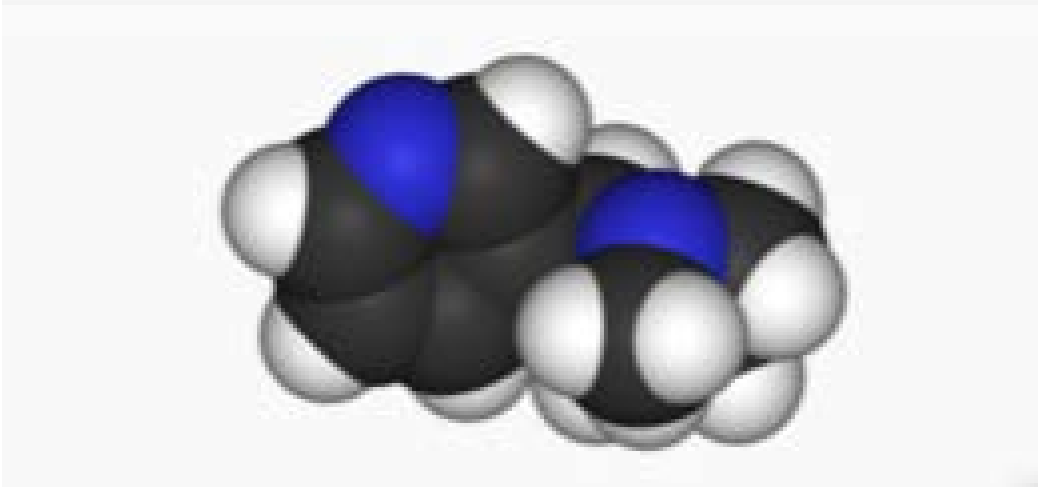
Nicotine and Vaping

December 11, 2019

Objectives

- Develop an understanding of the history of tobacco
- Review the pharmokinetic and pharmacodynamics effects of nicotine
- Demonstrate negative effects nicotine has on health
- Describe e-cig and current vaping trends


Nicotine
H
N
N



Tobacco: still the leading cause of preventable death in the United States

History

I st Peoples of Pre-Columbian Americas

- Known use of tobacco/nicotine
- Native Americans cultivated and smoked in pipes
  - Medicinal and ceremonial
- Christopher Columbus- brought it back to Europe
  - Didn't "get into it" until mid-16th century
    - France's Jean Nicot

History Continued…

- 1556- France
- 1558- Portugal
- 1559- Spain
- 1565- England
- 1612- Commercial crop in Virginia: John Rolfe
  - Colony's largest export
  - Slavery

History Continued…

- How it was used: Pipe, chewing, and snuff
  - Cigars early 1800s
  - Cigarettes not popular until after civil war (although were around in the 1600s)
  - Late 1880s 1st cigarette making machine

History Continued…

- 1930s- correlation between cancer and smoking
- 1944- American Cancer Society warnings
- 1950s- Tobacco industry research council= made it “healthier again”
- 1960s- Surgeon general “smoking and health” risks emphasized
- 1971- Broadcast advertising banned
- 1995- Clinton- FDA to regulate more

Nicotine Causes

- Psychostimulant
- Potent parasympathomimetic alkaloid
- Nightshade plant family
- Relaxation and relief from stress and hunger
- Arousal during fatigue
- Relaxation during anxiety

Nicotine Withdrawal

- Craving, irritability, frustration, anger, anxiety, depression, difficulty concentrating, restlessness, increased appetite
- Maximum withdrawal intensity 24-48 hours after last use
  - Diminishes over a few weeks

Forms

- Cigarette, bidis, cigars, pipes, snuff, chewing tobacco
- More addictive during rapid administration- smoke

Pharmokinetics

- Rapid delivery to brain with smoking
  - Precise dose titration by altering:
    - Puff volume
    - Number of puffs taken
    - Depth inhaled
  - Volume of distribution 180L, <5% binding to plasma proteins
  - T 1/2 = 2 hours
    - Accumulates during a day and persists 6-8 hours after smoking ceases (6-8 goes right after persist)
    - Renal excretion
    - PH dependent

Cotinine

- Metabolized to cotinine in liver/lung/brain
- CYP2A6
- Female faster than male
- African Americans obtain average 30% more nicotine per cigarette and clear more slowly than Caucasians
- Chinese Americans have lower nicotine intake per cigarette and smoke fewer cigarettes per day than Caucasians
  - Slower metabolisms CYP2A6

Biochemical Markers

- Blood, salivary, plasma cotinine
- Expired breath carbon monoxide
- Blood carboxyhemoglobin concentration
- Plasma or salivary thiocyanate

Biochemical Markers

- Cotinine: >14ng/mL =smoker
  - ≥100 ng/ml ~ 1/2ppd
  - Up to 900 ng/mL= regular smoker
  - Persist up to 7 days after stopping
- Breath carbon monoxide (CO)
  - > 10 ppm=indicated tobacco smoking within past 8-12 hours
- Thiocyanate- blood and saliva for weeks after stopping

Drug Interactions

- Nicotine accelerates metabolism of many drugs:
  - CYP1A2
    - Theophylline, propranolol, olan zapine, clozapine imipramine, haloperidol, pentazocine, estradiol
- Nicotine inhibits:
  - Reduction in BP from beta blockers,
  - Ulcer treatment with histamine H_2 receptor antag
  - Sedation from benzos
  - Analgesia from some opioids

Pharmacologic Actions

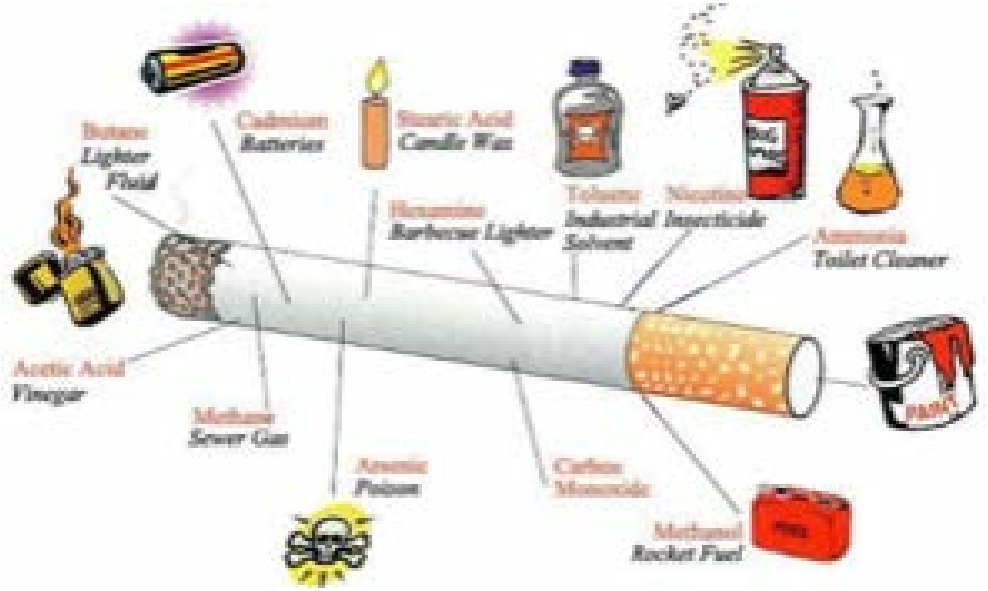
- Low doses/ acute: ↑ blood pressure/heart rate/cardiac output/cutaneous vasoconstriction
- ↑ ↑ ↑doses: hypotension, slowing HR
- CNS effects: arousal, relaxation during stress, enhancement mood/attention/reaction time
- Rapid metabolizers smoke more
- Variance in behavior and withdrawal = genetic effects- CHRNA5- CHRNA3- CHRNB4- CHRNB3

Mental Illness and Nicotine

- 36% current smokers (vs 20% no mental illness)
- Schizophrenics: 70-88% smokers
- ADHD: 40% smoke
- Depression: 59% lifetime prev. smokers vs 17% general population not smokers

Neurobiological Mechanism of Action

- nAChRs- nicotine acetylcholine receptors
- Ligand gated ion channels
- Closed at rest
- Opened by nicotine
- α4β2 containing nAChRs: primarily responsible for nicotine dependence
  - Innervation to nearly all areas in the brain including dopamine reinforcement pathways = potent enhancement
  - Withdrawal- α5 - containing nAChRs in habenula= adverse effects
  - ↓activity of MAOA and MAOB = perceived benefit of smoking by depressed patient


Butane
Lighter Fluid
Cadmium
Batteries
Stearic Acid
Candle Wax
Benzene
Barbecue Lighter
Toluene
Industrial Solvent
Nicotine
Insecticide
Ammonia
Toilet Cleaner
Acetic Acid
Vinegar
Methane
Sewer Gas
Arsenic
Poison
Carbon
Monoxide
Methanol
Rocket Fuel

Systemic Toxicity

- ≥ 50 known carcinogens
- Cardiovascular risk:
  - CO reductions in O_2 delivery to heart
  - Oxidant chemicals:
    - Endothelial dysfunction
    - Platelet activation
    - Thrombosis
    - Coronary vasoconstriction
  - Imbalance between proteolytic and antiproteolytic forces in lung
  - Heightens airway responsiveness
  - Chronic obstructive lung diseases

Systemic Toxicity

- Eyes
  - Increased rates of posterior subscapular cataracts
  - Macular degeneration
- Females
  - Lower levels of estrogen
  - Earlier menopause
  - Increased risk of osteoporosis
- Males
  - Impair penile erection
- Decreased appetite and increased metabolic rate: weigh 6-10 lbs less
- Increased LDL, Decreased HDL
- Delays healing of peptic ulcers

Pregnancy

- Nearly doubles relative risk of low birth weight in infant and relative risk of spontaneous abortion
- Perinatal and neonatal mortality increases of ~ 1/3
- Variation in CYP1A1 and GSTT1- roles of metabolizing and excreting toxic chemicals

Developing Fetus

- Nicotine arrests neuronal replication and differentiation
  - * Contribute to SIDS
- Activates nicotinic cholinergic receptors in fetal brain
  - Abnormalities of cell proliferation and differentiation=altered synaptic activity
- Increased susceptibility to hypoxia
  - Induced brain damage
  - Perinatal mortality
  - Sudden infant death

Second Hand Smoke

- Escaping smoke of burning tobacco and exhaled smoke
- Causally associated with
  - Acute and chronic coronary heart disease
  - Lung cancer
  - Sinus cancer
  - Eye and nasal irritation
  - If asthma: pneumonia/COPD
  - LBW and SIDS
- Salivary cotinine level 0.4 ng/mL=
  - Increased lifetime mortality risk 1/1000 lung cancer
  - 1/100 cardiovascular disease
- Prevalence of 28% unrestricted smoking in workplace
  - ~ 4,000 cardiovascular deaths
  - ~ 400 lung cancer deaths annually in US

Morbidity and Mortality

- Pack in US ~ $7.18 in medical care expenditures and lost productivity
- 440,000 premature deaths annually
  - 150,000 CV
  - 150,000 cancer
  - 100,000 non malignant pulmonary disease
- Male: 13.2 years lost
- Female: 14.5 years lost

Tobacco and Alcohol

- Increased medical complications
- Oral and esophageal cancers
- >1000 lives lost to household fires

Cessation

- Immediately
  - Decreased risk CV death
  - Decreased blood coagulability, improved tissue oxygenation
  - Decreased predisposition to cardiac arrhythmia
- Reduced risk of death continues for 10-15 years
- After 10-15 years abstinence, risk of all-cause mortality nearly that of non-smokers

Vaping and E-Cigarettes

Vaping and E-Cigarettes

- Inhaling and exhaling aerosol (vapor)
- 2007 introduced to mass market

Structures

- Mouthpiece, battery, cartridge for "e-liquid" heating component
  - Battery heats up heating component
    - Contents of e-liquid into aerosol that is inhaled
- E-liquid
  - Propylene glycol or vegetable glycerin-based with nicotine, flavoring and other chemicals and metals but not tobacco

Structures

- "Closed system device"- self contained e-liquids (cartridges/pods) not meant for modification (JUUL)
- "Open system device" – users add range of e-liquids including cannabinoids
- For established nicotine e-liquids=
- -lower concentrations of toxic substances per puff than conventional

Vaping Articles

- JAMA Original
- E- cig use among youth in the US, 2019

JAMA

- Cross sectional analyses of school based nationally based representative sample of 19, 018 students grades 6-12 in 2019 national youth tobacco survey (2/15/19- 5/24/19)

JAMA

- Outcomes:
  - Self reported current (last 30 days) HS and MS students
  - Frequent use (>20 days in past 30 days)
  - Usual e-sig brand
  - Flavors/types of exclusive e-cig users.

JAMA

- 10, 097 HS (mean 16.1 years old, 47.5 % female) 8,837 MS (mean 12.7 years old 48.7% female)
  - *Response rate 66.3 %
- Current e-cig
  - 27.5 % (95% CI, 25.3 %-29.7%) HS
  - 10.5% (95% CI, 9.4%-11.8%) MS
- Frequent e-cig
  - 34.2% (31.2 %-37.3%) HS
  - 18.0% (15.2%-21.2%) MS
- Exclusive e-cig
  - 63.6 % (59.3%-67.8%) HS
  - 65.4 % (60.6%-69.9%) MS
- “Usual” : JUUL primary brand
  - 59.1 % (54.8 %-63.2%) HS
  - 54.1 % (49.1 %- 59 %) MS
- No Usual Brand
  - 13.8% (12 %-15.9%) HS
  - 16.8 % (13.6-20.7%) MS
- Flavored
  - 72.2% (69.1%-75.1%) HS
  - 59.2% (54.8%-63.4%) MS
- Primarily= fruit, menthol/mint, candy, dessert, sweets

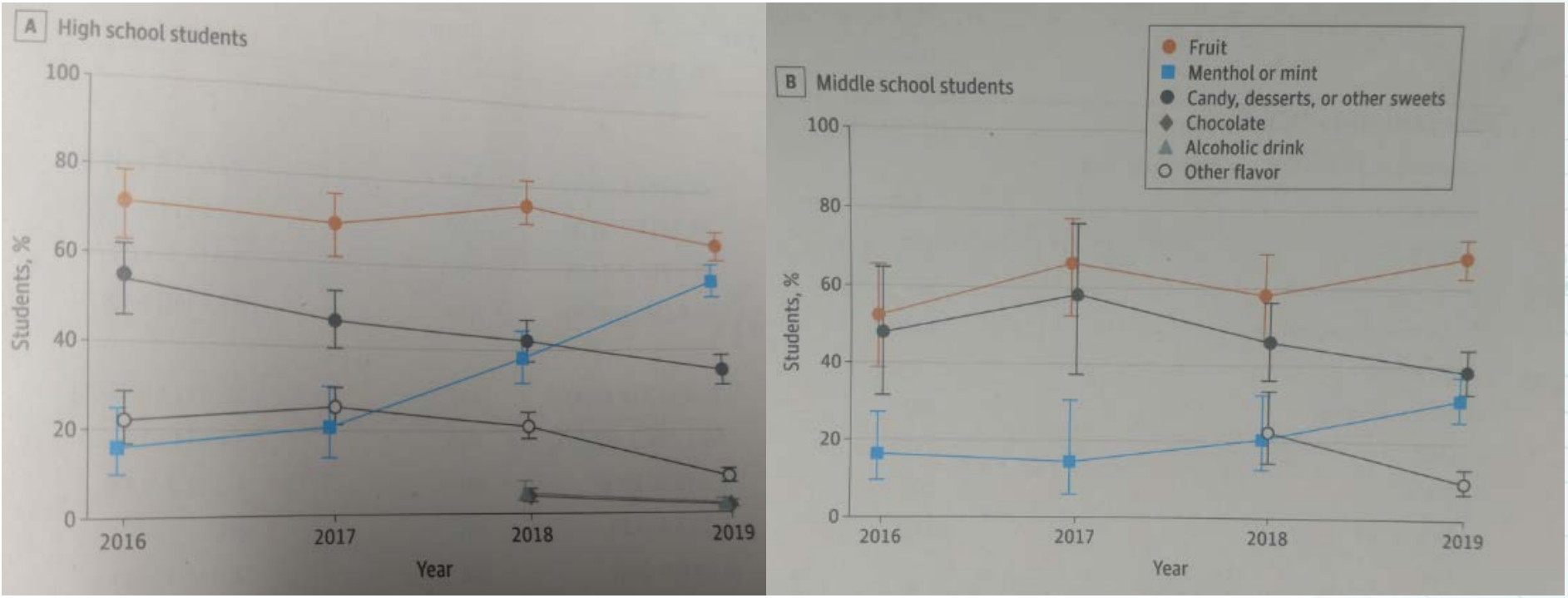
JAMA

- This project expanded nationally represents 4.1 million HS and 1.2 million MS that use e-cigs and 1.6 million youth with frequent e-cig use.

JAMA

- 2011-2015 e-cig HS use has increased 1.5 → 16%
- “ Epidemic” FDA and US Surgeon General e-cig youth use 2018

JAMA



2019- Cigarette smoking is at historic lows

JAMA

- E-cig popularity:
  - Small/discreet
  - Higher nicotine content
  - Flavors appeal to youth

JAMA

- Adolescent nicotine use effects learning, memory, attention, and increases risk of future drug use

JAMA

- Nicotine salt products like JUUL
- Increase levels of nicotine with less irritation than free base = easier dependence

JAMA

- Transition fruit → menthol/mint
- 2018 – FDA to protect by limiting flavors available to youth to menthol/mint

Youth Trends in Vaping

- E-Cigarettes: Youth and Trends in Vaping
- Karen G. Dederstandt phD, RN, CPNP, FAAN
- Journal of Pediatric Health Care, 2015-11-01, Volume 29, Issue 6, Pages 555-557, Copyright 2015 National Association of Pediatric Nurse Practitioners

Youth and Trends

- 61% of middle schoolers and 80% of high schoolers are dual users
- Vaping Increase
  - 2011→ 3.3% American youth
  - 2012→ 6.8 %

Youth and Trends

- Multiple studies show → e-cig use does not discourage, but may encourage cigarette use and may be a gateway to nicotine addiction

Youth and Trends

- Adolescent brain exhibits greater reward effects from nicotine exposure than the adult brain
  - youth are more susceptible to a lifelong battle with addiction

Youth and Trends

- History- FDA attempted to regulate (tobacco control act 2008) initially marketed as tobacco cessation product
- E-cig → sued FDA → Court ruled in 2010 that it could not be regulated as a drug if sold as a tobacco product

JAMA and EVALI

- JAMA article Nov 26, 2019 Volume 322, number 20
- As of 10/28/19 49 states >1600 severe pulmonary disease related to vaping
  - 34 deaths EVALI (e-cig or vaping associated lung injury)

JAMA and EVALI

- 84% OF 53 CASES OF EVALI in 3 studies involved use of THC – many acute lipoid pneumonia and chemical pneumonitis

CDC Recommendation

- CDC recommendation from 10/28/19
  - Avoid vaping THC
  - Avoid modified or street bought products
  - Consider refraining from all e-cigs/vaping
  - Use other FDA approved NRT for cessation
  - monitor from symptoms
- Need to monitor long term pulmonary status
- *** Smoking is still the leading cause of preventable death despite decreases in use
- *** Need to ask


THE VAPING CRISIS
Walker McKnight was just 19 years old when he bought his first e-cigarette. Two months later he was in a hospital fighting for his life
'Vaping Nearly Killed Me'
by JOHNNY DODD
TOP GUN ALL STARS
Photographs by AUDRA MELTON
W
Walker McKnight had never given much thought to vaping. In high school the health-conscious athlete—who often spent five hours a day working out—would occasionally take a drag off a friend's e-cigarette, but it wasn't until he started his freshman year at Valencia Community College that the 19-year-old student decided to purchase his first Juul. "It gave me a really intense, good feeling," says Walker, recalling how a couple of hits helped take the edge off the pressures of school. "I could feel my whole body throbbing and tingling."
Two months later Walker was fighting a desperate battle to stay alive. He spent nearly four months drifting in and out of consciousness, connected to a respirator in an Orlando hospital as doctors fought to keep his infected lungs from collapsing and his organs from shutting down. "I begged my parents to let me die," says Walker, now 20, as he fidgets with the oxygen tube under his nose. "I wouldn't wish this on anybody."
Tragically Walker—who estimates that nearly 90 percent of his friends still vape on a regular basis—is just one of thousands of young people across the nation who have been hospitalized with serious lung illnesses associated
A Life Forever Changed
"I thought, I'm not that type of person ... and then I was hooked on vaping like everybody else," says Walker (at home and, right, in his high school yearbook picture).