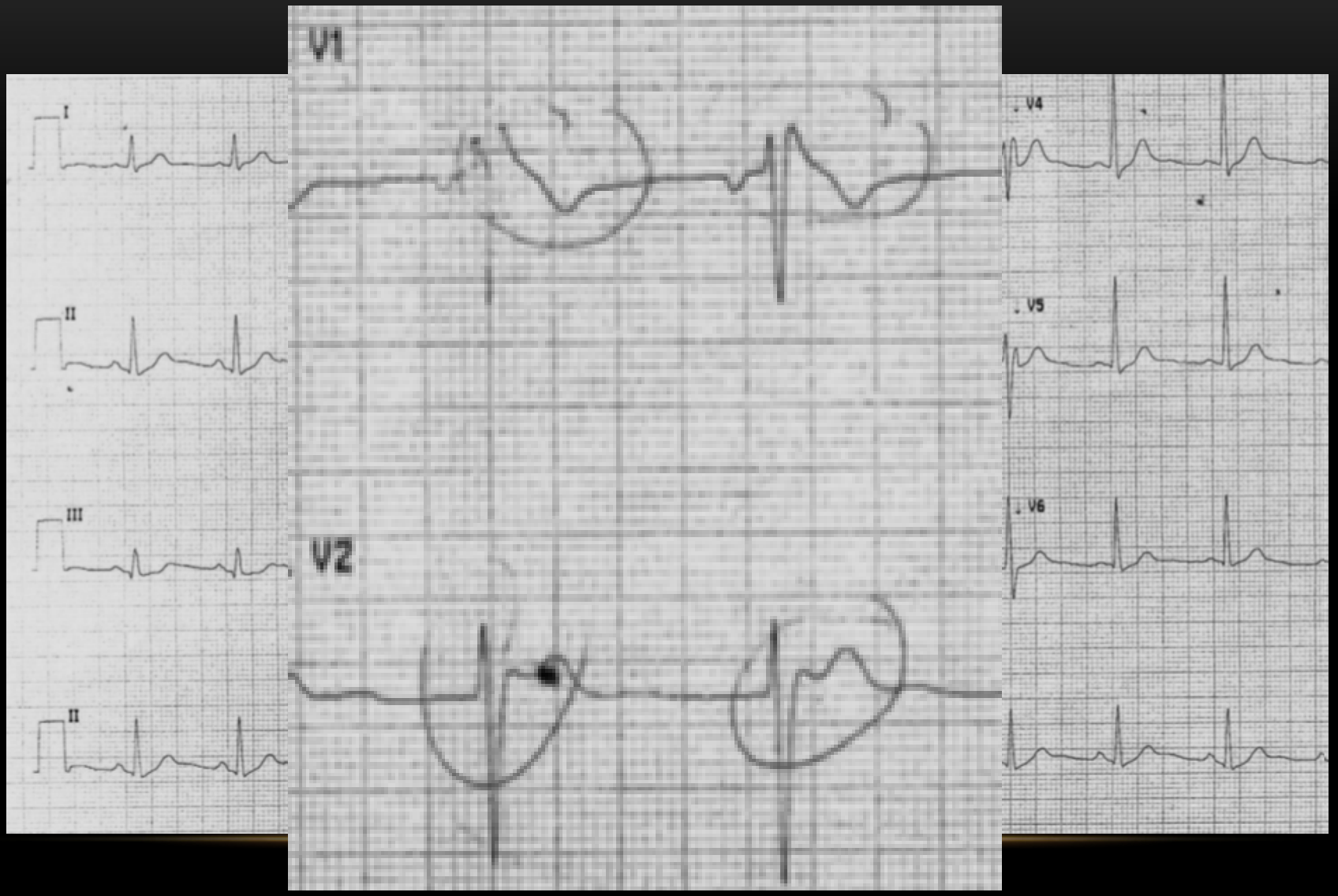
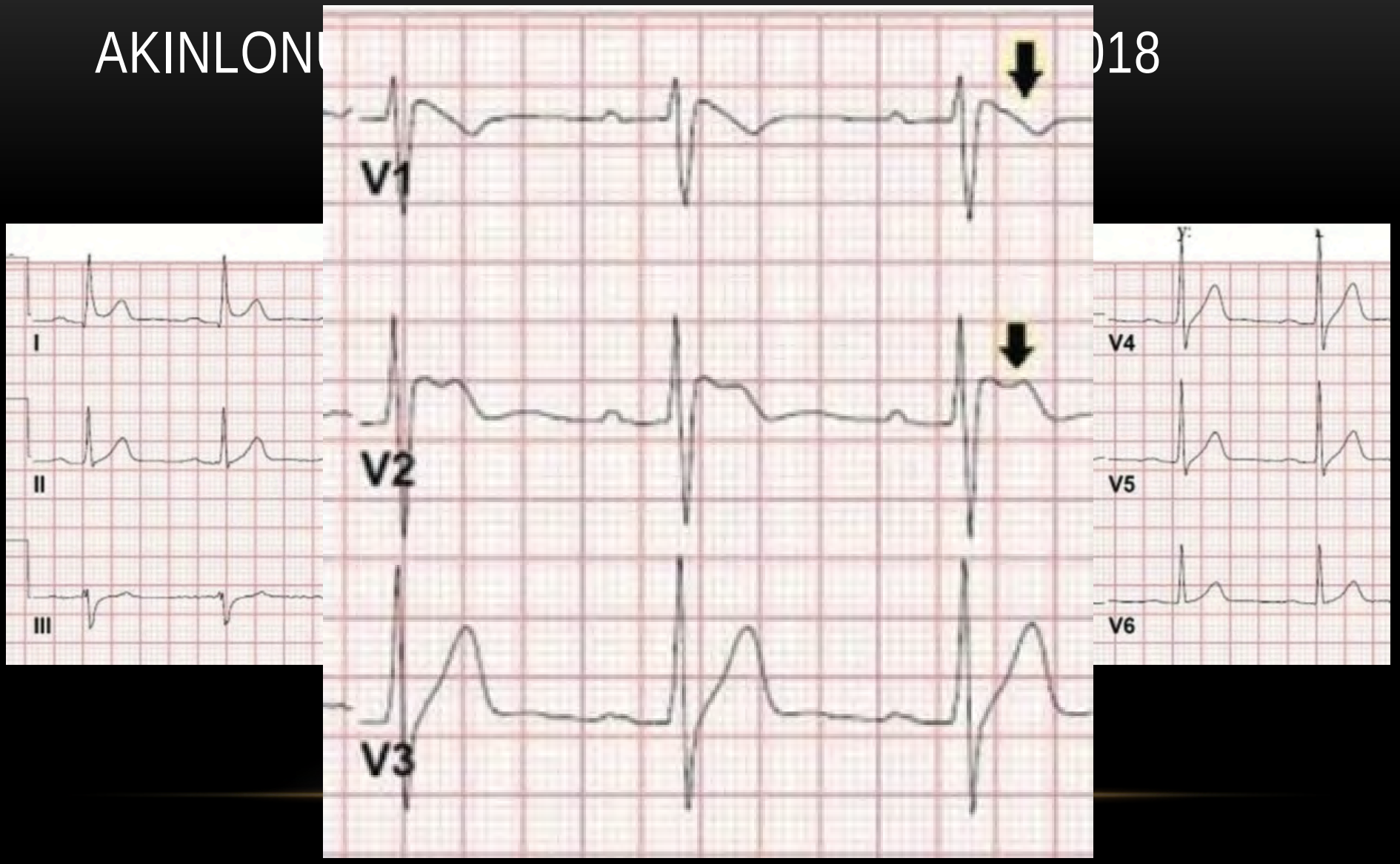


Figure 2. Electrocardiogram (V_1-V_3 leads). A and B, type I Brugada pattern that appeared at 2 visits in the emergency room after cannabis exposure. C and D, electrocardiogram in the outpatient clinic, no recent use. In D, the V_1 and V_2 leads were raised to the second intercostal space and type III Brugada pattern was observed. E, V_1-V_3 leads during flecainide infusion; type I Brugada pattern.

VALLE ET AL, AM J EMERG MED, 2016



AKINLONU 018



KARIYAN 018

5 CASE REPORTS: CANNABIS-INDUCED BRUGADA-LIKE T WAVE CHANGES

- (2007) 19 yo male – presented with syncope
  - Normal baseline ECG. Procainamide infusion test NEGATIVE
- (2012) 42 yo male – (+) palpitations and PVCs (RVOT origin)
  - Normal baseline ECG. Flecainide infusion test POSITIVE
- (2016) 19 yo male – (+) palpitations, dizziness
  - Normal baseline ECG. Flecainide infusion test NEGATIVE
- (2018) 49 yo male – (+) palpitations
  - Normal baseline ECG. Declinced provocative drug testing
- (2018) 36 yo male – (+) chest pain. Troponins negative.
  - Normal baseline ECG. Procainamide infusion test NEGATIVE

CANNABIS AND ION CHANNELS

BJP British Journal of Pharmacology

Br J Pharm 2014

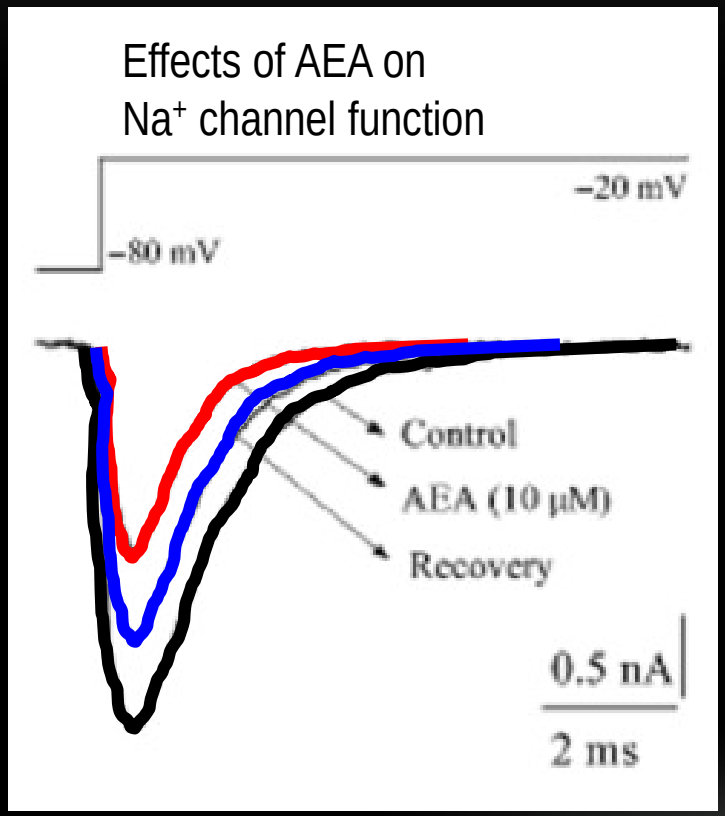
RESEARCH PAPER

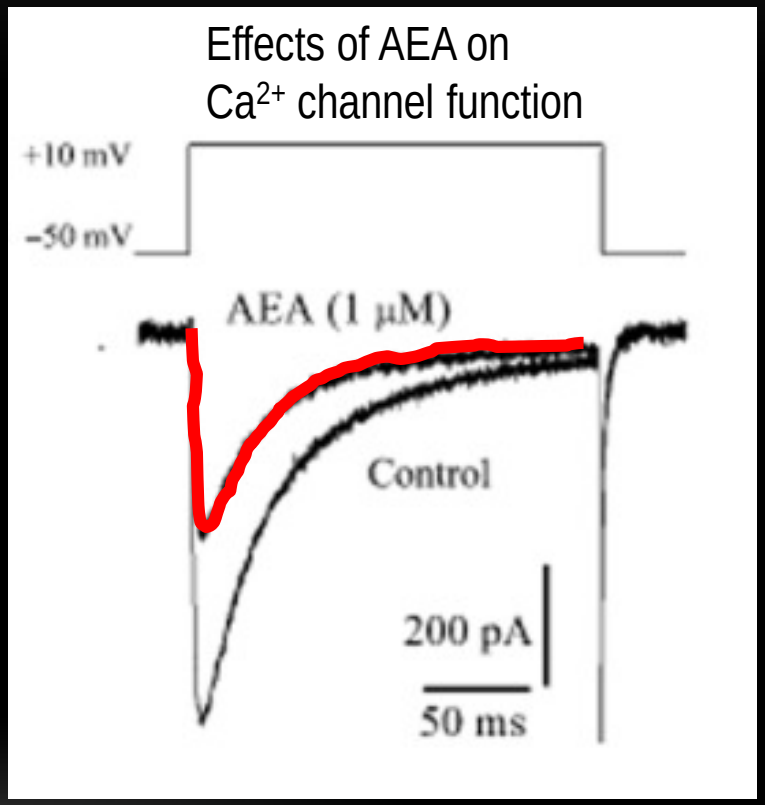
Effects of the endogenous cannabinoid anandamide on voltage-dependent sodium and calcium channels in rat ventricular myocytes

Lina T Al Kury[1], Oleg I Voitychuk[2], Keun-Hang Susan Yang[3], Faisal T Thayyullathil[4], Petro Doroshenko[1], Ali M Ramez[1], Yaroslav M Shuba[2], Sehamuddin Galadari[4], Frank Christopher Howarth[5] and Murat Oz[1]

[1]*Laboratory of Functional Lipidomics, Department of Pharmacology, UAE University, Al Ain, UAE,* [2]*Bogomoletz Institute of Physiology and International Center of Molecular Physiology, National Academy of Sciences of Ukraine, Kyiv, Ukraine,* [3]*Department of Biological Sciences, Schmid College of Science and Engineering, Chapman University, One University Drive, Orange,*

AL KURY ET AL, BR J PHARM 2014

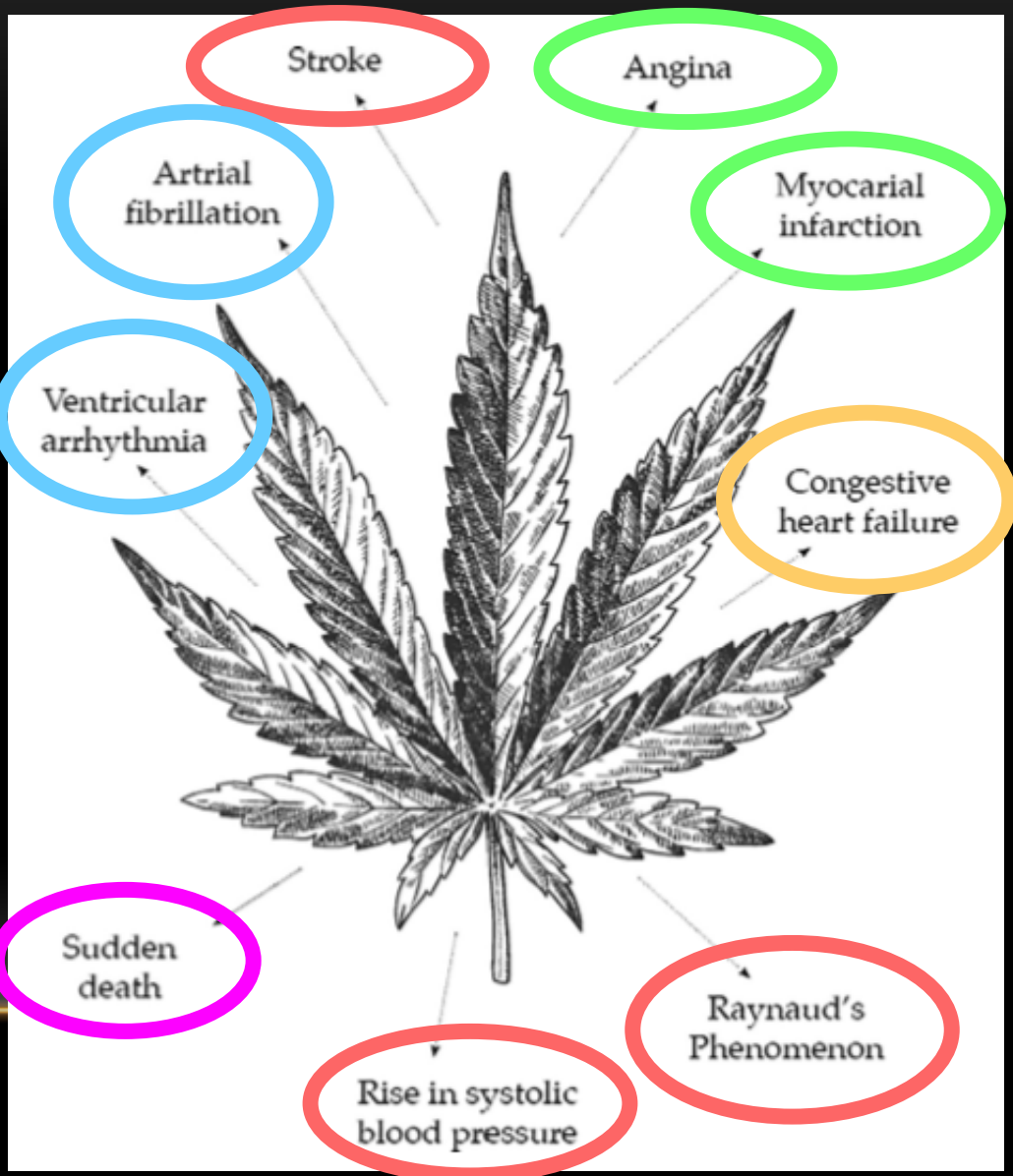




SOME EVIDENCE THAT CANNABINOIDS CAN INFLUENCE CARDIAC ION CHANNEL FUNCTION

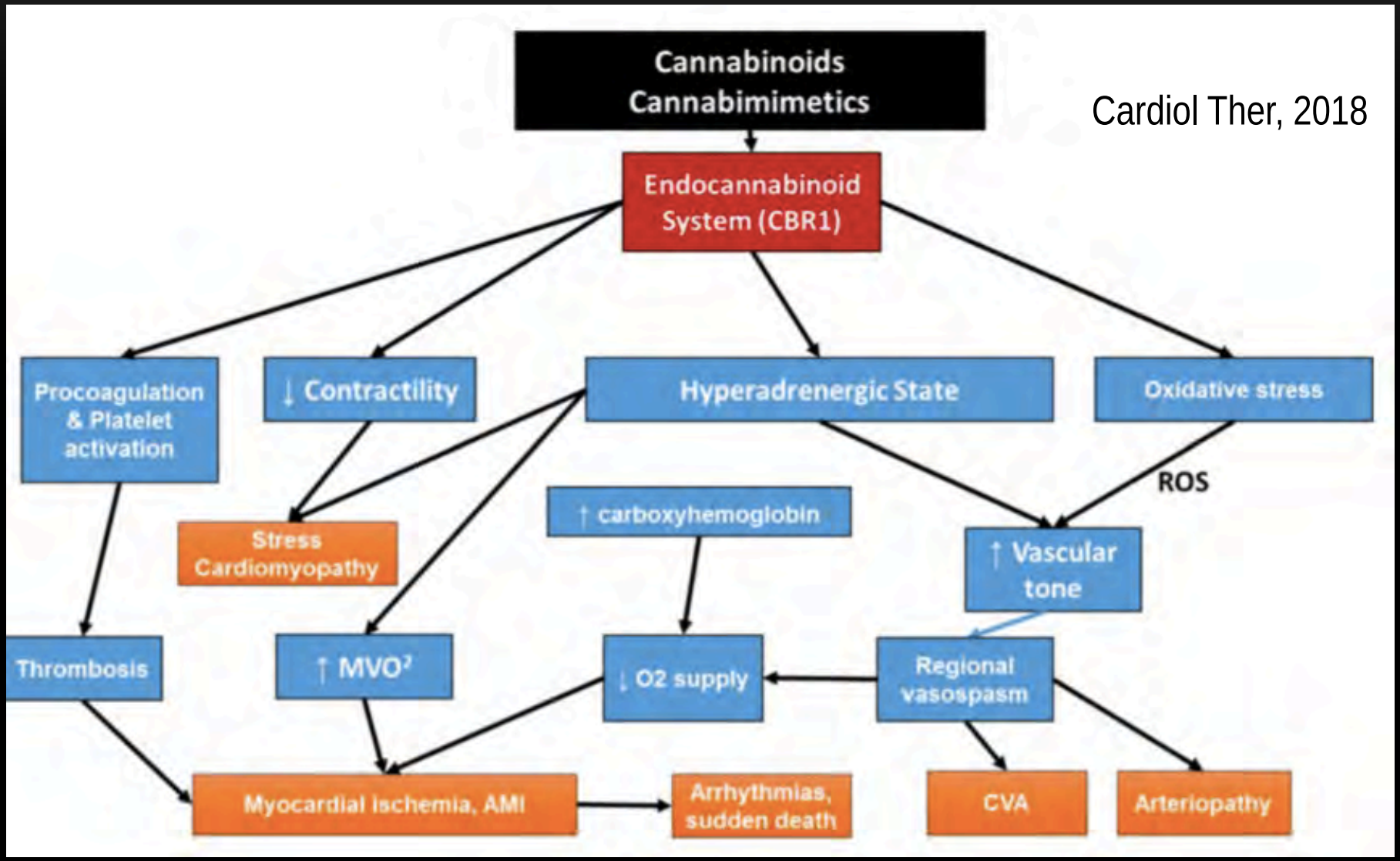
CANNABIS EFFECTS ON THE HEART

- Vascular
- Myocardial dysfunction
- Ischemia
- Arrhythmias
  - Atrial
  - Ventricular
  - Asystole
- Ion channel dysfunction



Trends CV Med, 2018

CANNABIS EFFECTS ON THE HEART

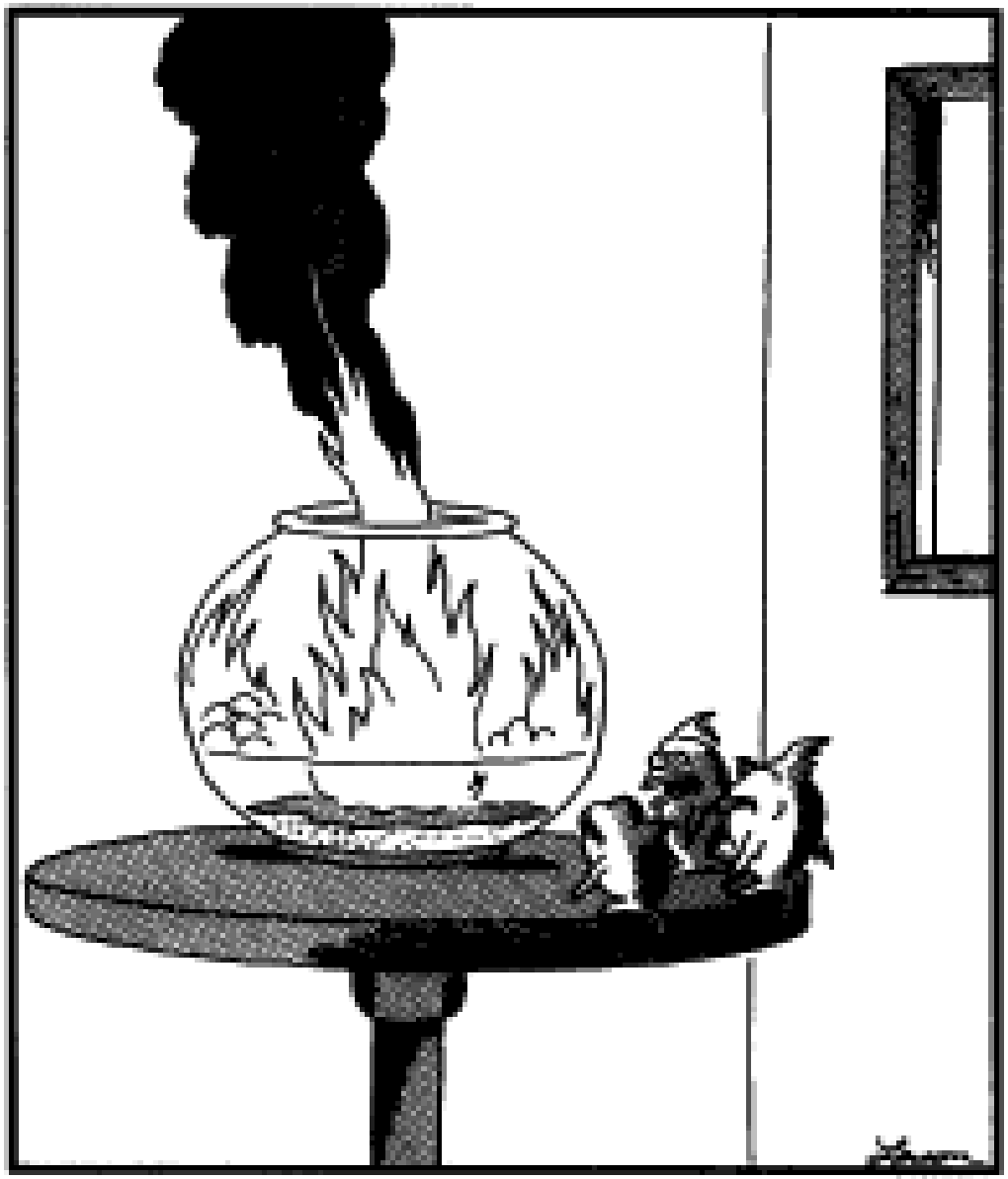


BACK TO OUR PATIENT: 16 YO MJ USER WITH SYNCOPE, PVCS

- Admitted to PICU, serial troponins negative
- PVCs persisted while abstaining in PICU x 2 days
- No Brugada pattern on ECG
- DC’d on atenolol
- No further syncope
- Holters show 8-10% ectopy burden
- Ectopy suppressed on treadmill testing
- Continues to smoke marijuana

CANNABIS AND ARRHYTHMIAS: TAKE HOME POINTS

- Do an H & PE!!
- Myocardial ischemia – a real thing!
- Arrhythmias
  - MI-related
  - Virtually every arrhythmia has been reported as occurring after cannabis use
- Concern for sudden death
  - Repeated observations of Brugada-like ECG
  - More research needed
- More clinical experience surely to come!!



Well, thank God we all made it out in time...