



Kratom tree

MARCH 21, 2018



Prehospital

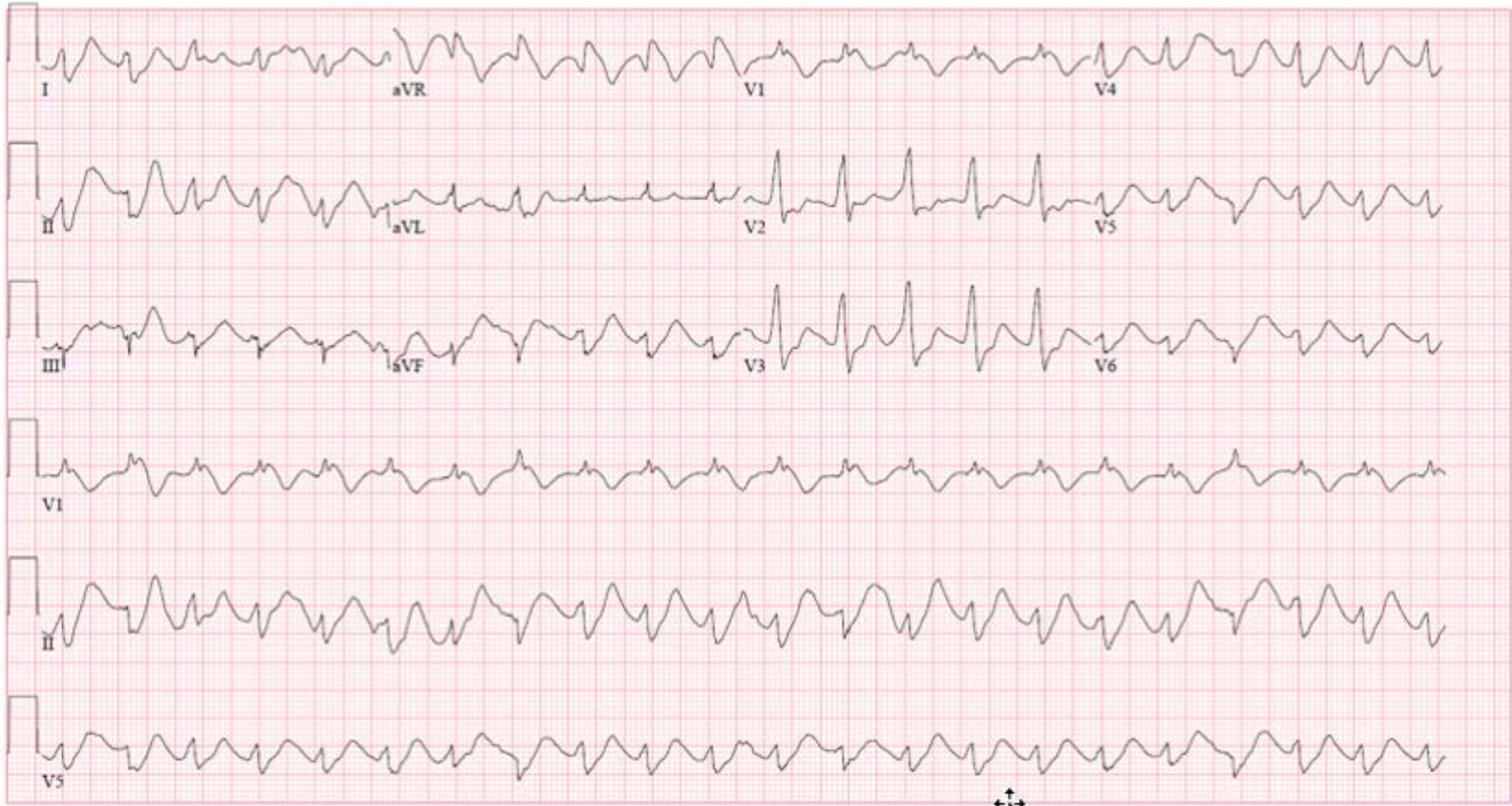
- **With family**
 - 23 y/o male having dinner with family at restaurant
 - Altered mental status and abnormal motor activity, ? seizure, “collapse” to floor
 - Unresponsive, apneic, pulseless
 - CPR initiated

- **Per EMS**
 - Intermittent, pulseless V-tach, PEA reported
 - CPR, defibrillation x 2-4, epinephrine 1 mg x 4
 - Bradycardia treated with atropine 0.5 mg
 - CPR en route to hospital

ED

- On arrival at 21:15, CPR in progress
- Pulse present following transfer from ambulance stretcher to ED stretcher
- Tachycardia, vomited
- Endotracheal intubation
- ECG
- Meds
 - Midazolam, ondansetron, sodium bicarbonate (100mEq)
 - Levetiracetam, dexamethasone, hydromorphone
 - Propofol, after patient beginning to follow commands
 - No antidysrhythmics

February 5, 2018
21:23



Notable Labs

- **ED 2/5/18**

- **21:24** Blood gas pH 6.85/pCO₂ 84/pO₂/106/HCO₃ 15/O₂ Sat 90%
K⁺ 3.2, glucose 301
- **21:30** Lactate > 13, Cr 1.93, AST/ALT 173/190, CK 2,989
- **22:14** UTox (IA) presumptive positive benzodiazepines

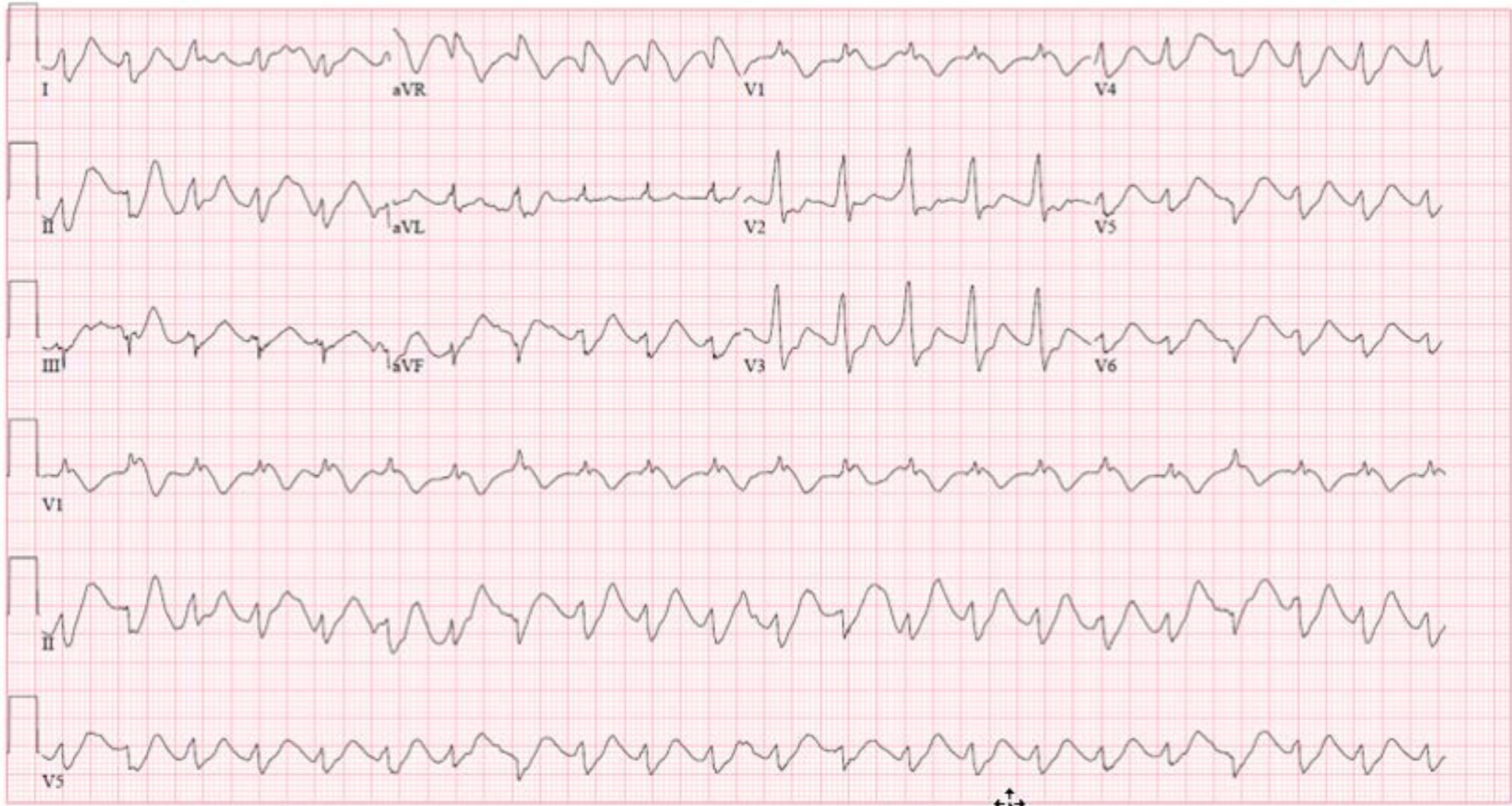
- **ICU 2/6/18**

- **0106** Blood gas pH 7.35, lactate 1.5
- **0428** Improving- All including LFTs, Cr, glucose

Inpatient Hospital Course

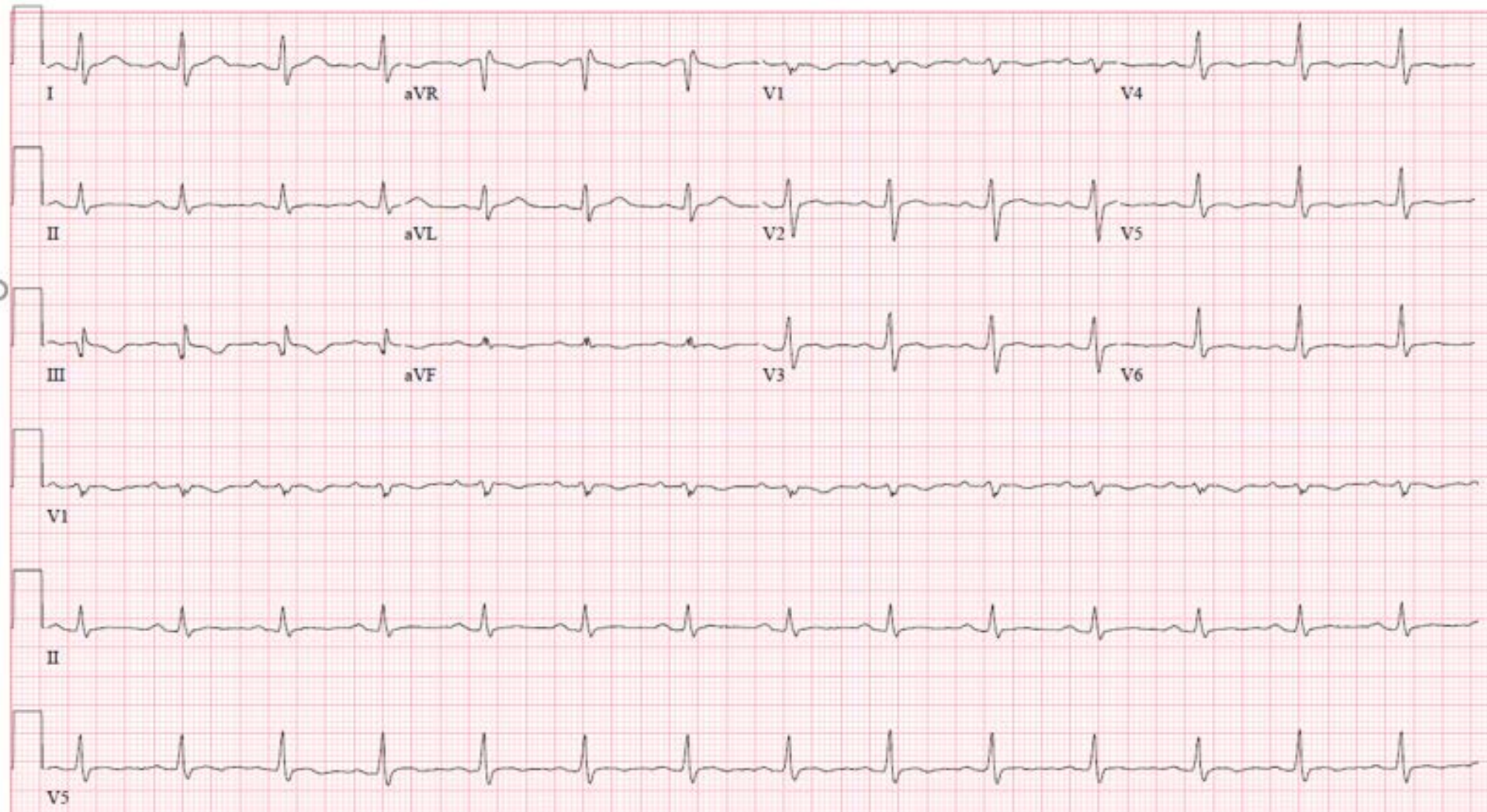
- **ICU**
 - Repeat ECG
 - Extubated, approximately 5 hours after hospital arrival
 - Denies drug overdose
 - Reports frequent Kratom and Robitussin[®] use
- **General Cardiac Floor**
 - Prehospital rhythm strips obtained

February 5, 2018
21:23



February 6, 2018

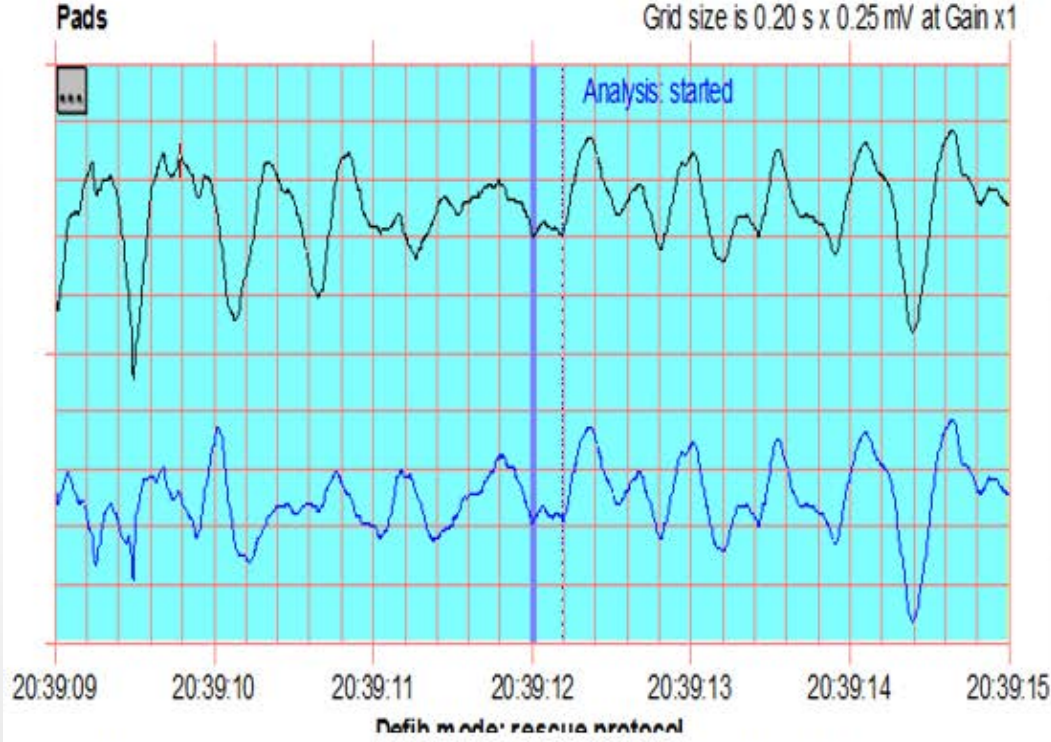
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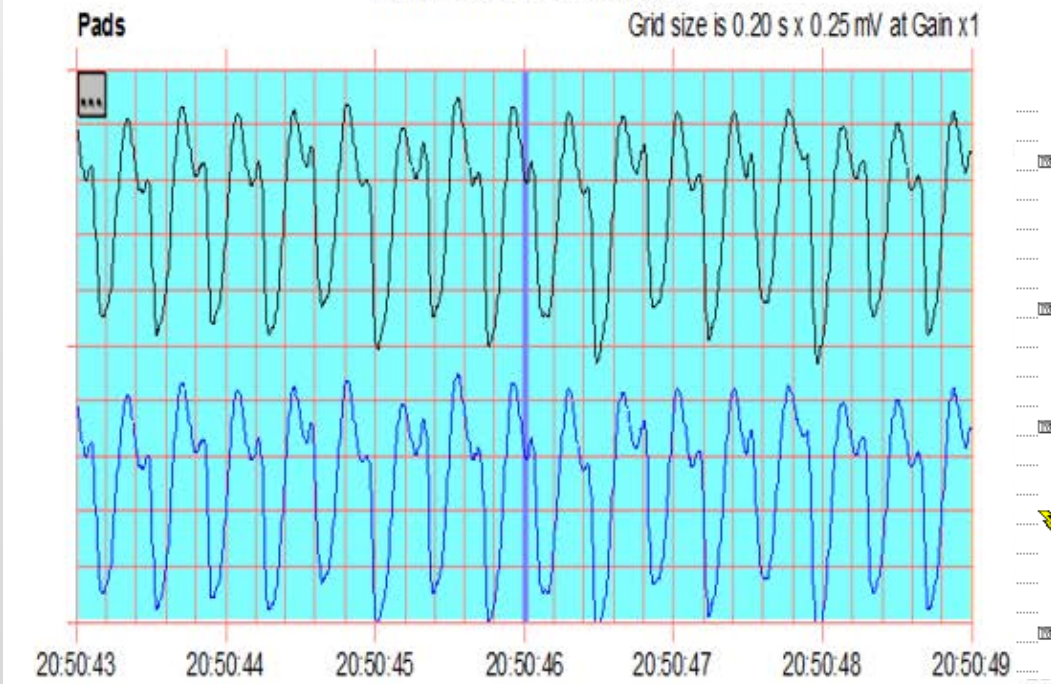
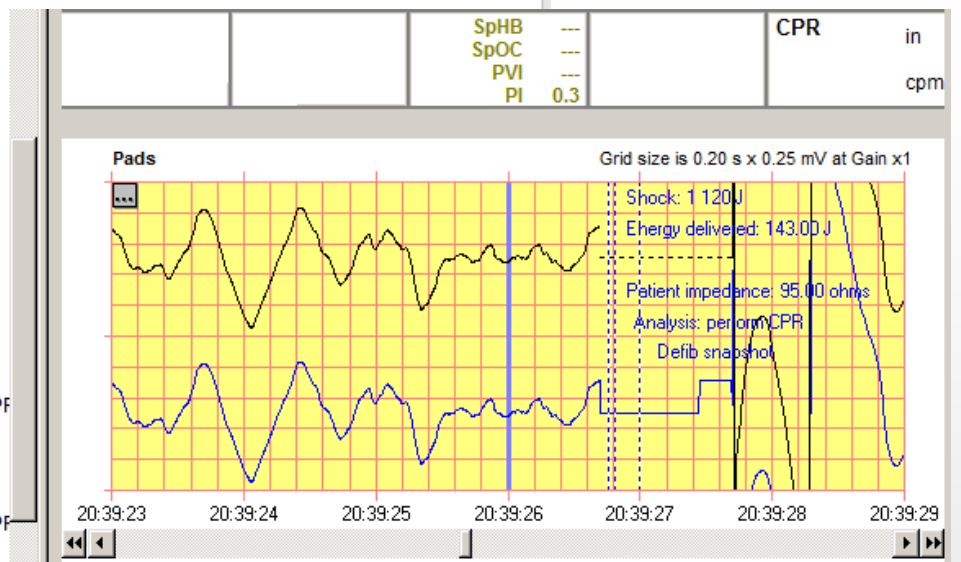
PMHx and Meds

- **PMHx**
 - Asthma – Exercised-induced
 - ADHD
 - Anxiety
 - Major depressive d/o
 - Per patient – Irritable bowel symptoms
- **PTA Meds – Takes as directed**
 - Albuterol MDI
 - Bupropion XL 300 mg since second week Jan 2018/Prior 150 mg since Dec 2017/Previously in 2010
 - Cimetidine prn
 - Clonazepam 0.5 mg BID prn (takes in this manner most days x few years)
 - Methylphenidate ER 54 mg daily

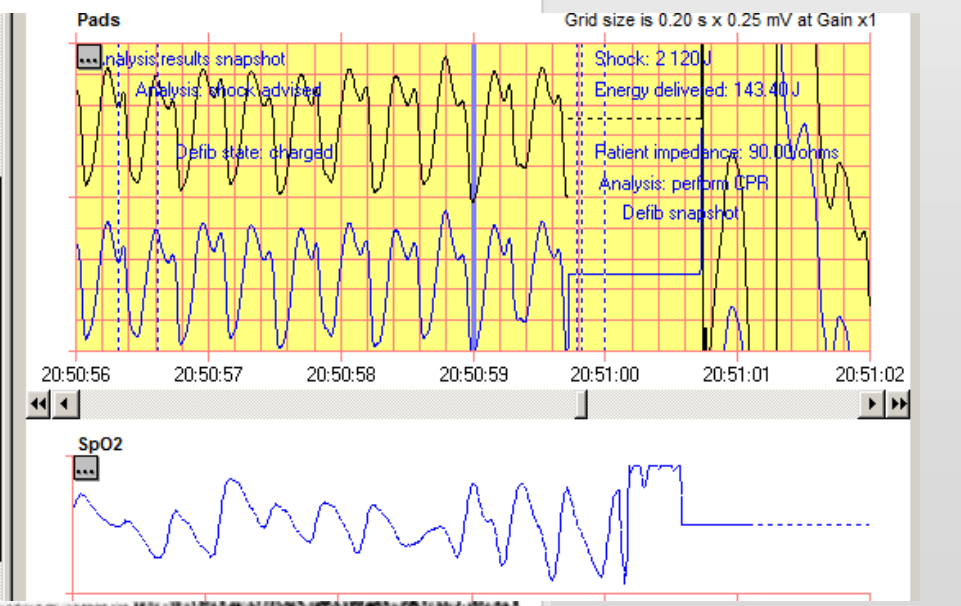
Prehospital Rhythm Strips



- 20:39:21 Analysis: shock advised
- 20:39:21 Defib state: charged
- 20:39:26 Shock: 1 120 J
- 20:39:26 Energy delivered: 143.00 J
- 20:39:26 Patient impedance: 95.00 ohms
- 20:39:26 Analysis: perform CPR
- 20:39:27 Defib snapshot
- 20:41:20 C: EVENT
- 20:41:21 Treatment snapshot
- 20:41:26 Analysis: stop CPR
- 20:41:31 Analysis: started
- 20:41:37 Analysis results snapshot
- 20:41:37 Analysis: no shock advised
- 20:41:37 Analysis: if no pulse, perform CPF
- 20:43:36 Analysis: started
- 20:43:42 Analysis results snapshot
- 20:43:42 Analysis: no shock advised
- 20:43:42 Analysis: if no pulse, perform CPF
- 20:45:42 Analysis: stop CPR



- 20:47:53 Analysis: stop CPR
- 20:47:58 Analysis: started
- 20:48:04 Analysis results snapshot
- 20:48:04 Analysis: no shock advised
- 20:48:04 Analysis: if no pulse, perform CPF
- 20:50:04 Analysis: stop CPR
- 20:50:09 Analysis: started
- 20:50:15 Analysis results snapshot
- 20:50:15 Analysis: no shock advised
- 20:50:15 Analysis: if no pulse, perform CPF
- 20:50:50 Analysis: started
- 20:50:56 Analysis results snapshot
- 20:50:56 Analysis: shock advised
- 20:50:56 Defib state: charged
- 20:50:59 Shock: 2 120 J
- 20:50:59 Energy delivered: 143.40 J
- 20:50:59 Patient impedance: 90.00 ohms
- 20:50:59 Analysis: perform CPR
- 20:51:00 Defib snapshot
- 20:52:59 Analysis: stop CPR



Additional Studies

- **ED 2-5-18 ~2200**
 - CXR – Poor inspiration, pulmonary vascular congestion, sharp angles/Interstitial pulmonary edema likely
 - Head CT – Negative
- **ICU 2-6-18 ~0930**
 - CXR – Improved aeration, post-extubation
- **General Floor 2-6-18**
 - Brain MRI – Negative
- **General Floor 2-7-18**
 - Cardiac Echo – Normal
- **General Floor 2-9-18**
 - CT Angiogram Coronary Arteries (IP) – No coronary anomaly
 - CT Chest – Dependent atelectasis bilaterally
 - MR Cardiac Function – Normal
- EEG planned OP, unable to perform inpatient due to patient discomfort

SHx

- College – Chemistry major
- Substance use
 - THC – Smokes frequently, “heavily” in high school
 - Kratom – Near daily, subsequently reported more than once a day, IV “once or twice”
 - Robitussin[®] – Frequent, ingests “like water”
 - EtOH – Occasional, “not like the way [he] feels the day after heavy use
 - Cigar smoking – Occasional, no cigarettes
- “Recreational” and “Experimental” use
 - Cocaine
 - Ethylphenidate–“Sometimes . . . rather than misusing prescriptions”
 - NBOMe
 - Opioids – Codeine and hydrocodone/APAP – Has used, limits to avoid excessive APAP exposure
 - IV drug use – Rare, “tried”

Delivered by mail from China to patient
? WI versus MN versus ND



Course – February 5 through February 16, 2018

- Continued chest discomfort, due to CPR and ICD placement
- Analgesia continued throughout hospitalization (Initially prn and later scheduled + prn)
 - APAP
 - NSAIDS
 - Opioids
 - Lidoderm® patch
- Consults
 - Cardiology, interventional and EP
 - Toxicology
 - Gastroenterology
 - Chemical dependency counselor – pt declined, resources provided in written discharge instructions
- Evaluation
 - Cardiac work-up found no underlying structural cause
- Procedures
 - 2-13-18 ICD Placement– subcutaneous
 - 2-14-18 ICD lead revision

DEA - *Mitragyna speciosa* (Rubiaceae family)



Kratom tree



Leaf of kratom tree



Kratom capsules

Indigenous to Thailand, Malaysia, Myanmar, Papua New Guinea, others



DrugFacts

www.drugabuse.gov

Kratom

What is kratom?

Kratom is a tropical tree (*Mitragyna speciosa*) native to Southeast Asia, with leaves that contain psychoactive (mind-altering) opioid compounds. The tree's bitter leaves are consumed for mood-uplifting effects and pain relief and as an aphrodisiac.

Kratom is not currently an illegal substance and has been easy to order on the Internet in recent years. It is sometimes sold as a green powder in packets labeled "not for human consumption." It is also sometimes sold as an extract or gum.



Photo by DEA/www.dea.gov/pr/multimedia-library/publications/drug_of_abuse.pdf#page=84

In recent years, some people have used kratom as an herbal alternative to medical treatment in attempts to control withdrawal symptoms and cravings caused by addiction to other opioids or to other addictive substances such as alcohol. There is no scientific evidence that kratom is effective or safe for this purpose (see "Medication-Assisted Treatment").

Kratom sometimes goes by the following names:

- Herbal Speedball
- Biak-biak
- Ketum
- Kahuam
- Ithang
- Thom



- Formulations
 - Leaves
 - Powder
 - Pills
 - Leaves
 - Liquid extract/tinctures
- Route
 - Drink
 - Chew leaves
 - Smoke
 - Ingest pills

Kratom-Pharmacodynamics*

- **Mitragynine** and **7-hydroxymitragynine** are the two active components of at least 25-40+ alkaloids
 - Mitragynine - 13 X potency of morphine in regards to opioid-like effects
 - 7-hydroxymitragynine - 4 X more potent in CNS stimulant and depressant effects than mitragynine
- **Opioid-like Effects**
 - *Full versus partial agonist and agonist versus antagonist*
 - Kappa-opioid (highest affinity)
 - Mu-opioid agonist
 - Delta-opioid
- **Stimulant Effects**
 - Stimulation of post-synaptic Alpha-2 receptors
 - Serotonin-Stimulation of 5-HT_{2A}
- Inhibit neuronal Ca²⁺ channels
- **Cardiac Effects** (QT prolongation, dysrhythmia)
 - Rapid delayed rectifier potassium current I_{kr}
 - Concern for sodium channel blockade (not documented)

*Varying reports

Kratom-Pharmacokinetics (Mitragynine)

- Human (N=10), ingested, tea (unless specified)
- Onset approx. 10-20 minutes after “use” of leaves, full effect 30-60 minutes after ingestion
- Time to maximum plasma concentration 0.83 (+/- 0.35) hour
- Duration of action 2-5 hours after “use” of leaves
- $t_{1/2}$ 23.24 (+/- 16.07) hours
- Vd 38.04 (+/- 24.32) L/kg
- Metabolism (in vitro)
 - Hepatic – phase I and II
 - Cytochrome P450 Interactions – Inhibitory CYP3A4, CYP2D6 > CYP1A2 > CYP2C19
 - P-glycoprotein inhibition
- Lipophilic and poorly water soluble (in vitro)

Reported Uses

Southeast Asian Countries

- Enhanced tolerance for work, reduce fatigue
- Analgesic
- Social and religious functions
- Self-treatment of opioid withdrawal
- Wound healing
- Aphrodisiac
- Recreational
 - Thailand 4 X 100 = cough syrup, kratom leaves, cola, ice

Western Countries

- Analgesic
- Self-treatment of opioid addiction/withdrawal
- Recreational
 - Krypton = O-desmethyltramadol + kratom
- Mood enhancer, antidepressant
- Increase energy levels
- Increase alertness
- Increase sociability
- Reduce anxiety
- Reduce stress
- Sleep aid
- Muscle relaxant
- Anti-inflammatory
- Anorectic
- Antidiarrheal

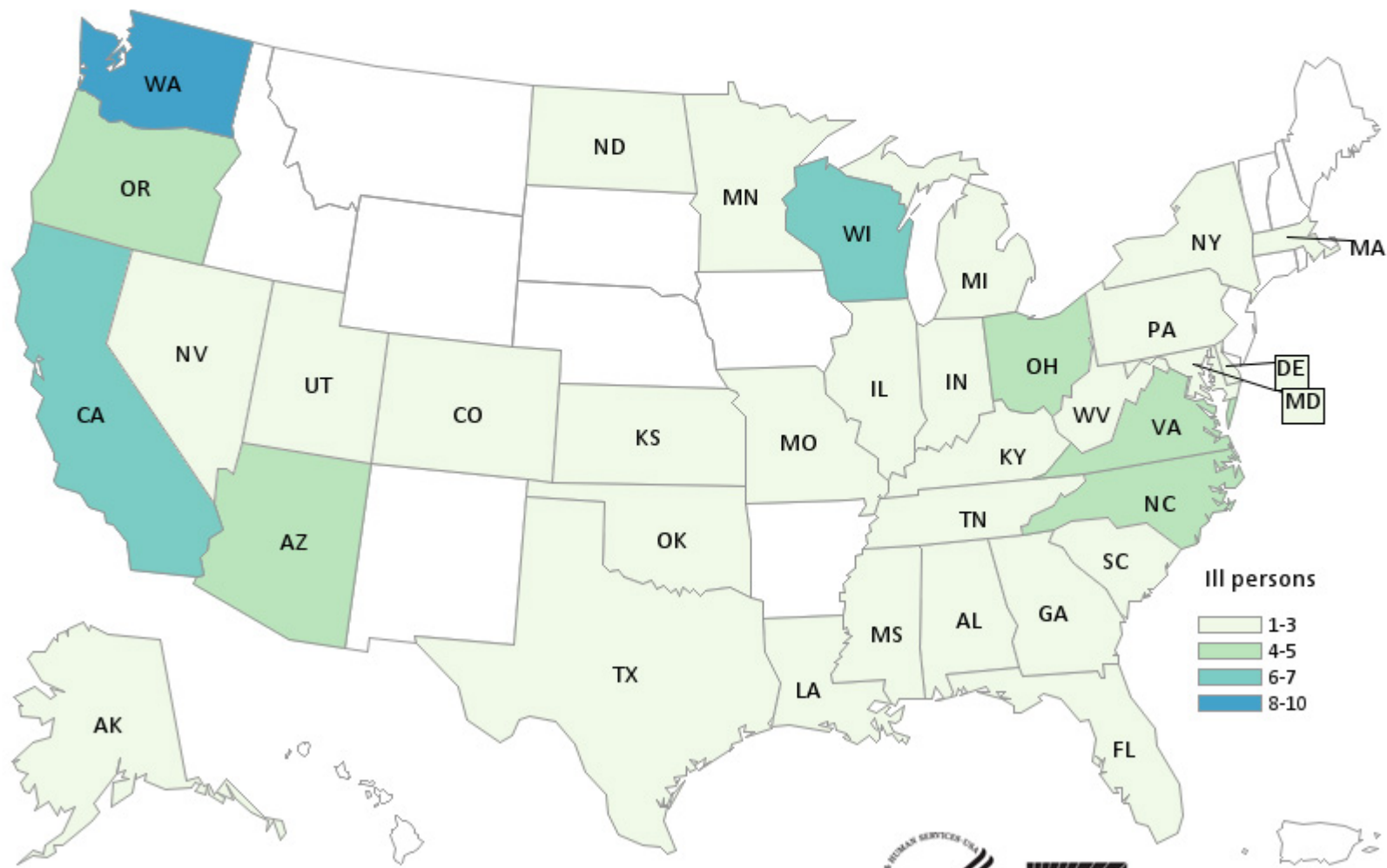
Effects

- **Dose-dependent (and likely strain dependent)**
 - Stimulant at low/moderate doses: 1-5 grams of raw leaves euphoric effects
 - Opioid-like at high doses: 5-15 grams (initial stimulant effects such as tachycardia, lower respiratory depressant effects)
- **Adverse (serious only reported in Western countries)**
 - Anorexia, dry mouth, nausea, weight loss, insomnia, urinary frequency, constipation, sweating, hyperpigmentation
 - Hepatic injury
 - Hallucinations, delusions, confusion
 - Seizure
 - e.g. modafinil
 - Cardiac
 - QT prolongation
 - Dysrhythmia, suspect TdP
 - In presence of some antidepressants
 - Death reported
 - Usually in presence of other substances e.g. SSRI, SNRI, benzodiazepine, diphenhydramine, ethanol, *Datura stramonium*, morphine, fentanyl, carisoprodol, caffeine, Krypton
- **Tolerance**
- **Withdrawal (Dependence/addiction-controversial)**
 - Emotional lability, irritability, insomnia, rhinorrhea, body aches, diarrhea, jerking movements

Case Count Maps

Posted March 15, 2018 4:45 PM ET

People infected with the outbreak strains of *Salmonella*, by state of residence, as of March 14, 2018 (n=87)



Department of Health



News Release: Salmonella cases linked to consuming kratom


Minnesota Department of Health sent this bulletin at 03/16/2018 09:15 AM CDT

Salmonella cases linked to consuming kratom

Plant used as stimulant, opioid substitute but should not be consumed in any form

Regulation

- Legal most countries
- Banned
 - Thailand
 - Myanmar
 - Malaysia
 - Australia
 - United Kingdom
 - Parts of United States



AMERICAN KRATOM ASSOCIATION

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March 07, 2018

The AKA and BEA will be working together for the common goal of saving kratom

"You can do what I cannot do. I can do what you cannot do. Together we can do great things" - Mother Theresa

Over the years, many questions have been positioned to us as to why this hasn't been done. While there may have been differences in the past on which paths to take, at the end of the day in our hearts we know the destination is the same for each of our organizations. We all want kratom to be legal for the community and in doing so for people to have the right to live better lives. No more, no less.

The AKA and BEA will be working together for the common goal of saving kratom in America.

This week there are two critical state actions on kratom that require the attention of the kratom community, in Kansas and Tennessee. The American Kratom Association (AKA) and the Botanical Education Alliance (BEA) both agreed to collaborate in each respective state. Resources and lobbying efforts in will be provided by the AKA for Kansas and by the BEA for TN. We believe this allows us to more efficiently allocate our resources and achieve our goals to protect consumer access to kratom.

The Kansas House Health and Human Services Committee will hold a Hearing today at 1 PM to address SB 282, a bill that will add kratom to the Kansas controlled substances list. On Monday, the Committee held an informational Hearing where the AKA was represented by Mac Haddow, our chief lobbyist, and following which Committee Chairman Daniel Hawkins committed to proposing an amendment to strip kratom from the proposed legislation.

In Tennessee, after a strong testimony from BEA board members Travis Lowin, Angela Watson, and 3 members of the kratom community, the Health Committee voted 6-3 to remove kratom from bill HB #1832. There is another hearing next week where the BEA will be attending to testify again in order to ensure the language does not get added back in the bill.

The AKA and BEA are committed to working together in these two states, and others, as we continue our fight for the right of consumers to make their own decisions on their health and well-being.

FDA Statement

Statement from FDA Commissioner Scott Gottlieb, M.D. on FDA advisory about deadly risks associated with kratom

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FDA Statement

For Immediate Release November 14, 2017

Statement from FDA Commissioner Scott Gottlieb, M.D., on the agency's scientific evidence on the presence of opioid compounds in kratom, underscoring its potential for abuse

Summary The FDA has issued regarding risks assoc

Additional adverse events associated with kratom use identified

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For Immediate Release February 6, 2018

FDA News Release

Summary FDA releases adverse events and sole evidence of kratom compounds' opioid

FDA oversees destruction and recall of kratom products; and reiterates its concerns on risks associated with this opioid

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For Immediate Release February 21, 2018

FDA In Brief: FDA objects to kratom compound intended for use as an alternative to prescription opioids and promoted with unproven claims to treat addiction

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For Immediate Release: Feb. 26, 2018

FDA Investigates Multistate Outbreak of Salmonella Infections Linked to Products Reported to Contain Kratom

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March 2, 2018

FDA

Regulation-United States

- FDA not approved for any medical use and advised against consumers use
- DEA
 - 2015 Labeled “drug of concern”
 - 2016 Initially listed in Schedule I Drug category, decision withdrawn
- State Bans
 - Alabama, Arkansas, Indiana, Vermont, Rhode Island, Wisconsin, Tennessee
 - Sarasota County, Florida/San Diego, California/Jerseyville, Illinois/Denver, Colorado
 - Age restrictions in Illinois, New Hampshire, New York
- Minnesota
 - Legal
 - Bill being considered that would make gross misdemeanor to sell kratom to those under 18 y/o

Case Follow-Up

- Phone calls to clinics
- Office visits (primary physician and electrophysiologist)
- EEG – Negative
- Compliance drug test, confirmatory from February 5, 2018
 - Positives
 - Methylphenidate
 - Midazolam
 - Bupropion
 - Negatives: Clonazepam, guaifenesin etc
 - Clonazepam and 7-aminoclonazepam cut off 50 ng/mL
 - Guaifenesin (parent only) cut off 300 ng/mL
- MDH samples ordered from February 5, 2018, testing pending

Follow-up: Readmission March 4, 2018









- **Prehospital**
 - In street, requesting assistance because of “pain from defibrillator firing”
- **ED Course**
 - ICD interrogation – no firing events
 - Admission due to altered mental status and tachycardia
 - Reported use of synthetic cannabinoid, kratom, and poppy seed extract
- **Hospital Course**
 - Mental status cleared
 - Telemetry – no ICD firing, patient describes recurrent discomfort as experienced prior to admission
 - Urine drug (hospital) – presumptive positive opiates
- **Discharged March 2, 2018 with diagnosis: Drug-induced delirium**
- **PDMP Accessed March 12, 2018– Recent prescriptions**

▪ 2-23-18	Clonazepam 0.5 mg #60, methylphenidate ER 54 mg #30	ND
▪ 2-22-18	Hydrocodone/APAP 5/325 mg # 10	MN
▪ 2-19-18	Hydrocodone/APAP 5/325 mg # 8	MN
▪ 2-16-18	Hydrocodone/APAP 5/325 mg # 20	MN
▪ 1-15-18	Clonazepam 0.5 mg #60, methylphenidate ER 54 mg #30	ND

Additional Questions/Considerations

- Suggestions for treatment for opioid use
 - Options
 - Transition from full opioid agonists, post-procedure pain control
 - Outpatient availability
- Communication with outpatient clinicians
 - Protected health information versus Safety concerns
- Placement of ICD
 - Controversial
- Regulation of kratom
 - South East Asian countries versus Western countries reports
 - Risks versus potential benefits, potential harm reduction tool

Kratom Powder

	Maeng Da Kratom COASTLINE KRATOM	SHOP NOW
	Red Thai Kratom COASTLINE KRATOM	SHOP NOW
	Red Bali Kratom COASTLINE KRATOM	SHOP NOW
	Green Malay Kratom COASTLINE KRATOM	SHOP NOW
	Green Borneo Kratom COASTLINE KRATOM	SHOP NOW
	White Borneo Kratom COASTLINE KRATOM	SHOP NOW
	Premium Indo Kratom COASTLINE KRATOM	SHOP NOW
	Ultra Enhanced Indo COASTLINE KRATOM	SHOP NOW

Reporting



1-800-222-1222

Minnesota Poison Control System



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