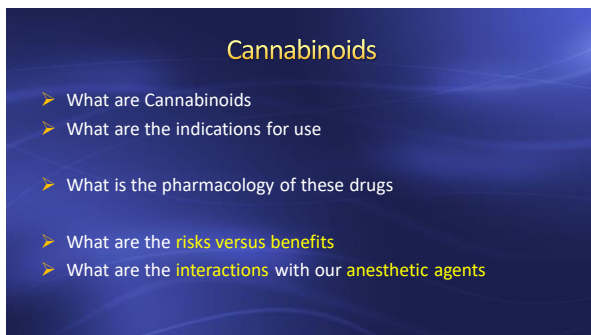




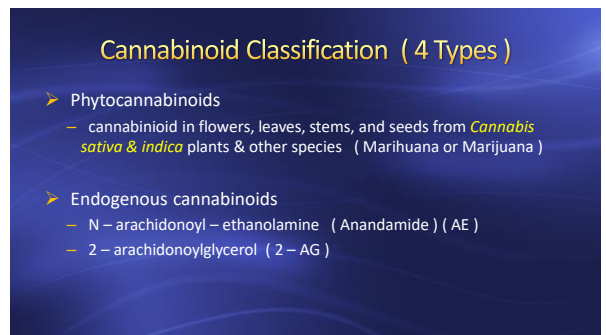
1



2



3



4

## Cannabinoid Classification ( 4 Types )

- Purified naturally occurring Cannabinoids
  - plant derived, purified compounds
  - delta – 9 – tetrahydrocannabinol ( THC )
  - cannabidiol ( CBD )
  - Sativex ( CBD + THC ) & Epidiolex ( CBD ) → purified extract medications
- Synthetic Cannabinoids
  - synthetic medications → Dronabinol & Nabilone ( Rx meds )
  - synthetic THC ( K2 or spice )

National Institute on Drug Abuse

5

## Endocannabinoid System

- Neurotransmission system identified in early 1990s
  - G – protein – coupled cannabinoid receptors ( CB 1 & CB 2 )
  - endocannabinoids to bind to receptors CB 1 and CB 2
    - N – arachidonoyl – ethanolamine ( Anandamide )
    - 2 – arachidonoylglycerol ( 2 – AG )
- System is therapeutic target for numerous physiologic conditions
  - appetite stimulation, pain modulation, blood pressure, N/V, memory, learning, coordination, GI motility, and immune response

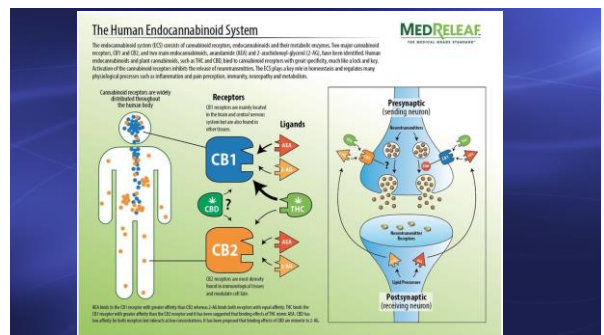
6

## Endocannabinoid System

- Potential treatment target for pathological conditions
  - Parkinson's Disease
  - Huntington's Disease
  - Alzheimers and Multiple Sclerosis
- Plant cannabinoids & synthetic cannabinoids activate this system
  - Marijuana, THC, CBD, Dronabinol, Nabilone, K2 & spice

Acta Pharmacologica Sinica. 2019;40:297-299

7



8

## CB 1 Receptors

- Concentrated in the Brain
  - cortex → orbitofrontal cortex: form new memories & shift focus
  - hippocampus → memory storage
  - cerebellum → balance, posture, coordination, & reaction time
  - medulla → minimal CB 1 receptors → respiratory function is preserved → explains low death rate from toxic THC levels
- Levels in Peripheral Nervous System, liver, heart, and kidneys

9

## CB 1 Receptors

- Activation can inhibit or activate the release of
  - GABA, Dopamine, Norepinephrine, Ach, & Serotonin
- Activation modulates response of opioid & NMDA receptors
- Location of CB 1 receptors → presynaptic & post synaptic

AANA Journal. 2019;87(6): 451 AANA Journal.2020;88(3):237 Goldfranks: Toxicological Emergencies, Marijuana

10

## CB 2 Receptors

- CB 2 receptors mainly expressed on
  - immune system → T cells, B cells, and macrophages
  - hematopoietic cells
- Functions
  - antinociception → relief of pain
  - anti-inflammatory & inhibit immune function

JAMA Surgery.com Am J Surgery 2018

11

## CB 1 & CB 2 Receptors

- THC → agonist at CB 1 & CB 2 receptors
- CBD → does not truly bind to CB 1 or 2 receptors
- CBD at CB 1 receptor
  - allosteric modulator → changes the receptor activity without binding
  - has inhibitory effect on agents that bind to CB1 → alters effect
- CBD at CB 2 receptor
  - inverse agonist → occupies receptor to produce opposite effect of agonist

12

# Marijuana

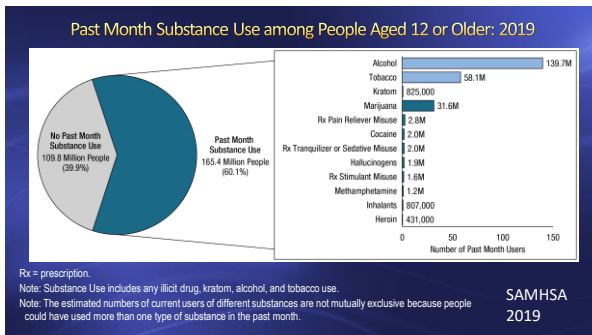
13

## Marijuana

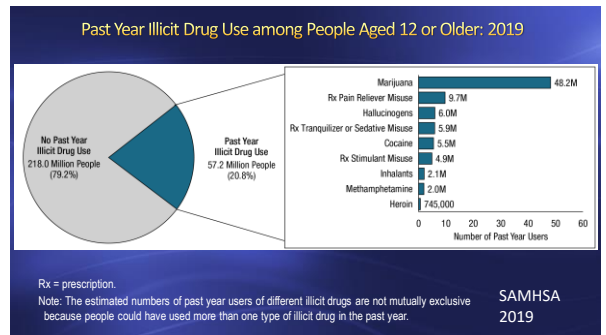
- 2020 Substance Abuse in United States
  - #1 Alcohol
  - #2 Tobacco
  - #3 Marijuana
    - 2018 → 11.8 million young adults used Marijuana
    - 2002 to 2014 → 455% increase in US adults → age 55-64
    - 2002 to 2014 → 333% increase in US adults → age > 64
- Need to monitor use & effects in older population
  - not much data out there

J Clin Med. 2020;9, 1925; doi: 10.3390/jcm9061925

14



15



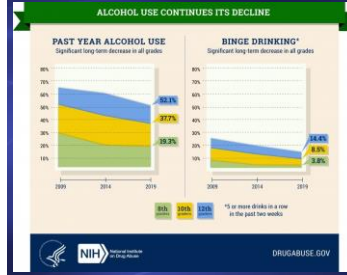
16

## Substance Abuse Adolescents & Young Adults

- What about the adolescent & young adult population?
- Third molar & orthodontic patients → What substances may they be abusing?
  - alcohol?
  - marijuana?
  - opioids?
  - Adderall and methamphetamines?
  - Club drugs?

17

## Alcohol



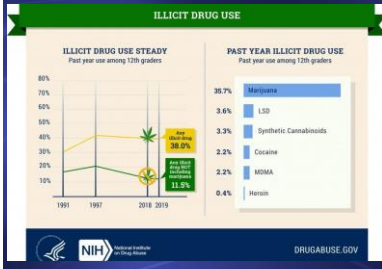
See decline in the use of alcohol

Decline includes binge drinking

Still is a problem at 19% to 52% use by 8<sup>th</sup>, 10<sup>th</sup>, 12<sup>th</sup> graders

18

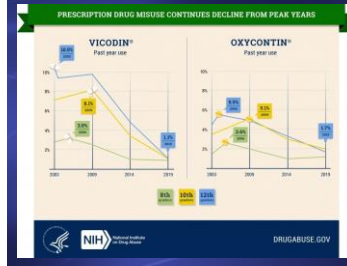
## Illicit Drug Use



Illicit Drugs excluding Marijuana have about halved in use

19

## Opioid Abuse



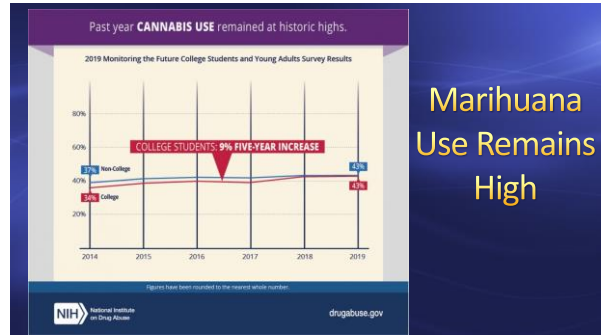
Opioid Abuse has decreased

Potential Good News

20

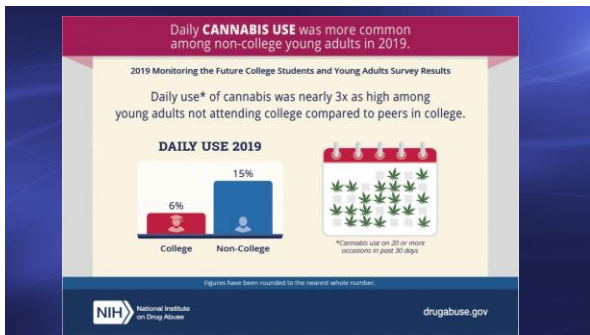


21

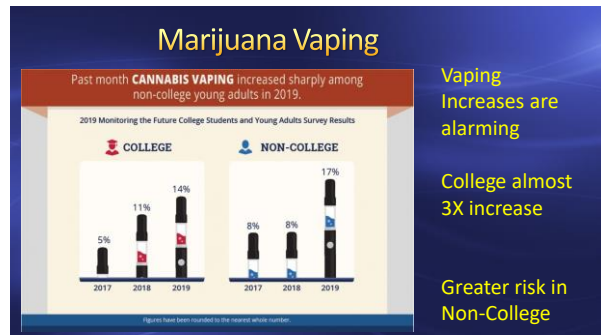


Marihuana Use Remains High

22



23



Vaping Increases are alarming

College almost 3X increase

Greater risk in Non-College

24

## Vaping

- Public perception → vaping is safer than smoking
  - vaping = no carbon monoxide and lack of tar
- Vaping lung injury is problem
- Vaping allows for higher concentrations of THC exceeding what is found in “flower” smoking
- Vaping allows free mobility from place to place

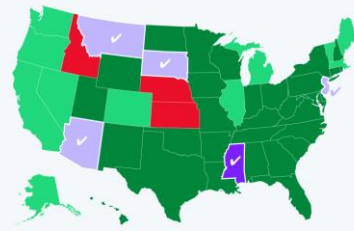
J Clin Med. 2020

25

## WEED LEGAL IN MOST OF AMERICA

✓ 5 states passed weed measures

● MEDICAL ONLY ● RECREATIONAL ● MEDICAL ONLY APPROVED ● RECREATIONAL APPROVED ● LEGAL



Yahoo finance.  
Internet accessed  
December 2020

26

## History of Cannabis

- Used for centuries
  - Chinese, Hindi, and Greeks
- Western Medicine 1800s → O’Shaughnessy → physician
  - treatment for rabies, tetanus, seizures, and delirium tremors
- Criminalized → Narcotic Act of 1914
  - OTC preparations available until 1941
- Controlled Substance Act 1970 (DEA)
  - Schedule I drug

27

## Marijuana

- Cannabis plants → 4 species
  - *Cannabis sativa* plant → common source
  - *Cannabis indica* plant
- Marijuana → entire plant is used
  - flowers, leaves, stems, and seeds → flower is an excellent source of THC → hence the nickname “flower”
- Street Names
  - weed, herb, pot, grass, ganja, & Mary Jane



28

## Marijuana

- More than 100 Cannabinoids in the plant
- THC is primary psychoactive agent →  $\delta$ -9 – tetrahydrocannabinol
- Cannabidiol (CBD) & Cannabinol
  - lack psychoactive properties
  - wide range of other pharmacologic activity
- More than 500 other compounds in plant
  - terpenes, flavonoids, & terpenoids

29

## How is Marijuana Used

- Delivery systems
  - smoking → “joint” cigarette
  - pipes
  - “bongs” → water pipes
  - “blunts” → cigar wrapper filled with Marijuana
  - vaporizers → eliminate smoke → “dabbing” on heated titanium nail or quartz glass container
  - edibles
  - transoral

30



31

## Marijuana Extracts & Concentrates

- Hemp extracts → yield high levels of CBD
- Marijuana extracts → yield high levels of THC
- Techniques → grind flowers, leaves, & stems
  - use heat, pressure, or solvents to remove contaminants
  - get a higher concentration of THC & CBD

32



## Marijuana Extracts & Concentrates

- Trying to remove impurities & increase THC content
- Budder → soft texture “stick of butter”
- Crumble → brittle version of budder “honeycomb”
- Shatter → brittle glass like texture → amber color
  - high THC content → 60 to 90%
- Delivery system → typically vaporization with dab rig or vape pen

33



34

## Marijuana Distillates

- Using organic chemistry distillation columns
  - isolate specific compounds in marijuana
- THC concentrations now → 98 to 99%

35

## THC Content of Marijuana

- THC in “flower” ( plant for smoking )
  - 1980’s → 1 to 3%
  - 1990’s → 6 to 20%
  - 2020 → up to 33% readily available
- “Flower” Trade names
 

– The Toad	37%	Godfather OG	25 to 34%
– GG4	25 to 30%	Bubba Kush	27 to 28%

Proc Bayl Univ Med Cent. 2019;32(3):364

36

## THC Content in Other Cannabinoids

- Budder 60 to 80%
- Crumble 60 to 90%
- Shatter 70 to 90%
- Distillates 95 to 99%
  
- Hybrids & Concentrates: THC to CBD ratio is increasing
  - CBD content is far less than THC content
  - CBD content attenuates psychoactive effects of THC
  - Customers want a better “high”

37

## CBD & THC Commercial Content

- THC & CBD content in “flower”
  - THC content → 8% to 29%
  - CBD content → 0.26 to 10.24%
- Customer has a choice
  - buy 1:1 product → less euphoria
- Shatter
  - THC content → 70 to 90%
  - CBD content → 1.1 to 3.6%

Internet Shopping California &amp; Colorado

38

## Inhaled Cannabinoids

- Onset Immediate
- Peaks 15 to 30 minutes
- Duration 1 to 3 hours depending upon dose
  
- Elimination half life
  - Occasional User 20 to 30 hours
  - Chronic User 72 hours

39

## THC Concentration in Blood

- Smoking or Vaporization & Blood concentration depends on
  - THC content of the product used → 20 to 99%
  - Tidal Volume → deep breaths increase THC content
  - Breath Holding → allows time to diffuse into blood
  
  - hot temperature of smoking → 13 to 30% available for lung absorption
  - vaporization yields lung absorption → > 70% → more effective inhalation technique

JAMA Surgery on line doi:10.1001/jamasurg.2020.5545

40

## “Synthetic Cannabinoids”

- Synthetic chemicals that bind to cannabinoid receptors
  - see effects similar to THC → but more pronounced
- Classification: NPS → new psychoactive substances
- Administration methods
  - Spray on any plant and smoke
  - Bongs
  - Vape pens

41

## “Synthetic Cannabinoids”

- Adverse Effects
  - psychosis, paranoia, & hallucinations
  - tachycardia, hypertension, seizures, and death
- Addictive agent
- Not a cannabinoid → similar structure
- Illegal most states
- Brand names: K2, Spice, Joker, Black Mamba, & Kronic

42

## Marijuana Edibles

- Variety of products
  - brownies, cookies, candy bars, & gummy bears
- Onset → 45 to 90 minutes
- Peak → 2 to 5 hours
- Duration → 5 to 10 hours
- Redosing → no effects felt → wait 2 hours before redose

43

## Marijuana Edibles

- Right edible dose varies person to person
  - tolerance from frequent use of marijuana
  - not enough science to use BMI to determine dose
- Empty stomach & edibles
  - expect more of an effect
- Beginners → 5 or 10 mg to start
  - 10 mg for frequent use → slight buzz

44

## Marijuana Edibles

- Adding CBD to edibles → enhance medical benefits
  - analgesia and antianxiety
  - decrease elevated heart rate
- CBD to THC ratio → 4:1 or higher
  - decrease likelihood of unwanted effects
  - improve medical benefits

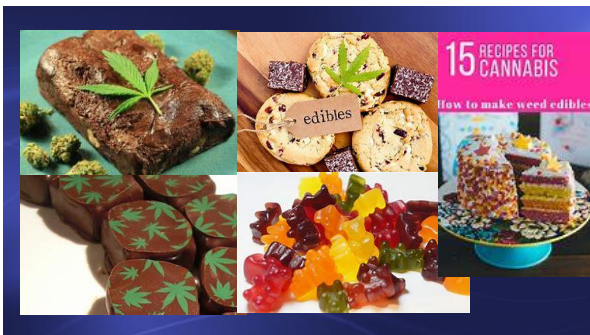
45

## Marijuana Edibles

TOLERANCE	USER EXPERIENCE	SUGGESTED DOSAGE
Very Low	Beginner	THC: >5 mg
Low	Some Experience	THC: 6-10 mg
Medium	Experienced	THC: 11-25 mg
High	More Experienced	THC: 26-80 mg
Very High	Expert	THC: 80+ mg

Edibles > 100 mg → 150, 200, even 500 mg → risks of nausea and paranoia increase significantly

46



47

## Cannabidiol CBD

- CBD
  - no psychomotor effects
  - anti emetic
  - anti convulsant
  - anti psychotic
  - can attenuate THC psychomotor effects

48

## Psychoactive Component THC

- Primary psychoactive component is → THC
  - $\delta$ -9 – tetrahydrocannabinol
- Euphoria → “High”
  - varies with dose, mode of administration, & personality of user

49

## CNS Effects

Euphoria	Heightened sensory perception
Relaxation	Laughing
Drowsiness	Dizziness
Anxiety	Dysphoria
Loss of Control	Impaired short-term memory

50

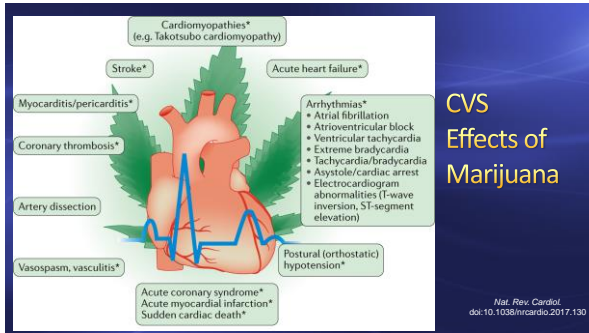
## CNS Effects

- Dysphoria
  - not uncommon especially in naïve users
  - severe anxiety & panic, loss of control, fear of dying
  - sometimes euphoria & dysphoria alternate

51



52



53

### Acute CVS Effects of Marijuana

- Dose dependent: CB 1 mediated **↑ sympathetic activity & ↓ parasympathetic activity**
  - increase in HR & SBP → range of 20 to 50% → up to 100%
  - onset immediate with smoking → peaks 10 to 15 minutes → lasts 1 to 3 hours after stop smoking
- NEpi levels → peak plasma levels in 30 minutes → duration of 120 minutes after stop smoking
  - ↑ CO & myocardial contractility
  - ↑ myocardial oxygen consumption

J Clin Anesthesia 2019 J. Clin Med. 2020

54

### Acute CVS Effects

- Cardiac Dysrhythmias
  - Males and patients  $\geq 45$  → most common is Atrial Fibrillation
  - Reports → Atrial flutter, 2<sup>nd</sup> Degree AV Block, PVCs, V tach & fib
  - Brugada ECG pattern → only ECG pattern not the syndrome
  - Multifocal Atrial Tachycardia & Junctional Tachycardia
- Heavy marijuana use & daily use → increased risk dysrhythmias
- High THC content & synthetic THC (K2) ↑ risk

J Clin Med 2020 Indian J Anaesth 2020;64: S210 J Clin Anesth.2019;57:41

55

### Type I Brugada Pattern

- Coved ST elevation  $\geq 2$  mm above baseline
- Inverted T wave
- Seen in V1 & V2

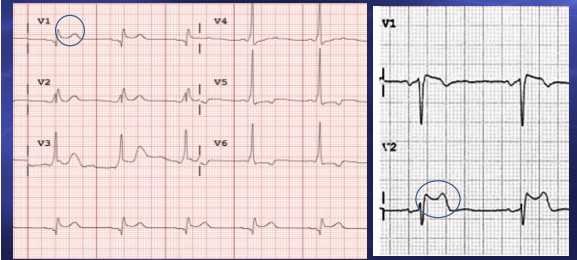
56

### Brugada Type II ECG Pattern

- Saddle back ST elevation
  - 1<sup>st</sup> phase is high take off ST elevation  $\geq 2$  mm
  - 2<sup>nd</sup> phase of saddle back is a trough  $\geq 1$  mm
- T wave is not inverted
- T wave is positive or biphasic

57

### Type II



58

### Cardiac Issues with Marijuana

- Tachycardia issue: literature reviews of past based upon lower THC content of cigarettes (4 to 8%)
  - tachycardias were tolerated in healthy and young
- Issue in 2020: Older patients & Increase THC concentration
  - Unanswered → but needs addressed & should raise concern

J Gen Intern Med. 2019;35(3):969-74

59

### Chronic Users and CVS Effects

- Higher doses of THC
  - increased parasympathetic responses & baroreceptor dysregulation → bradycardia & postural hypotension due to vasodilation
- Appears develop tolerance to CVS effects in chronic users after few weeks → again need to distinguish between young and old

AANA J. 2020;88(3):237

60

## AMI with Marihuana

- Several reports linking Marijuana use to AMI
  - for young patients without risk factors → possible → not common
  - National Academy of Science → found limited evidence for link
  - 32% increase in admissions for patients > 40 with primary diagnosis of AMI & secondary cannabis use disorder
- Mittelman ( 2001 ) → 4.8 X increased risk of AMI
  - in 1<sup>st</sup> hour of marijuana exposure
  - risk decreases to 1.7 X in 2<sup>nd</sup> hour
  - compared to 24 X increased risk of AMI → 1<sup>st</sup> hour after cocaine

West J Emerg Med.2019;20(4):557-572 Nature Reviews Cardiology.2018; 15:151

61

## AMI Marijuana

- Mechanism #1
  - tachycardia causes ↑ myocardial oxygen demand
  - elevated BP → **increases afterload** → increases cardiac work
  - smoking decreases oxygen delivery to heart
  - ↑ carboxyHb levels → **5 X greater than tobacco smoking levels**
  - marijuana causes ↑ platelet aggregation
- Mechanism #2
  - marijuana causes coronary vessel vasospasm
  - explanation for young AMI patients with negative cardiac cath

Am J Med Case Rep.2018;6(8):163

62

## AMI & Marijuana

- AMI
  - STEMI and NSTEMI
- Chronic Anginal Patients
  - time to onset of anginal symptoms → time ↓ by 48% after just → 1 marijuana cigarette
  - mechanism → ↑ carboxyHb levels → decreased myocardial O<sub>2</sub>

J. Clin Med. 2020 West J Emerg Med.2019 Heliyon 2018

63

## AMI or Unstable Angina

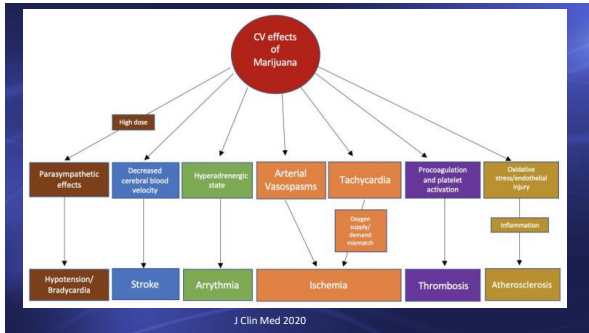
- Marijuana use
  - Patients with known CAD
  - Older age patients
  - Heavy users of marijuana & cannabis use disorder patients
  - High THC content products
- Marijuana would be a risk factor for an AMI or Unstable Angina
- Synthetic THC ( K2 ) → risk of AMI in younger patients

Anesthesiology.2020;132:625

Nature Review Cardiology. 2018

64





65

## CVA & Marijuana

- Ischemic stroke in young patients
  - age 25 to 34
  - 2.3 to 2.9 fold increase for marijuana vs tobacco users
- Ischemic stroke & TIA → far more common than hemorrhagic stroke
- Heavy users → greater risk than occasional users
- Mechanism: cerebral vasospasm

Nature Reviews Cardiology 2018 Curr Opin Anesthesiol. 2020;33:318 J Clin Anesth. 2019;57:41

66

## Respiratory Effects Marijuana

- Smoking → exposes airway & lung to
  - high concentration → irritants & carcinogens
    - benzopyrene & benzanthracene (carcinogens)
  - tar content of marijuana
    - 3 X more concentrated than tar from tobacco
    - 33% greater deposition in respiratory tract

Heliyon 2018 accessed online Proc Bayl Univ Cent. 2019 accessed online

67

## Respiratory Effects of Marijuana

- Smoking
  - marijuana burns at higher temperature than tobacco
  - heat is direct irritant to respiratory mucosa especially with smoking short butts (“roach clip” heat)
- Smoking technique is different than tobacco
  - 66% greater → puff volume
  - 33% greater → depth of inhalation
  - 4 X greater → breath holding

68

## Respiratory Effect of Marijuana

- Effects of Smoking Techniques
  - 5 X amount of carboxy – hemoglobin in lungs than tobacco
  - Greater diffusion of THC into blood
- 3 to 4 cannabis cigarettes over the course of time → yields the same amount of lung damage as chronic use of → 20 tobacco cigarettes

West J Emerg Med. 2019 Curr Opin Anesth. 2020;33:318

69

## Respiratory Effects Marijuana

- Bronchodilation
  - non-users of marijuana or new users
  - CB 1 mediated response
  - occurs in smokers or with PO use
  - duration of action → 1 hour
  - likely to produce → ↑ FEV1 & FVC on acute exposure
  - chronic use → no longer seen

AANA J. 2019;87:451 J Clin Anesth. 2019;57:41

70

## Respiratory Effects of Marijuana

- Chronic Use Respiratory Effects → 6 to 10 weeks of marijuana use
  - Onset of bronchial irritation & hyperactivity
  - ↓ FEV1 & FEV1/FVC ratio
  - FVC & Functional Residual Capacity → no change
  - ↑ Cough, Wheeze, & Mucus production

71

## Chronic Respiratory Changes

- Develop COPD
  - ↑ Goblet Cell Hyperplasia
  - ↑ Mucus Production
  - ↑ Loss of Ciliated Epithelium
  - ↑ Squamous metaplasia
- Increased incidence of bronchitis → occurring 10 years earlier than tobacco bronchitis
- Increased incidence of pneumonia as well

72

## Other Effects of Marihuana

- Anticholinergic
  - blurred vision due to dilated pupils ( may or may not occur )
  - possible dry mouth or difficulty voiding
- Gastric Emptying Time
  - prolongs emptying time on average by 30 to 120 mins
- Schizophrenia
  - long term use → ↑ risk if have genetic vulnerability

73

## Anti Emetic Use of Marijuana

- Mechanism of action
  - CB 1 receptor stimulation → inhibit release of 5HT3
  - CB 1 receptor → may inhibit the ability of 5HT3 to induce vomiting

74

## Addiction & Gateway

- Potential for addiction
  - chronic use → 7%
  - chronic use started during teen years → up to 17%
- Chronic use → increased risk of developing alcohol & tobacco dependence
- Majority of users do not advance to “harder” drugs

75

## Cannabis Use Disorder

- DSM – 5 Criteria: Drug for at least 1 year + 2 of following
- Repeatedly tried to stop
- Used larger amts over longer time than intended
- Cravings & obsession for drug
- Kept using despite negative consequences
- Drug more important than other aspects of life
- Developing tolerance

76

## Overdose Deaths

- Marijuana risk of overdose death
  - 4000 years of use → no reports of cannabis overdose
  - J Opioid Management.2009;5(3): 153
- Synthetic THC ( K2 ) → reports of death
- What about newer hybrids, purified products, & distillates plus older patients with co morbidities ??
  - remains to be seen

77

## Marijuana Withdrawal

- Symptom onset → 1 week after stop marijuana
- Need to express 3 or more symptoms
  - anger, irritability, aggressiveness, anxiety, nervousness, sleep disturbances, decreased appetite, depressed mood, or restlessness
- Need 1 or more physical finding
  - abdominal pain, fever, chills, headache, or tremors
- Peaks in 10 days

Marijuana internet sites

78

## Marihuana & Anesthesia

79

## Marijuana & Surgery

- Historically → Marijuana was a Schedule I drug
  - most of the literature is case reports or retrospective reviews
  - other than that → anesthesia data mostly anecdotal
- University of Mississippi National Center for Natural Products Research
  - THC content 13 to 14% → far less than hybrids sold at legal marijuana dispensaries
  - study drug less potent than commercial product → poor correlation

80

## Preoperative Considerations

Frequency	Technique	Marijuana
Monthly	Smoking	Flower – THC Content
Weekly	Vaporize	Concentrate
Daily	Vape Pen	K2 - Spice

History	Hyperemesis Episodes
	Cough, Sputum, Wheeze
	Palpitations
	Irregular rhythm ( Skipped Beats )
	History of Heart Disease and Respiratory Disease

81

## Examination

### New User

<b>Tachycardia</b>
↑ SBP
Dysrhythmias
Dyspnea & Sputum
Wheeze

### Chronic User

<b>Bradycardia or Tachycardia</b>
Postural or Orthostatic Hypotension
Dysrhythmias
Dyspnea & Sputum
Wheeze

82

## Anginal Patients

- Middle aged & older anginal patients
- Ask about anginal free functional capacity both before and after marijuana use
- Elevated risk of AMI → 1<sup>st</sup> hour after using marijuana  
Proc Baylor Med Center 2019
- Patients with cannabis use disorder ( heavy use can't stop )
  - marijuana used perioperatively → ↑ risk of perioperative AMI  
Anesthesiology 2020;132:625

83

## Aspiration Risk

- Marijuana decreases gastric emptying time
  - delayed additional 30 to 120 minutes
- Consider longer NPO time especially for solids
- Consider use of famotidine ( Pepcid ) → H2 blocker
  - 20 mg PO at HS before surgery → 20 mg PO 2-3 hours preop
  - alternative → 20 mg IV preop
  - Akla Setzer Gold ( no aspirin or particulates )

84

## Airway Reactivity

- Smoking = airway irritability & hyperresponsiveness
- Management → same as chronic tobacco smoking
- Stop smoking → 24 to **72 hours**
  - carboxyHb levels 5X greater than tobacco
  - 72 hrs best but difficult → minimum is 24 hrs
- Rare reports → severe edema & airway obstruction
  - oropharyngeal & uvular edema secondary to smoke

85

## Airway Reactivity

- Marijuana smoking → ↑ risk of laryngospasm for 4 hours
- Cough, sputum, or wheeze
  - Glycopyrrolate to decrease airway secretions
  - IV lidocaine → reduce airway hyperresponsiveness
  - Albuterol pretreatment → improves lung function
  - Dexamethasone → 4 to 8 mg IV preop
  - wheezing may require pre op optimizations days in advance

86

## Anesthetic Agents

- Anecdotal reports are abundant
  - anesthetic agents → patients require significant increased doses
  - excessive intraoperative movement & restraint issues
  - bizarre emergence reactions
- Growing evidence → regular cannabis use → resistant to sedative hypnotics
- Require ↑ induction dose → maintenance dose varies

Proc Baylor Med Center. 2019 Curr Opin Anesth. 2020

87

## Anesthetic Agents

- Marijuana used weekly for 6 months
  - required increased doses of propofol to place LMA
  - no difference between groups to get to BIS < 60
- Cannabis → may increase tolerance to sevoflurane

J Clin Anest. 2020. 67:109980 Curr Opin Anesth. 2020;33:832 Heliyon. 2018

88

## Marijuana & Sedation

- Moderate & Deep Sedation for Endoscopy

Sedative	Non-Cannabis User 255 pts	Cannabis User 25 pts	Greater Requirements %
Fentanyl mcgs	109.91	125.93	14%
Midazolam mg	7.61	9.15	19.5%
Propofol mg	13.83	44.81	220.5

J. Am Osteopath Assoc. 2019;119(5):307

## Anesthetic Agents

- Marijuana users vs non – users → drug doses
  - Intraoperative fentanyl → no difference
  - Postoperative fentanyl → marijuana users required more
  - Propofol, ketamine, & dexmedetomidine → no difference
- Need more data
  - Tachycardia, Hypertension, Dysrhythmias secondary to drug
  - avoid ketamine & sympathomimetics → synergistic effects
  - why are you still doing the case??

J Clin Anesth. 2020: 67

Curr Opin Anesth. 2020;33:832

89

90

## Marijuana & PONV

- Marijuana → anti emetic effect by CB 1 receptors in CTZ & VC of medulla
- Potential risk of PONV for daily users of marijuana
- Mechanism
  - held marijuana preop → onset withdrawal +
  - anesthetic agents → emetogenic additional risk of PONV
- Result → potential ↑ risk for PONV

BMC Anesthesiology. 2020;20:115

## Postoperative Issues

- Postoperative pain requirements
  - acute pain required higher doses of opioids
- Reports of increased pain & sleep disturbance postop
- Cannabis use → may experience hyperalgesia

Eur J Anaesthesiol. 2019;36:623 Eur J Anaesthesiol.2019;36:705 J Clin Anest 2020:66

91

92

## Elective Anesthesia & Marijuana

- Acute Intoxication → Defer elective surgery
- How long do you hold marijuana preop??
  - chronic users → ask about withdrawal episodes in past
- Current literature
  - Elective surgery → Hold the drug for 72 hours
  - Heliyon 2018; J Clin Anest 2019; AANA J 2019
- Will the patient do it??      What will you accept??

93

## Elective Surgery

- Does patient know the THC content of his product?
  - street weed vs commercial dispensary
- What is risk of withdrawal symptoms?
  - reports → takes a week → other reports suggest sooner
- If you stop for 72 hours → possible withdrawal
  - do we need to substitute THC “gummy bears” → at lower dose to prevent withdrawal starting 72 hours preop

94

## Elective Surgery

- Heavy THC content + multiple daily doses of marijuana
  - will holding for 72 hours increase irritability day of surgery
  - will it cause a more reactive patient thrashing around the chair
- High content THC → will require increased anesthetic drug doses intraoperatively
  - if completely stop days before → still need increased anesthetic doses but it may still be a “rodeo anesthetic”
  - will “gummy bears” prevent this
  - will allowing normal THC dose up to night before prevent this

95

## Anesthetic Medications

- Midazolam as per usual → 1 to 3 mg IV
- Propofol → infusion preferred over bolus bumping
  - 100 mcg/kg/min to start → increase as needed
- Opioid → prefer remifentanyl infusion
- Ketamine → decreases hyperalgesia
- Dexmedetomidine for “hyperactivity” and emergence
  - mini bolus or infusion

96



## Case Presentation

- 25 y.o. male
- PMH: no significant history except marijuana use
- Chief Complaint
  - pain in tooth #30
- Secondary complaint
  - cyclic episodes of severe N/V
  - multiple vomiting episodes per day
  - lasts for several days then stops then recurs in few months
  - severe abdominal pain
  - only relief is taking hot showers

97

## Cannabinoid Hyperemesis Syndrome (CHS)

- Cyclic episodes of emesis
- 1<sup>st</sup> reported in Australia in 2004
- Colorado → since legalization → ER visits have doubled
- Often requires admission for hydration & analgesia
- Most cases → cannabis inhalation is cause
- Usually unresponsive to typical antiemetics

98

## CHS

- Onset after Cannabis use for more than 1 year
  - most cases → range is 1 to 5 years
- Cannabis Frequency of Use

< Weekly	2.4%	<b>Daily Use Most Common</b>
Weekly Use	19.4%	
Daily Use	47.9%	
Greater Than Daily	23.7%	

J. Med  
Toxicol. 2017;13:71

99

## Signs & Symptoms

Severe N/V	100%
Cyclic Vomiting over months	100%
Resolution when stop cannabis	96.8%
Symptoms ↓ with Hot Shower/Bath	92.3%
Abdominal Pain	85.1%
Caucasian	80%
Males	72.9%

Many Patients Report Marijuana Use Started as Teenager

100

## 4 Phases of CHS

- Inter – episodic phase
  - No symptoms
- Prodromal
  - Triggers → stress, noxious stimuli, infections, others
  - Develop nausea
  - Can use oral anti-nausea agents

101

## 4 Phases

- Vomiting Phase
  - may be < 12 hours of vomiting
  - duration 1 to 2 days → can persist for 7 days
  - hot showers/bath or seek emergency care
  - abdominal pain
- Recovery Phase
  - vomiting stops
  - resume oral intake
  - duration = days to months

102

## Management of CHS

- Hot showers or hot bath
- Anxiety issues → benzodiazepines in ER or hospital
- IV Proton Pump Inhibitors ( PPI ) to reduce acid
- Saline IV for hydration
  - 1 to 2 Liters in ER then 150 to 200 ml/hr
- Typical antiemetics → ineffective
- Solution = stopping the use of cannabis = most effective

103

## TRPV 1 Receptors

- Transient Receptor Potential Vanilloid 1 Receptors
  - TRPV 1 Receptor
  - found in the endovanilloid system → system interacts with endocannabinoid system
- TRPV 1 and CB 1 receptors
  - located on same neurons in CTZ & VC of medulla
  - located on same peripheral enteric & vagal sites
  - both receptors are activated by cannabinoids
  - TRPV 1 is also found in skin

J.Med Toxicol.2017;13:71

104

## Mechanism of Action

- Cannabis activates TRPV 1 receptors
  - result = antiemetic
  - prolongs gastric emptying time
- Cannabinoids activate CB 1 receptors
  - act as antiemetic
  - prolongs Gastric Emptying Time

105

## Mechanism of Action

- Excessive cannabinoid use
  - Gastric Emptying Time → additional emptying delays
  - down regulates or desensitizes → CB 1 receptor
  - desensitizes or downregulates → TRPV 1 receptor
- Develop Cyclical Vomiting

**No Case Reports Linking CHS to Increased PONV**

106

## Capsaicin Topical Cream

- Capsaicin → plant extract from chili peppers
  - medical use → topical pain relief
  - topical cream → 0.025%, 0.075%, & 0.1%
  - activates TRPV 1 receptors found in skin
- Apply 1 inch strip on abdomen → 3 to 4 times day
  - relief after 1 or more doses
  - prevents admission to hospital
  - side effects → burning & erythema skin

J Pharmacy Practice.2020; 1-8. doi: 10.1177/0897190020934289

107

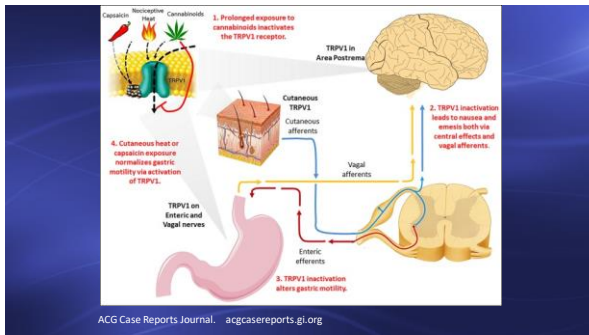
## Capsaicin & TRPV 1 Receptors

- Prolonged marijuana exposure inactivates TRPV 1 receptors
  - receptors in CTZ, VC, enteric, and vagal neurons
  - gastric emptying time increased + nausea & vomiting
- Capsaicin or heat → temperatures > 43 C
  - activate TRPV 1 receptors in skin
  - restore anti emetic effects & normalizes gastric motility

**81% Success Rate**

Clin Toxicol.2020;58(6):471 J Pharm Practice2020

108



109

## Haloperidol for CHS

- Haldol → Dopamine antagonist in CTZ D2 site
  - 1 to 5 mg IV → most case reports → 5 mg IV
  - relief of symptoms in about 1 hour (11 patients in study)
  - relief of symptoms in 1 to 2 hours (4 patients)

**82% Success Rate**

- Haldol for PONV relief
  - 0.5 to < 2 mg IV or IM 2020 Consensus Guidelines PONV
  - 0.5 to 1 mg IV SAMBA
- Could consider droperidol 0.625 mg IV

Am J Therapeutics.2017;24:e64 Am J Emerg Med.2013;31:1003e5

110

## Cannabinoid Medications

- Marinol & Syndros (Dronabinol = generic)
  - synthetic THC
  - Oral capsule & oral liquid
  - Approved for CINV & HIV/AIDS anorexia
- Cesamet (Nabilone = generic)
  - synthetic cannabinoid that mimics THC
  - Oral capsule
  - approved for CINV

111

## Cannabinoid Medications

- Sativex (Nabiximols = generic) (UK & Canada, not US)
  - plant, purified extract of THC & CBD → ratio of 1:1
  - Oromucosal spray → buccal or sublingual
  - Use → pain & spasticity in MS & cancer pain
- Epidiolex
  - plant, purified CBD
  - Oral solution for specific types of epilepsy
    - Lennox-Gastaut & Dravet Syndrome

Anesth Analg.2019;129:1339  
Cancer ChemotherPharmacol.2017;80:441  
J Clin Med.2020

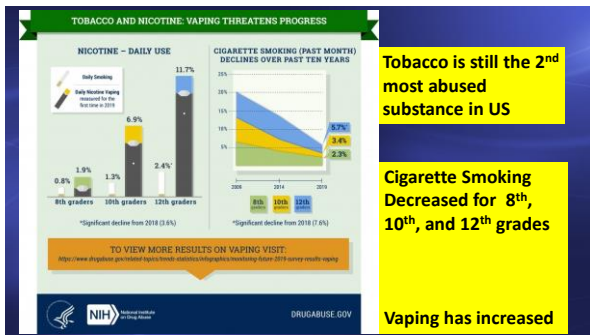
112

# E – Cigarettes & Vaping

113

- ### Summary of E-Cigarettes
- No tar or CO
  - Nicotine > tobacco nicotine
  - Nicotine → ↑ HR, BP, myocardial O2 consumption
    - ↑ risk for AMI in patients with risk factors → versus non users
  - Thermal burns from explosions
  - EVALI → Vit E is cause
  - Hold nicotine vaping for at least 10 hrs.

114

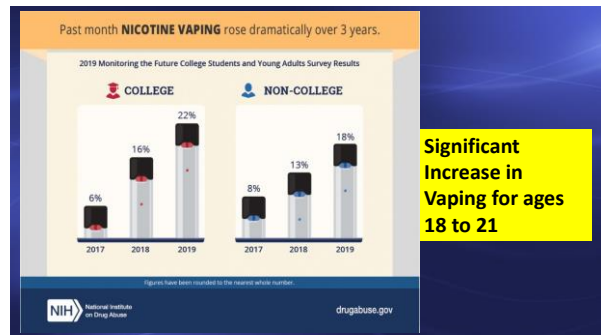


**Tobacco is still the 2<sup>nd</sup> most abused substance in US**

**Cigarette Smoking Decreased for 8<sup>th</sup>, 10<sup>th</sup>, and 12<sup>th</sup> grades**

**Vaping has increased**

115



**Significant Increase in Vaping for ages 18 to 21**

116

## Electronic Cigarettes

- Developed in China in 2003
- Introduced in US in 2007
- Designed to deliver nicotine
- Electronic Nicotine Delivery Systems (ENDS)
- Term → E cigarette is for nicotine products
- Term → Vaping is for cannabis products → THC & CBD
  - new concern: cannabis extracts, oils, & dabbing distillates
  - even more alarming → methamphetamine, ecstasy, crack, fentanyl, & heroin

117

## E cigarettes

- 1<sup>st</sup> Generation
  - looked like a cigarette
- 2<sup>nd</sup> Generation
  - larger battery & refillable tank
- 3<sup>rd</sup> Generation
  - improved lithium battery
  - disposable cartridges
  - alter temperature to control amount of vapor
  - dabbing modifications available for cannabis extracts

118

## Popularity & Web Claims

- Compared to tobacco → User claims
  - Healthier 95%
  - Cheaper 93%
  - Cleaner 95%
  - Smoke Anywhere 88%
- Don't burn or smolder like cigarette
  - less waste → cheaper
  - no secondhand smoke
  - possible secondhand vapor

119

## ENDS Components

- Replaceable cartridge for liquid
  - 1<sup>st</sup> Nicotine only → now → cannabis “flower”, oil, & concentrates
- Heating element run by Lithium battery
- Atomizer or vaporization chamber
- Mouthpiece



120

## E cigarettes

- Nicotine content
  - equals or exceeds nicotine content in tobacco
  - young ENDS users → 3 to 4 X → more likely to progress to cigarettes than non-ENDS users
- Solvents
  - propylene glycol or glycerin
- Over 7000 flavoring compounds available
- Carbonyls, toluene, benzene, & heavy metals

121

## E Cigarettes

- No combustion or burning
  - no tar deposits like burning tobacco
  - eliminating some tobacco carcinogens
- No burning
  - eliminates carbon monoxide
  - no carboxy – hemoglobin to affect oxygen delivery
  - benefit over smoking

122

## CVS Issues with ENDS

- Nicotine activates nicotinic Ach receptors
  - catecholamine release → sympathetic stimulation
  - ↑ HR, ↑ BP, ↑ CO, ↑ Myocardial Oxygen Consumption
- Patients with CAD
  - decreased coronary blood flow
  - increased risk of Heart Failure from β adrenergic stimulation
  - ↑ risk of Ventricular dysrhythmias

123

## CVS Issues with ENDS

- Nicotine → activate renin angiotensin aldosterone system
  - nicotine upregulates ACE → convert angiotensin I to II
  - BP increases
  - Aldosterone is released to retain Na
  - Vasopressin also raises BP & fluid retained
- Nicotine by ENDS → 79% higher risk of AMI than non-users
- ENDS → decreased cutaneous blood flow

AANA J. 2020;88:135

124

## Respiratory Issues with ENDS

- Propylene glycol & glycerin in heated vapor
  - form acetaldehyde & formaldehyde → inhaled by lung
  - cause cough & ↓ FEV1/FVC ratio
- Aerosolized propylene glycol → produces ultrafine particulates ( PM 2.5 ) in lung
  - decreased lung function & exacerbate wheezing in asthmatics
  - equals or exceeds that seen in tobacco smoking

AANA J. 2020

125

## Respiratory Issues with ENDS

- Chronic ENDS use → 6 months or longer
  - ↓ FEV1 & FEV1/FVC ratio
  - ↓ Forced expiratory flow in lungs
- Increased incidence of Bronchitis in adolescents
  - 2 X as likely as non-ENDS users

126

## Diacetyl

- Flavoring compound → butter taste
- Diacetyl inhalation → “popcorn lung”
  - bronchiolitis obliterans → rare untreatable pulmonary fibrosis
  - develop fibrosis of distal & terminal bronchioles
  - airway collapse from fibrosis → small airway disease
- 76% of sweet ENDS flavorings → contain Diacetyl
- Propylene glycol, glycerin, & diacetyl can be ingested BUT NOT INHALED

127

## Thermal Injuries with E-Cig-Vap

- Battery thermal burns
 

Thigh	Carry in Pocket	62% cases
Hand	Using device	33%
Genitalia	Carry in pocket	19%
Mouth/face	Using device	20%
- Battery explosions
  - avulsed teeth, facial burns, nasal fractures & soft tissue, & orbital blow out from missile effect

Case Reviews 2016-2018 93 cases. AANA J 2020

128



## Anesthesia Implications

- General preoperative evaluation
  - Treat like a chronic smoker
  - Identify Comorbidities → especially respiratory & cardiac
- Physical & Vital Signs
  - Wheeze, cough, dyspnea, & airway reactivity
  - Heart rate, BP, SpO2, METS, & ECG
- Nicotine half life = 2 hours → no nicotine 10 hours

129

## Anesthesia

- LMA or intubated GA → volatile agents over TIVA
- Open airway
  - Propofol, Ketamine, Dexmedetomidine, Midazolam
  - Opioid → short on & off → Remifentanyl
  - Glycopyrrolate for secretions
- Albuterol preop for lungs
- Dexamethasone
  - may need steroid prep for few days preop for lungs

130

## Electronic Vaping

- Vaping Cannabis
  - THC/CBD plant vaping → grind up flower & place in vape pen
  - THC concentrate or CBD concentrate → cartridges or dabbing
  - delivery system → vaporization of highly concentrated product
- Other added components
  - propylene glycol, glycerin, flavoring agents
  - terpenes
  - Vit E acetate

131

## Terpenes

- Hydrocarbon found in essential oil of cannabis plant
- Increases absorption of inhaled CBD & THC
- Heat from vaporization
  - degrade terpene to methacrolein & benzene
  - these cpds cause acute lung injury and pulmonary edema

J Investigative Medicine High Impact Case Reports.2020;8:1

132

## Vitamin E Acetate

- Vit E → PO intake is benign just like PO diacetyl on popcorn
- Vit E in marijuana bongs & vape pens
  - used to dilute the marijuana for vaporization
- Heating and vaporization of Vit E
  - releases ketene gas → toxic to lungs
- Causative agent in EVALI

Curr Opin Anesthesiol.2020;33:318

133

## EVALI

- EVALI → Electronic Cigarette and Vaping Associated Lung Injury
- Introduction
  - 1<sup>st</sup> reports → early 2012 → lung injury secondary to vaping
  - July 2019 → young males ( age 10 to 19 ) in 10 states
    - ER visits for Dyspnea & Chest Pain
    - Non-Contributory Medical History
    - All used E cigarettes or vaping in past 90 days
    - Mostly cannabis concentrates but some nicotine

134

## EVALI

- EVALI cases through February 2020
  - 2807 cases → 68 deaths → involved all 50 states
  - Agent vaped → **THC** → comprised majority of cases
    - Nicotine → 8 to 24% of cases
    - No Nicotine or THC → 2 to 7% of cases
  - Most patients → 86 to 92% vaped THC → past 90 days
- Vit E → identified in 90% of cases by bronchial lavage (BAL)
  - mechanism unclear → heated Vit E injury

N Engl J Med.2020;382:903

135

## EVALI

- Patient Data
 

Males	62 to 79% cases
Age < 30	Median ( 23-27 )
THC past 90 days	76 to 91% cases
Caucasian	46 to 79% cases
Hispanic	12 to 47%
- Daily use of THC → significantly increases risk of EVALI

136

## Clinical Presentation

Respiratory	Dyspnea, Tachypnea, Cough
Cardiovascular	Tachycardia, Chest Pain
GI	N/V, Abdominal Pain, Diarrhea
Constitutional	Fever, Fatigue, Headache

SpO2	< 95	< 90 not uncommon
CXR	Opacities & infiltrates	
CT	Ground Glass Opacities	

Case Reports in Pulmonology, 2020;

137

## Pathology of EVALI

Acute Fibrinous Pneumonitis  
Diffuse Alveolar Injury  
Pneumonia & Bronchiolitis

138

## Diagnosis

- E cigarette or vaping in past 90 days
- Radiographic opacities & infiltrates
- No evidence of infection
- Medical history does not indicate another diagnosis
- Treatment: mostly inpatient care
  - oxygen, BIPAP or CPAP, empiric antibiotics, & steroids
  - most patients recover & discharged to home
  - mortality: 0.6 to 3%

J Thoracic Oncology, 2020;15(11):1727

139

## Anesthetic Management of Vape Pens

- Combination of E cigarettes + high dose THC
- Similar cardiac & respiratory issues as high dose marijuana by other means

140



141