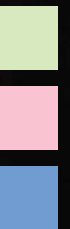


*two photon art.com*

**nicotine**



# FURTHER READING

[WWW.CDC.GOV/TOBACCO](http://WWW.CDC.GOV/TOBACCO)

[TOBACCO.UCSF.EDU](http://TOBACCO.UCSF.EDU)

[TOBACCOFREEKIDS.ORG](http://TOBACCOFREEKIDS.ORG)

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THROUGH [SCHOLAR.GOOGLE.COM](http://SCHOLAR.GOOGLE.COM)

IF YOU ARE ASKED TO PAY FOR THE ARTICLE, TRY  
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HOSPITALS & UNIVERSITIES) & MANY WOULD BE  
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**LAMMEL**  
LABORATORY

 **TOBACCO-RELATED DISEASE  
RESEARCH PROGRAM**



**hhmi**  
Howard Hughes  
Medical Institute



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Written and illustrated by Christine Liu  
Edited by the Lammel Lab

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NICOTINE IS A PROFOUNDLY POWERFUL MOLECULE THAT CARRIES POTENTIAL FOR BOTH BENEFIT & HARM. METHODS FOR NICOTINE INTAKE WILL CONTINUE TO EVOLVE WITH HUMAN SOCIETY. WITH MORE RESEARCH & UNDERSTANDING OF HOW NICOTINE & ITS DELIVERY METHODS IMPACT OUR MINDS & BODIES, WE CAN MAKE BETTER CHOICES & CREATE BETTER TREATMENTS FOR ADDICTION & DISEASE.



FROM BURNING LEAVES TO COTTON CANDY FLAVORED VAPOR, HUMANS HAVE DEVELOPED METHODS TO ENJOY NICOTINE OVER THOUSANDS OF YEARS.

## WHAT CAN WE DO?

UNFORTUNATELY, NICOTINE IS HIGHLY ADDICTIVE AND IS THE LEADING CAUSE OF PREVENTABLE DEATH WORLDWIDE, LARGELY DUE TO THE BODILY HARM CAUSED BY CIGARETTE SMOKE.



★ SUPPORT BASIC SCIENTIFIC RESEARCH TO ENSURE THAT SCIENTISTS CAN STUDY NICOTINE, DIFFERENT DELIVERY METHODS, & THE CHEMICALS ASSOCIATED WITH THEM IN ORDER TO ENSURE THAT CONSUMERS HAVE ENOUGH INFORMATION TO MAKE CAREFUL & INFORMED DECISIONS ABOUT THEIR HEALTH.

★ ENGAGE WITH POLICYMAKERS & VOTE TO HELP SHAPE HOW NICOTINE PRODUCTS ARE REGULATED & ADVERTISED.

★ LASTLY, STAY INFORMED & SHARE WHAT YOU'VE LEARNED WITH OTHERS! SEND THEM A COPY OF THIS ZINE!



AS TECHNOLOGY & OUR METHODS OF NICOTINE INTAKE EVOLVE, WILL THIS EPIDEMIC BE LEFT IN THE PAST?

OR WILL WE CONTINUE TO GRAPPLE WITH THE CONSEQUENCES OF NICOTINE ADDICTION FOR AS LONG AS HUMANITY PERSISTS?



TOBACCO PLANTS ARE PART OF THE DIVERSE SOLANACEAE PLANT FAMILY, WHICH CONTAINS DEADLY NIGHTSHADE & DELICIOUS POTATO.



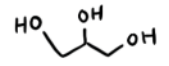
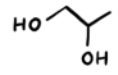
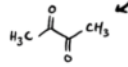
# SO... WHAT'S NEXT?

IN SEPTEMBER 2019, THE NUMBER OF MYSTERIOUS ILLNESSES & DEATHS ASSOCIATED WITH VAPING REACHED A TIPPING POINT & CALLS FOR BANNING FLAVORED E-LIQUIDS ARE INCREASING. IT IS CURRENTLY UNKNOWN HOW & WHY HUNDREDS OF YOUNG PEOPLE ARE FALLING ILL.

MANY PLANTS IN THE SOLANACEAE FAMILY CONTAIN A TYPE OF CHEMICAL CALLED AN ALKALOID (CHARACTERIZED BY A NITROGEN ATOM & STRONG EFFECTS ON ANIMALS IN SMALL AMOUNTS) — NICOTINE IS ONE OF THESE ALKALOIDS. ALKALOIDS ACT AS NATURAL PESTICIDES & THEIR CONSUMPTION CAN HURT HUMANS TOO, WHICH IS WHY HUMANS USE NICOTINE IN SMALL AMOUNTS.

CALIFORNIA HAS URGED PEOPLE TO STOP VAPING IMMEDIATELY.

THE CHEMICALS IN VAPE JUICES NEED TO BE RIGOROUSLY INVESTIGATED. A RARE CONDITION CALLED "POPCORN LUNG" AFFECTED WORKERS IN POPCORN FACTORIES, CAUSED BY A CHEMICAL CALLED DIACETYL, WHILE SAFE FOR INGESTION, THIS BUTTERY FLAVOR CHEMICAL IS PRESENT IN VAPE LIQUIDS (~70% OF THOSE TESTED IN A 2015 HARVARD STUDY) & ITS LONG TERM HEALTH RISKS ARE UNKNOWN, INCLUDING A POTENTIAL LINK TO ALZHEIMER'S. SOME POPCORN BRANDS HAVE STOPPED ADDING DIACETYL TO THEIR PRODUCTS & THE EUROPEAN UNION HAS BANNED ITS USE IN E-LIQUIDS BUT IT REMAINS LEGAL IN THE USA. THE MAIN INGREDIENTS OF E-LIQUIDS (VEGETABLE GLYCERIN & PROPYLENE GLYCOL) MAY ALSO CARRY HEALTH RISKS WHEN INHALED OVER LONG PERIODS OF TIME. THIS CURRENT GENERATION OF YOUNG VAPE USERS MAY BE HARMED IN WAYS SCIENTISTS HAVEN'T EVEN BEGUN TO PREDICT.



THE TWO MAIN TOBACCO PLANTS

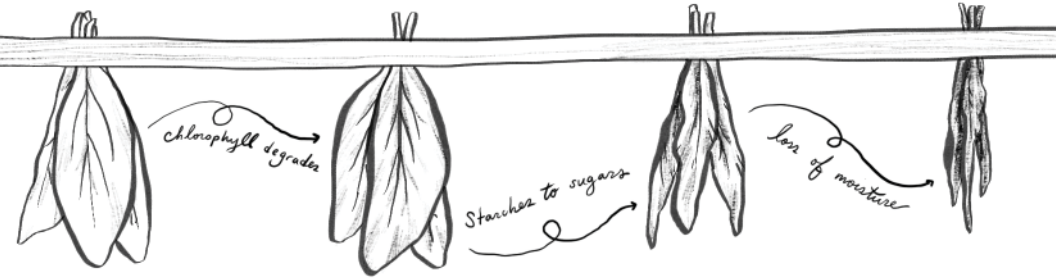
NICOTIANA TABACUM

MOST WIDELY GROWN FOR CIGARETTES & CHEWING TOBACCO. CONTAINS 3-9X LESS NICOTINE THAN N. RUSTICA.



NICOTIANA RUSTICA

MOSTLY USED IN SHAMANIC PREPARATIONS & FOR EXTRACTING NICOTINE FOR E-LIQUIDS & OTHER NICOTINE PRODUCTS DUE TO HIGH LEVELS OF NICOTINE THAT MAKES SMOKING TOO INTENSE.



TOBACCO LEAVES START OUT LARGE & GREEN BUT EXPOSURE TO OXYGEN SLOWLY SHRINKS & YELLOWS THE LEAVES, CONVERTS STARCHES INTO SUGARS, & ALLOWS FOR FLAVOR-IMPROVING CHEMICAL REACTIONS TO OCCUR. THIS PROCESS IS CALLED "CURING." THE EXACT METHODS FOR CURING & FERMENTING DEPEND ON THE DESIRED FINAL PRODUCT.



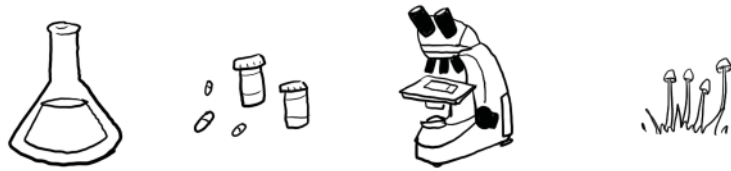
IN ADDITION TO GOVERNMENTAL REGULATION, COMMUNITIES THEMSELVES ARE TAKING STEPS TO PREVENT ADDICTION & DISEASE. NATIVE AMERICAN COMMUNITY LEADERS ARE PROPOSING CHANGES TO TREAT TOBACCO AS THE SACRED CEREMONIAL PLANT IT ONCE WAS, BEFORE COMMERCIALIZATION CHANGED THE WAY INDIGENOUS PEOPLE USED TOBACCO.

learn more at:  
KEEPITSACRED.ITCMI.ORG

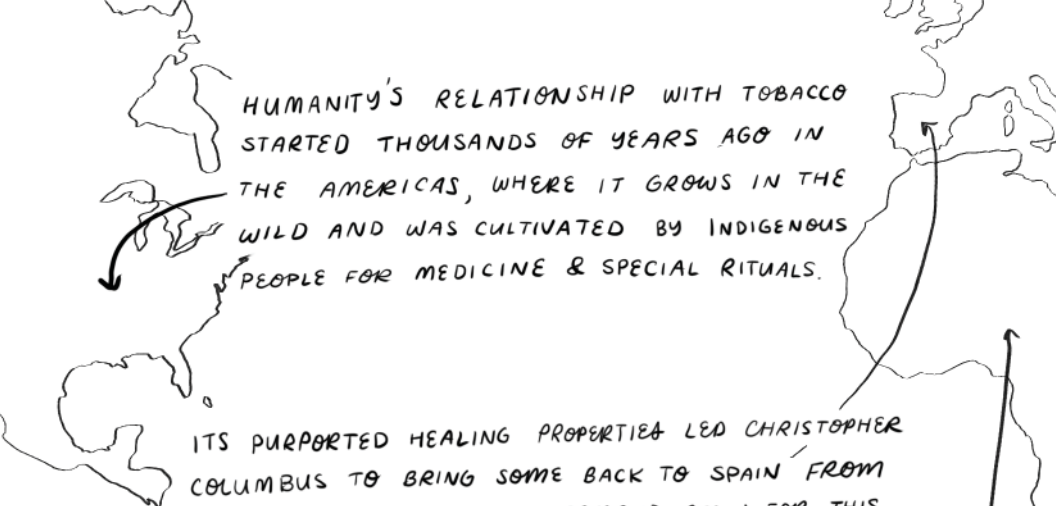
HUMANITY'S RELATIONSHIP WITH TOBACCO HAS EVOLVED OVER THE PAST THOUSANDS OF YEARS, WITH THE MOST RAPID CHANGES IN THE LAST CENTURY. NOWADAYS, SOMEONE CAN DEVELOP A NICOTINE ADDICTION WITHOUT EVER COMING INTO CONTACT WITH THE PLANT THAT NICOTINE COMES FROM.



IN 2018, ~20% OF HIGH SCHOOL STUDENTS WERE VAPING & ABOUT 5% OF MIDDLE SCHOOL STUDENTS HAD STARTED TOO. SOME ARE UNAWARE THAT THEY'RE CONSUMING NICOTINE & MANY DON'T KNOW THAT ONE JUUL POD CONTAINS AS MUCH NICOTINE AS A PACK OF CIGARETTES. MORE EDUCATION & REGULATION ARE NEEDED AS E-CIGARETTES BECOME MORE POPULAR.



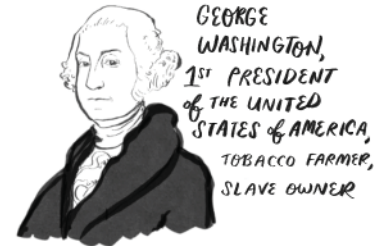
THE FDA AIMS TO REDUCE THE IMPACT OF DISEASE & ADDICTION WITH SEVERAL GOALS. THEY HOPE TO REDUCE THE AMOUNT OF NICOTINE IN TOBACCO CIGARETTES, DECREASE THE AVAILABILITY OF FLAVORED TOBACCO & NICOTINE PRODUCTS, & CONTINUE TO ALLOW INNOVATION OF PRODUCTS THAT CAN HELP ADULTS OVERCOME A DEPENDENCE ON COMBUSTIBLE TOBACCO PRODUCTS. E-CIGARETTES, PHARMACEUTICAL DRUGS, & OTHER ADVANCES HOLD A LOT OF PROMISE. RESEARCHERS ARE ALSO CONTINUING TO INVESTIGATE HOW NICOTINE ACTS ON THE BRAIN TO DEVELOP TOOLS TO TACKLE ADDICTION.



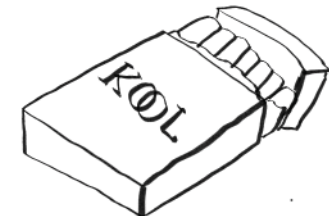
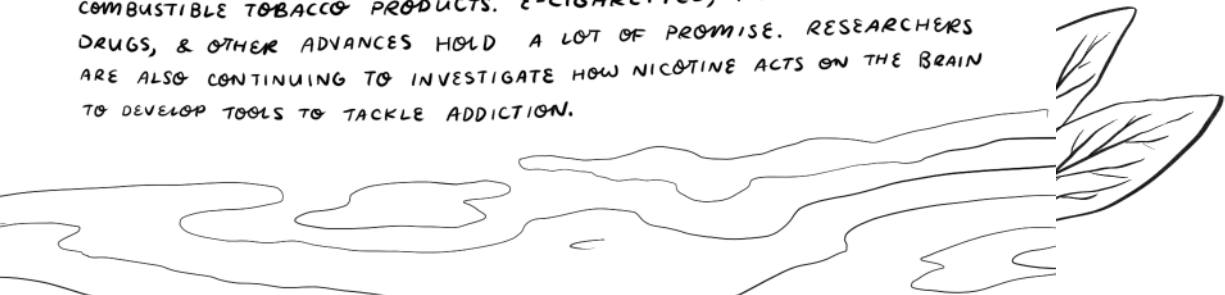
HUMANITY'S RELATIONSHIP WITH TOBACCO STARTED THOUSANDS OF YEARS AGO IN THE AMERICAS, WHERE IT GROWS IN THE WILD AND WAS CULTIVATED BY INDIGENOUS PEOPLE FOR MEDICINE & SPECIAL RITUALS.

ITS PURPORTED HEALING PROPERTIES LED CHRISTOPHER COLUMBUS TO BRING SOME BACK TO SPAIN FROM HIS FAMOUS 1492 VOYAGE. DEMAND GREW FOR THIS "CURE-ALL", WITH EUROPEAN SCHOLARS AND NOBLES EAGER TO GET MORE OF THIS SPECIAL PLANT.

WHILE TOBACCO WAS TABOO IN BRITAIN, AMERICA BECAME A LAND OF OPPORTUNITY FOR BRITISH COLONISTS. THEY TOOK CLAIM OF NATIVE AMERICAN LAND AND BUILT TOBACCO PLANTATIONS, RELYING ON THE LABOR OF ENSLAVED AFRICANS TO KEEP PROFITS HIGH.



TODAY, LAND THEFT & SLAVERY ARE LESS PREVALENT BUT TOBACCO STILL HARMS NATIVE AND BLACK PEOPLE IN THE U.S. WITH DISPROPORTIONATELY HIGH SMOKING AND DISEASE RATES. TOBACCO COMPANIES HAVE A HISTORY OF TARGETING KIDS IN BLACK COMMUNITIES AND EXPLOITING SOVEREIGN STATUS OF TRIBAL LANDS TO SELL TOBACCO TAX-FREE.





TOBACCO WAS VALUED AS MORE THAN A DRUG. IN THE 1600s IT WAS OFTEN USED AS A PESTICIDE. BY SOAKING TOBACCO LEAVES IN WATER, NICOTINE WOULD DISSOLVE INTO THE SOLUTION TO CREATE AN EFFECTIVE DETERRENT AGAINST INSECTS. AN ENGLISH PHYSICIAN & BOTANIST, NICHOLAS CULPEPPER, EVEN RECOMMENDED TOBACCO WATER TO KILL LICE.



NICOTINE DOESN'T KILL ALL INSECTS THOUGH. IN FACT, IT MIGHT EVEN BE ATTRACTIVE TO SOME! IN A STUDY PUBLISHED IN 2005, RESEARCHERS FOUND THAT BEES PREFERRED TO EAT NECTAR LACED WITH A LITTLE NICOTINE.



AS WITH ALL OTHER SUBSTANCES, THE DOSE MAKES THE POISON. HUMANS CAN SUFFER & EVEN DIE IF TOO MUCH NICOTINE ENTERS THE BODY. WHEN EXPOSED TO TOO MUCH NICOTINE, ONE MIGHT START EXPERIENCING QUICK & HEAVY BREATHING, FASTER HEART RATE, HEAD & STOMACH ACHES, VOMITING, & DIZZINESS. AFTER THIS INITIAL STAGE, THE BODY WILL REACT BY SLOWING DOWN BREATHING & HEART RATE AND THE RISK OF LOSING CONTROL OF MUSCLES & HAVING A SEIZURE INCREASES.



MINDSET IS VERY IMPORTANT FOR THOSE WHO WANT TO QUIT SMOKING. THOSE WHO ARE ABLE TO QUIT COLD TURKEY MAY HAVE HAD A "WAKE UP CALL" THROUGH A SCARY EXPERIENCE OR EVEN A BOOK.

MANY RECOMMEND:



SOCIAL SUPPORT THROUGH GROUPS IN PERSON & ONLINE CAN HELP, AS DOES USING APPS TO TRACK PROGRESS

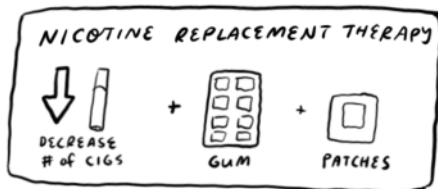


THUS, GUIDED COGNITIVE THERAPY IS ALSO AN EFFECTIVE METHOD FOR THOSE TRYING TO QUIT. RESEARCHERS ARE EVEN INVESTIGATING THE POWER OF PSYCHEDELIC DRUGS, PARTICULARLY PSILOCYBIN WHICH IS FOUND IN "MAGIC MUSHROOMS", GIVEN DURING PSYCHOTHERAPY BY TRAINED PSYCHIATRISTS TO TREAT ADDICTION.



IT'S UNCLEAR WHETHER THE SUCCESS OF PSYCHEDELIC-ASSISTED THERAPY IS DUE TO A COGNITIVE SHIFT IN PERSPECTIVE, A BIOCHEMICAL PROPERTY OF PSILOCYBIN, OR BOTH. COGNITIVE THERAPY TENDS TO BOOST THE EFFECTIVENESS OF ANY QUIT METHOD, REGARDLESS OF WHETHER OTHER DRUGS OR NICOTINE REPLACEMENT ARE USED.

SOME LUCKY PEOPLE ARE ABLE TO QUIT SMOKING "COLD TURKEY" WITHOUT ANY WEANING OR CESSATION AIDS, BUT THIS DOESN'T WORK FOR EVERYONE. OTHERS START BY TAPERING DOWN THEIR USE BY DECREASING THE AMOUNT OF CIGARETTES THEY SMOKE, THEN USING NICOTINE GUM & PATCHES TO GET THEIR BODIES USED TO LOWER & LOWER LEVELS OF NICOTINE.



PHARMACEUTICAL DRUGS CAN ALSO BE PRESCRIBED TO HELP WITH QUITTING. BUPROPRION (AKA WELLBUTRIN) IS EFFECTIVE AS AN ANTIDEPRESSANT DUE TO ITS ABILITY TO BLOCK DOPAMINE AND NOREPINEPHRINE REUPTAKE, WHICH KEEPS THESE NEUROTRANSMITTERS AVAILABLE. BUPROPRION ALSO BLOCKS NICOTINE ACETYLCHOLINE RECEPTORS, WHICH MAKES IT HELPFUL FOR SOME PEOPLE TRYING TO QUIT SMOKING.



MORE RECENTLY, PHARMACEUTICAL DRUGS LIKE CHANTIX & CHAMPIX HAVE BEEN DESIGNED TO BIND LOOSELY TO THE SAME RECEPTORS THAT NICOTINE BINDS TO, KEEPING THEM SLIGHTLY ACTIVATED SO THAT NICOTINE ONLY HAS A WEAK EFFECT WHEN INTRODUCED BACK INTO THE BODY.

( SCIENTIFICALLY SPEAKING, THESE DRUGS CONTAIN VARENICLINE AS THE ACTIVE INGREDIENT WHICH IS A PARTIAL AGONIST SELECTIVE FOR  $\alpha 4 \beta 2$  NICOTINIC ACETYLCHOLINE RECEPTORS. )



GREEN TOBACCO SICKNESS IS A FORM OF NICOTINE POISONING THAT HAPPENS WHEN WET LEAVES ARE HANDLED. WHILE NICOTINE POISONING THROUGH SKIN USED TO HAPPEN MOSTLY TO AGRICULTURAL WORKERS, CASES ARE NOW HAPPENING WHEN PEOPLE ARE EXPOSED TO NICOTINE VAPING LIQUIDS.



EACH YEAR, HUNDREDS OF CHILDREN ARE RUSHED TO THE EMERGENCY ROOM FOR NICOTINE POISONING.

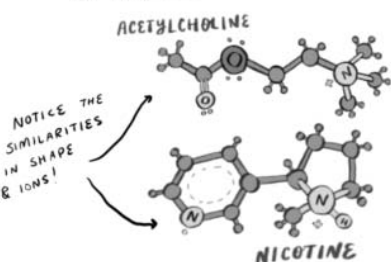
A SINGLE TEASPOON OF VAPE JUICE CAN POISON A TODDLER, & IN SOME CASES, CHILDREN HAVE DIED.



IT IS ESPECIALLY IMPORTANT TO KEEP E-LIQUIDS AWAY FROM PETS & KIDS AS THEY BECOME MORE COMMON & COME IN MORE APPEALING SCENTS.



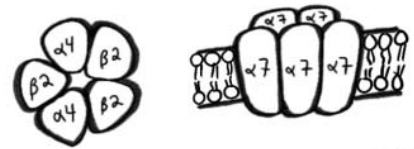
SMOKING TOBACCO ALLOWS NICOTINE TO RAPIDLY ENTER THE BLOOD & WITHIN SECONDS, NICOTINE IS DISTRIBUTED ALL OVER THE BRAIN & BODY. NICOTINE BINDS TO RECEPTORS THAT EVOLVED TO BIND A SIGNALLING MOLECULE THAT'S MADE IN OUR OWN BODIES - ACETYLCHOLINE.



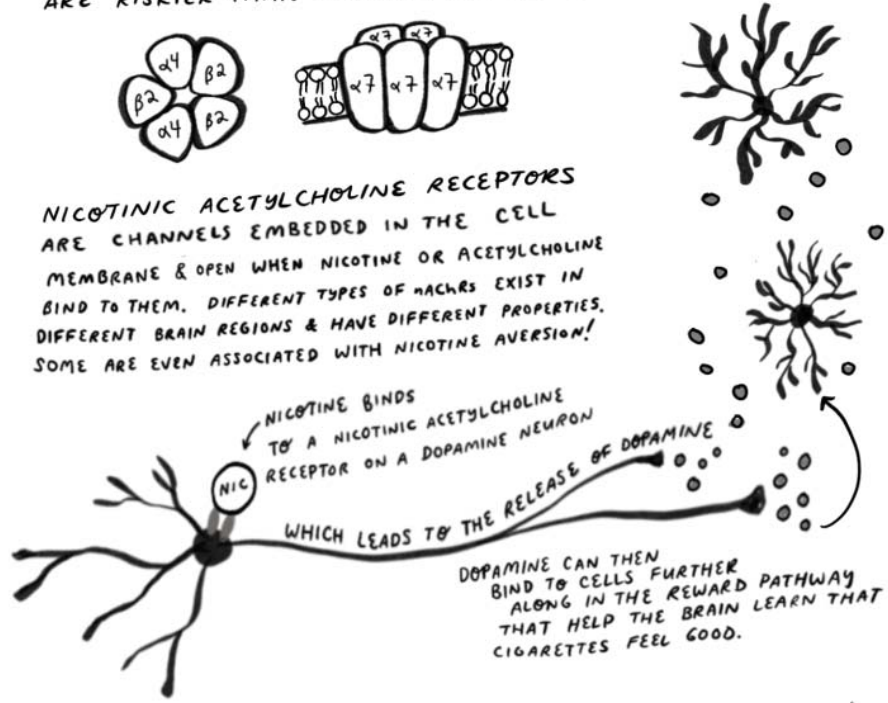
ACETYLCHOLINE MOVES OUR MUSCLES & PLAYS A ROLE IN SLEEP, FEAR, & PLEASURE.

NICOTINE'S MOLECULAR STRUCTURE IS SIMILAR ENOUGH TO ACETYLCHOLINE THAT IT CAN BIND TO ACETYLCHOLINE RECEPTORS. THE RECEPTORS MOST SENSITIVE TO NICOTINE ARE CALLED NICOTINIC ACETYLCHOLINE RECEPTORS.

NICOTINE'S RAPID & DIRECT EFFECT ON THE BRAIN'S NATURAL REWARD SYSTEM MAKES IT EXTREMELY ADDICTIVE. LIKE OTHER ADDICTIVE DRUGS, NICOTINE CAUSES SOME NEURONS TO RELEASE A LOT OF DOPAMINE WHICH CREATES A RUSH OF PLEASURE. THE FASTER A DRUG GETS TO THE BRAIN, THE BIGGER THE RUSH. THIS IS WHY SMOKING & VAPING ARE RISKIER THAN PATCHES OR GUM.



NICOTINIC ACETYLCHOLINE RECEPTORS ARE CHANNELS EMBEDDED IN THE CELL MEMBRANE & OPEN WHEN NICOTINE OR ACETYLCHOLINE BIND TO THEM. DIFFERENT TYPES OF nAChRs EXIST IN DIFFERENT BRAIN REGIONS & HAVE DIFFERENT PROPERTIES. SOME ARE EVEN ASSOCIATED WITH NICOTINE AVERSION!



A NICOTINE HABIT IS NOTORIOUSLY TOUGH TO QUIT. IT OFTEN TAKES MANY ATTEMPTS OVER MANY YEARS BEFORE SUCCESSFULLY ABSTAINING FOR A YEAR. WHILE 6-7 ATTEMPTS IS A COMMONLY SHARED STATISTIC, IT ISN'T UNCOMMON TO NEED OVER 30 ATTEMPTS.

"Quitting smoking is easy: I've done it thousands of times."

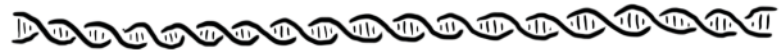
MARK TWAIN

IT MIGHT EVEN BE HARDER TO QUIT SMOKING THAN QUITTING OTHER DRUGS. WHEN SCIENTISTS LOOKED AT 28 DIFFERENT STUDIES OF PEOPLE TRYING TO OVERCOME THEIR ADDICTION FOR 6 OR MORE MONTHS,



BUT ONLY 8% OF PEOPLE TRYING TO QUIT SMOKING WERE ABLE TO.

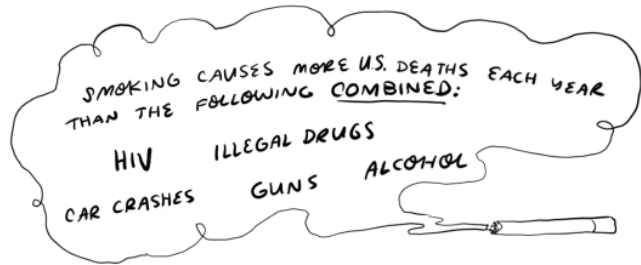
THIS LIKELY HAS TO DO WITH HOW EASY IT IS TO PURCHASE NICOTINE PRODUCTS COMPARED TO ILLEGAL DRUGS LIKE HEROIN. SMOKING ISN'T JUST AN ADDICTION INVOLVING MOLECULES & THE BRAIN. IT'S A LEGAL, SOCIAL DRUG THAT IS DESIGNED TO APPEAL. OUR SOCIAL RELATIONSHIPS & LIVING ENVIRONMENTS PLAY A ROLE, AS DOES GENETICS!



PEOPLE WITH DIFFERENCES IN THE CHRNA5-CHRNA3-CHRN4 GENE CLUSTER THAT ENCODES NICOTINIC ACETYLCHOLINE RECEPTORS VARY IN RISK FOR ADDICTION & DISEASE.



NICOTINE ADDICTION HAS TAKEN BLAME FOR CAUSING THE MOST PREVENTABLE DEATHS BOTH IN THE U.S. & WORLDWIDE. MOST OF THESE DEATHS ARE DUE TO DISEASES CAUSED BY SMOKING CIGARETTES. THE CHEMICALS IN THE SMOKE DAMAGE NEARLY EVERY ORGAN OF THE BODY - MORE THAN JUST THE LUNGS & HEART.

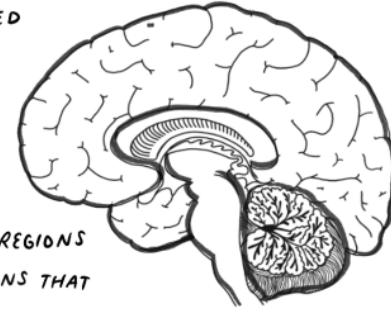


BUT EVEN WHEN DELIVERED WITHOUT CIGARETTE SMOKE, NICOTINE INCREASES HEART RATE & CAUSES BLOOD VESSELS TO CONSTRICT. IT'S UNCLEAR WHETHER NICOTINE PATCHES & GUM CAUSE LONG-TERM CARDIOVASCULAR HARM, BUT BOTH CIGARETTES & E-CIGARETTES INCREASE THE RISK OF HEART ATTACK. USING BOTH IS EVEN WORSE.



NICOTINE CAN ALSO HARM THE DEVELOPING BRAINS OF YOUNG PEOPLE BY POTENTIALLY PRIMING THE BRAIN FOR ADDICTION TO OTHER SUBSTANCES & INTERFERING WITH LEARNING & EMOTIONAL STABILITY. WHEN FETUSES ARE EXPOSED TO NICOTINE THROUGH THEIR PREGNANT MOTHERS, THE BABIES WEIGH LESS WHEN BORN & ARE AT RISK FOR ATTENTION & LEARNING DEFICITS.

WHILE ADDICTIVE DRUGS ALL INCREASE DOPAMINE IN SOME WAY, DRUGS AFFECT MORE THAN JUST DOPAMINE NEURONS. THE BRAIN IS AN INTERCONNECTED NETWORK OF CELLS WITH DIFFERENT REGIONS PERFORMING SPECIFIC ROLES.



FOR EXAMPLE, THE REGIONS IMPORTANT FOR PROCESSING REWARD & PLEASURE INFORMATION HAVE LOTS OF DOPAMINE NEURONS BUT OTHER REGIONS MIGHT CONTAIN MOSTLY EXCITATORY NEURONS THAT RELEASE GLUTAMATE OR INHIBITORY CELLS THAT RELEASE GABA. MORE OFTEN THAN NOT, BRAIN REGIONS CONTAIN MANY CELL TYPES.



WHEN NICOTINE BINDS TO RECEPTORS ON A DOPAMINE NEURON, THE NEURON BECOMES MORE LIKELY TO FIRE AN ACTION POTENTIAL TO RELEASE DOPAMINE IN BRAIN REGIONS WHERE THE NEURON SENDS PROJECTIONS. NEURONS RECEIVING DOPAMINE CAN BECOME EXCITED OR INHIBITED DEPENDING ON THE RECEPTOR & CELL PROPERTIES.

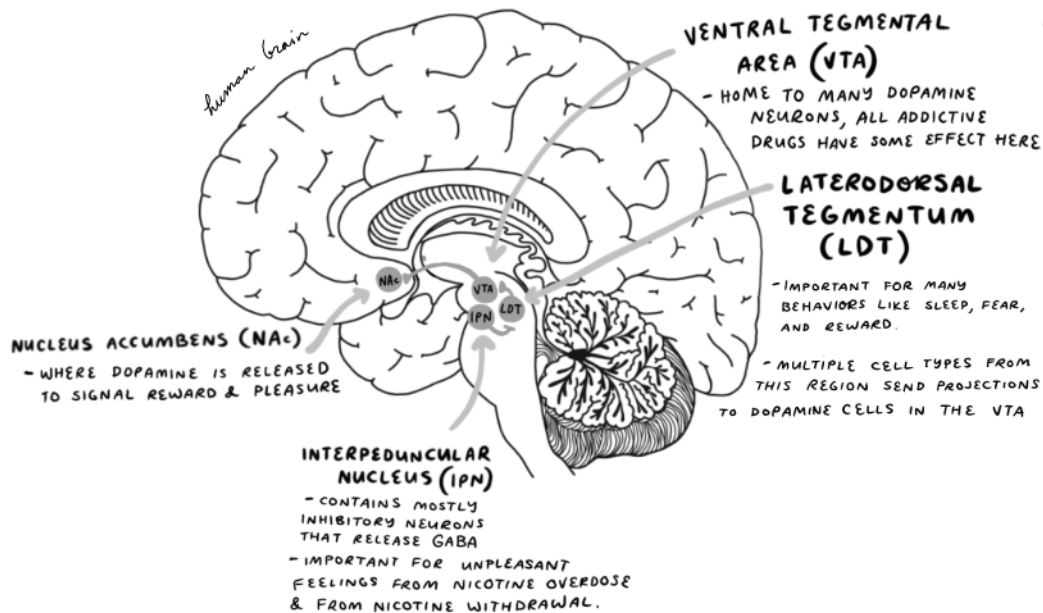
THUS, DRUGS HAVE COMPLEX EFFECTS ON THE BRAIN & SCIENTISTS ARE TRYING TO UNTANGLE THE CIRCUITS OF NEURONS THAT DRUGS ACT ON. THE STORY GETS EVEN MORE COMPLICATED WHEN INVESTIGATING LONG-TERM EFFECTS OF DRUGS.

EVEN AFTER A SINGLE EXPOSURE, NICOTINE BEGINS CHANGING THE BRAIN. CONNECTIONS BETWEEN NEURONS STRENGTHEN & NICOTINE RECEPTORS BECOME MORE ABUNDANT, SHAPING PARTS OF THE BRAIN TO RESPOND MORE STRONGLY TO NICOTINE. ADDICTION OCCURS WHEN THE REWARD SYSTEM IN THE BRAIN BECOMES DYSFUNCTIONAL TO THE POINT WHERE DRUG-SEEKING BECOMES A PRIORITY OVER FOOD, SOCIAL RELATIONSHIPS, & OTHER HEALTHY REWARDS & THE USER IS UNABLE TO ABSTAIN FROM THE DRUG, CAUSING CONSEQUENCES.

NICOTINE IS A PARTICULARLY INTERESTING DRUG TO STUDY BECAUSE UNLIKE OTHER ADDICTIVE DRUGS, IT BECOMES UNPLEASANT & AVERSIVE AT HIGH DOSES. ADDICTION MIGHT ACTUALLY BE TREATABLE BY TAPPING INTO THE BRAIN'S NATURAL AVERSION RESPONSE TO NICOTINE IF DESIGN DRUGS TO ACTIVATE IT.

OUR RESEARCH IN THE LAMMEL LAB AT UC BERKELEY TEASES APART THE NETWORK OF NEURONS THAT COMMUNICATE WITH THE DOPAMINE SYSTEM IN RESPONSE TO NICOTINE.

WE FOCUS ON A FEW REGIONS OF THE BRAIN KNOWN TO RESPOND TO NICOTINE:



OUR GOAL IS TO TRACE A PATH OF COMMUNICATION THROUGH THE BRAIN THAT SIGNALS WHEN NICOTINE MAKES US FEEL GOOD, AND HOW THIS COMPARES TO THE SIGNALS THAT OCCUR WHEN HIGHER DOSES MAKE US FEEL BAD.



NICOTINE CAN ALSO CAUSE A PROFOUNDLY "grounding" EXPERIENCE AND CAN EASE ANXIETY, BUT THE ANXIETY MAY BE CAUSED BY ADDICTION & WITHDRAWAL, PERPETUATING A DEPENDENCE ON NICOTINE FOR RELIEF. AT HIGH DOSES, NICOTINE CAN EVEN CAUSE ANXIETY & DISCOMFORT.

SMOKING MAY SIMPLY EASE SOME SYMPTOMS BUT THE RISK OF ADDICTION & BODILY HARM LIKELY OUTWEIGH POTENTIAL BENEFITS.



EVEN WITHOUT RELYING ON NICOTINE AS A TREATMENT FOR DISORDERS, A HEALTHY PERSON IS ALREADY EXTREMELY VULNERABLE TO BECOMING DEPENDENT & ADDICTED TO NICOTINE. THE HEALTHY BRAIN & BODY'S NATURAL LEARNING & REWARD MECHANISMS ARE HIJACKED BY ADDICTIVE DRUGS.

DRUGS TEND TO BE A QUICK & RELATIVELY EASY WAY TO FEEL PLEASURE, BUT THE BODY ADAPTS QUICKLY TO FEEL UNPLEASANT IN THE ABSENCE OF DRUGS. THIS IS CALLED WITHDRAWAL, & THE ONLY WAY TO GET RID OF IT IS TO EITHER TAKE MORE DRUGS OR ABSTAIN FROM DRUGS LONG ENOUGH FOR THE BODY TO RECOVER FROM THE CHANGES DRUGS HAVE CAUSED.

FOR MANY, KEEPING UP A DRUG HABIT IS FAR EASIER THAN QUITTING.

WHILE A LOT OF RESEARCH HAS BEEN CONDUCTED ON NICOTINE & THE BRAIN, WE HAVE A LONG WAY TO GO BEFORE FULLY UNDERSTANDING NICOTINE'S IMPACT ON US.



DISORDERS LIKE SCHIZOPHRENIA & PARKINSON'S ARE CHARACTERIZED BY ABNORMAL LEVELS OF DOPAMINE AND PATIENTS TEND TO SELF-MEDICATE WITH NICOTINE. THEORETICALLY, NICOTINE CAN BE A TOOL FOR INCREASING DOPAMINE IN THE BRAIN TO COUNTERACT DEFICIENCIES CAUSED BY DISEASE. HOWEVER, A PROMISING YEAR-LONG STUDY EXPLORING WHETHER NICOTINE PATCHES COULD SLOW PARKINSON'S DISEASE DID NOT YIELD ANY DIFFERENCES BETWEEN PATIENTS GIVEN NICOTINE PATCHES VERSUS PATIENTS GIVEN A PLACEBO.



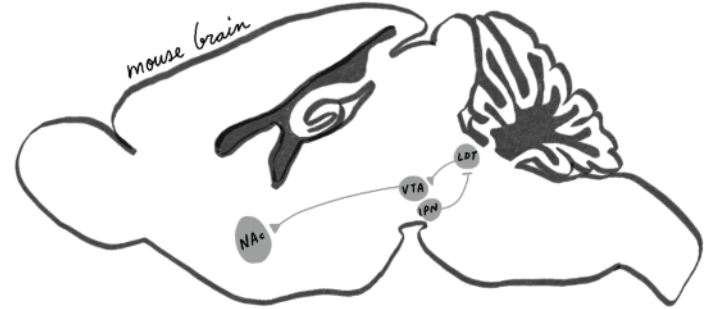
THERE ARE SOME POSITIVE EFFECTS OF NICOTINE. NICOTINE HAS BEEN SHOWN TO IMPROVE PERFORMANCE IN SOME COGNITIVE TASKS IN SOME HEALTHY ADULTS, PEOPLE WITH MILD COGNITIVE IMPAIRMENT, & ADOLESCENTS WITH ADHD. HOWEVER, THE EFFECTS TEND TO BE MILD & DON'T AFFECT EVERYONE THE SAME WAY.



HAMILTON MORRIS, WHO EXPERIMENTS WITH DRUGS ON HIS TV SHOW "HAMILTON'S PHARMACOPEIA", LIKES TO CHEW NICOTINE GUM WHILE HE WRITES.



OUR LAB STUDIES THESE BRAIN REGIONS IN MICE BECAUSE THEIR BRAINS ARE CONSIDERED SIMILAR ENOUGH TO HUMANS IN TERMS OF HOW IT FUNCTIONS IN RESPONSE TO DRUGS.



THERE ARE EXTREMELY POWERFUL NEUROSCIENTIFIC TECHNIQUES AVAILABLE TO USE WITH MICE & OUR LAB USES THEM TO TARGET SPECIFIC CELL TYPES BASED ON WHICH BRAIN REGION THE NEURONS ARE IN, WHERE THEY SEND PROJECTIONS, & WHAT KIND OF NEURON THEY ARE.



GENETICALLY ENGINEERED MICE ALLOW TARGETING OF NEURONS BY CELL TYPE

VIRUSES TO INFECT NEURONS TO EXPRESS SPECIAL PROTEINS LIKE LIGHT-SENSITIVE ION CHANNELS

MICROSCOPY COMBINED WITH FLUORESCENT LABELING TOOLS LET US SEE WHERE NEURONS SEND & RECEIVE PROJECTIONS FROM



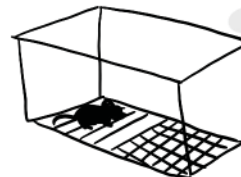
STEREOTACTIC SURGERY TO INJECT VIRUSES & FLUORESCENT TRACERS INTO THE BRAIN WITH PRECISION

THEN, WE CAN RECORD HOW DIFFERENT GROUPS OF NEURONS RESPOND TO NICOTINE & EVEN MANIPULATE THEM TO SEE IF TURNING CERTAIN CELL POPULATIONS ON OR OFF WILL AFFECT HOW NICOTINE FEELS TO THE MICE.



OPTOGENETICS ALLOW US TO CONTROL NEURON ACTIVITY WITH LIGHT BY OPENING LIGHT-SENSITIVE CHANNELS THAT ARE INTRODUCED TO NEURONS

FIBER PHOTOMETRY RECORDS THE ACTIVITY OF NEURONS WHEN A MOUSE RECEIVES NICOTINE



MOUSE BEHAVIOR TESTS CAN TELL US IF A DOSE OF NICOTINE IS REWARDING OR AVERSIVE.



SLICE ELECTROPHYSIOLOGY ENABLES THE RECORDING OF INDIVIDUAL NEURONS

# CIGARETTES



**1969:** ADVERTISING OF CIGARETTES ON TV & RADIO IS BANNED & PACKAGING MUST INCLUDE WARNING

**2010:** BRANDING CIGARETTES AS "LIGHT" & "LOW-TAR" IS BANNED

**1987:** SMOKING ON DOMESTIC FLIGHTS LESS THAN 6 HOURS IS BANNED

**2009:** BANNED ALL FLAVORS EXCEPT MENTHOL (WHICH MAY INCREASE DANGER OF SMOKING BOTH DUE TO APPEAL & TO REDUCING SENSITIVITY TO PAIN FROM SMOKE INHALATION)

HAVE BEEN THE MOST POPULAR TOBACCO PRODUCT. BITS OF TOBACCO LEAVES ARE WRAPPED WITH THIN PAPER & TOPPED WITH A FILTER.

SOMETIMES EXTRA NICOTINE & OTHER ADDITIVES LIKE GLUE & FILLERS & FLAVORS ARE ADDED.



**2010:** PACKAGING MUST INCLUDE HEALTH WARNINGS

SMOKELESS TOBACCO IS USUALLY CHEWED OR PLACED BETWEEN THE LIP & TEETH FOR ORAL ABSORPTION OF NICOTINE. USING SMOKELESS TOBACCO CAN LEAD TO CANCER OF THE MOUTH, ESOPHAGUS, & PANCREAS IN ADDITION TO NICOTINE ADDICTION & ORAL DECAY.

"DIP" or "CHEW"

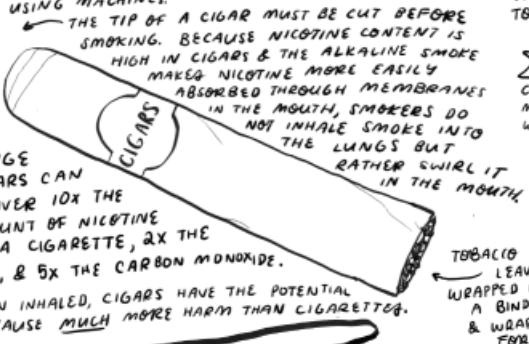
MORE RECENTLY, TOBACCOLESS & SMOKE-FREE NICOTINE HAS BEEN DEVELOPED BY ONE OF THE LEADING CHEWING TOBACCO MANUFACTURERS. THE POUCHES ARE MADE WITH SOLID NICOTINE SALT CRYSTALS AND BULKING, SWEETENING, & FLAVORING CHEMICALS. THESE POUCHES MIGHT POSE FEWER HEALTH RISKS THAN CHEWING TOBACCO, BUT THEY HAVEN'T EXISTED LONG ENOUGH FOR ENOUGH LONG-TERM RESEARCH TO BE CONDUCTED.



**CIGARS** ARE LARGE CYLINDERS PACKED & WRAPPED WITH TOBACCO LEAVES. SOME MAKERS PRIDE THEMSELVES ON HAND-ROLLING CIGARS INSTEAD OF USING MACHINES.

**2016:** FDA BEGINS REGULATION TO COVER ALL TOBACCO PRODUCTS

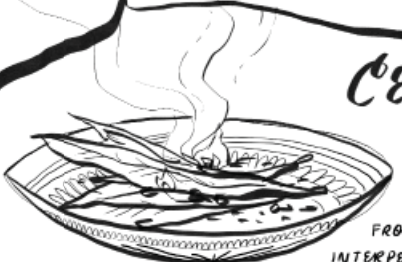
**2018:** CIGAR PACKAGING MUST INCLUDE HEALTH WARNINGS



WRAPPED WITH "TOBACCO PAPER" (tobacco pieces pressed & glued to form a sheet)

TOBACCO LEAVES WRAPPED WITH A BINDER LEAF & WRAPPED AGAIN FOR SMOOTH LOOK

# CEREMONIAL BURNING

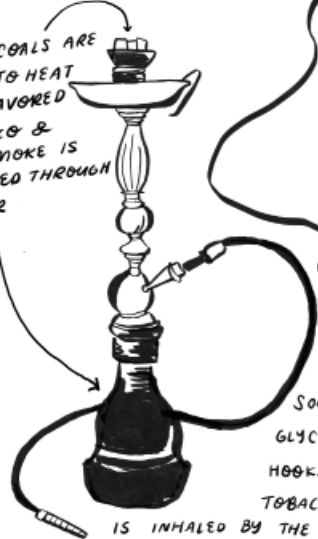


IN CULTURES INDIGENOUS TO THE AMERICAS, TOBACCO WAS SMOKED IN PIPES OR BURNED IN A DISH OR IN AN OPEN FIRE. THE PRIMARY MOTIVE WAS NOT TO GET HIGH OR BUZZED FROM THE NICOTINE BUT TO FOSTER A SPIRITUAL AND/OR INTERPERSONAL CONNECTION.

# HOOKAH

ORIGINATED IN INDIA & PERSIA ABOUT 500 YEARS AGO

HOT COALS ARE USED TO HEAT UP FLAVORED TOBACCO & THE SMOKE IS FILTERED THROUGH WATER



# LITTLE CIGARS/CIGARILLOS



BIGGER THAN CIGARETTES AND SMALLER THAN CIGARS, CIGARILLOS HAVE AN APPROPRIATE NAME. THEY ARE WRAPPED WITH TOBACCO LIKE CIGARS & HAVE HIGH NICOTINE LEVELS THAT ARE ALSO NOT MEANT FOR INHALING DEEPLY. HOWEVER, PEOPLE DO TEND TO INHALE, WHICH MAKES THESE LITTLE CIGARS, OFTEN FLAVORED WITH SWEET AROMAS LIKE FRUIT & VANILLA, VERY DANGEROUS TO HEALTH.

CIGARILLOS ARE ALSO OFTEN CUT OPEN TO MIX THE TOBACCO CONTENTS WITH CANNABIS TO CREATE A "SPLIFF" OR "BLUNT".

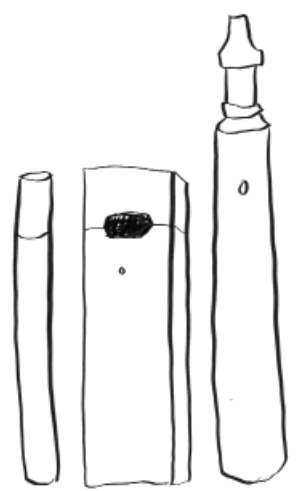
HOOKAHS ARE WATER PIPES THAT ARE TYPICALLY SMOKED AS A SOCIAL ACTIVITY. TOBACCO IS MIXED WITH MOLASSES, VEGETABLE GLYCEROL & FLAVORS AND PLACED IN A COMPARTMENT AT THE TOP OF THE HOOKAH WITH ALUMINUM FOIL AND HOT CHARCOAL ON TOP, ALLOWING THE TOBACCO TO BURN SLOWLY. THE SMOKE PASSED THROUGH WATER AS IT IS INHALED BY THE USER. IN ADDITION TO THE HIGH DOSES OF NICOTINE & TOXIC CHEMICALS CONSUMED, THE CUSTOM OF SHARING A MOUTHPIECE CAN ALSO TRANSMIT DISEASE.

# E-CIGARETTES

THIS NEW, TOBACCO-LESS, ELECTRONIC METHOD OF NICOTINE DELIVERY IS TURNING THE LANDSCAPE OF NICOTINE ADDICTION & DISEASE UPSIDE-DOWN. WHILE IT'S A PROMISING TOOL FOR QUITTING CIGARETTES, THEY ARE ALSO INCREASING NICOTINE INTAKE AMONG YOUNG PEOPLE & THE INGREDIENTS IN E-LIQUIDS MAY POSE THEIR OWN DANGERS.

MORE YOUTH & TEENS ARE VAPING EACH YEAR, ENTICED BY FUN FLAVORS. MANY ARE UNAWARE THEY ARE EVEN CONSUMING NICOTINE & BECOMING ADDICTED.

AS A GROWING, LUCRATIVE MARKET, COMPANIES & LAWMAKERS ARE RACING TO SHAPE POLICY AROUND THIS EMERGING TECHNOLOGY. WHILE A FULL-FLEDGED BAN ON FLAVORED E-LIQUID OR PODS IS HEAVILY DEBATED, JUUL (THE LEADING COMPANY WITH 70% OF THE MARKET SHARE) HAS DECIDED TO PULL FLAVORS OFF SHELVES & SELL THEM ONLINE ONLY, WHICH SHOULD DECREASE ACCESS TO YOUTH & TEENS.



**2016:** BANNED SALES TO CUSTOMERS UNDER 18 YEARS OLD