

TOPIC 8 REVIEW – TOBACCO

→ Tobacco is the most dangerous substance in the world

- kills more people than

- DDT
- PCB's
- industrial chemicals
- pesticides
- cocaine
- alcohol
- homicide
- suicide

→ COMBINED!

- tobacco is basically linked to all forms of death listed above. In fact, 1/3 of all cancer deaths are associated with the use of tobacco.

- the number one risk factor associated with stroke is tobacco smoke!

- tobacco kills 420,000 per year in North America

- estimated that 6 billion deaths/year, more specifically in third world countries where as much as 70% people smoke

History of Tobacco

→ **Columbus** discovers tobacco 1492

- Natives drank smoke from tobaggos (name of tobacco for the natives Columbus saw on his trip to the Caribbean)

- first shipments to Spain from Tobago

- theory that "tobacco" comes from the shipment to Spain from the island "Tobago"

→ **Jean Nicot** introduced tobacco to France

- "l'herbe nicotaine"

- Jean Nicot introduced tobacco to France. He used it as an herbal medicine – in fact, one of the first treatments of asthma was tobacco!

→ Tobacco was used to revive drowning victims

→ Tobacco smoking in clubs

- smoking a long time ago was expensive and unpleasant (tobacco was very harsh because of the acids in it).

- people consumed tobacco primarily using a pipe with a long stem

- point is to have the acid gas to cool down in the long stem to allow smoking to be possible

- crude processing of tobacco back then

→ Water pipes popular in Eastern countries

- water pipes is a way to smoke tobacco in Eastern countries.

- while it may prevent some organic substances going into the smoke, it is not MUCH safer

→ Snuff became popular with aristocracy

- snuff = powdered tobacco leaves

- you had to be rich because the supply of tobacco back then was low

→ Chewing tobacco popular with the masses

→ First depiction of cigarette smoking

- Cigarette is in fact a relatively new invention (late 1700s)

- cigarettes were originally rolled by hand

- making them expensive

- Bonsack machine reduced production cost

- first machine to manufacture cigarettes!

- drove down the cost dramatically

- Flue-curing reduced harshness of smoke
- flue-curing = heating up tobacco in an oven.
 - when you heat it rapidly in this flue process, it is not acidic anymore (i.e. it does not hurt your throat anymore). Now possible to smoke in a modern way (without the long stem!)

- Cigarettes become dangerous!
- machine manufacturing reduced cost
 - could afford to smoke a lot
- flue curing reduced irritants in smoke
 - smoke brought deep into lungs
 - cigarettes now addictive
- these two factors increase exposure to toxic substances
 - risk = toxicity x exposure
- early cigarette ads emphasized “mildness”

Cigarette smoking today

- Average smoker smokes 10, 000 cigarettes each year
 - data from today
- cigarette consumption then and now:
 - late 1800s:
 - 80 cigarettes a year
 - did not inhale
 - today:
 - 10,000 cigarettes a year
 - inhale deeply
 - hold smoke in lungs

How It Works

- Nicotine is the addictive substance
 - 2 mg per cigarette required to addict smoker
 - as a result, cigarettes (or nicotine gums for ex) typically contain 2 mg per cigarette or per gum
 - therefore cigarette delivers 2 mg nicotine to addict
- Nicotine acts on acetylcholine receptors
 - nicotine = acetylcholine agonist
 - messenger-receptor interaction
 - 2nd messenger system signal transduction to go from the receptor to the biological response
 - agonist at low doses, resulting in excitatory signal without the presence of acetylcholine
 - agonist sends message without the normal messenger
 - antagonist at high doses
 - blocks chemical messages
 - smokers regulate the dose
 - if you want to get stimulated, you puff on the cigarette, but to get relaxed, you inhale deeply
 - nicotine stimulates dopamine release
 - remember, dopamine is involved in the “reward” system of the brain
 - part of the reason why nicotine is so addictive!
 - smoking cues add to the addiction
 - “ritual” or “cue” of smoking
 - ex: coffee in the morning = cigarette!
 - nicotine use as a pesticide
 - lethal dose is 60 mg
 - cigar, however, contains 120 mg! Why people don’t die – temperature of the cigar smoke causes thermal decomposition of nicotine to a biologically safe level
 - common form of poisoning in children

- lethal dose is 60 mg
- lethal dose of cyanide is 70 mg
- nicotine to kill elephants
 - nicotine is concentrated in “dart guns” to kill elephants and other animals
- nicotine stimulate the heart muscle
 - because nicotine stimulates the heart muscle, heart attack is a very real possibility, though it is very rare that nicotine would result in a heart attack

- Toxic substances in tobacco smoke – CO
- carbon monoxide!!
- CO reduces oxygen carrying capacity of blood
 - sticks to haemoglobin – affinity of CO is 20 X higher than that of oxygen

Smoking and Cancer

- Polonium 210 in tobacco smoke
- causes cancer (see cancer lecture)

- Carcinogens in tobacco smoke
- benzopyrenes
 - converted by Cyt P450, and before hydrolase activity, the intermediate can intercalate with DNA to cause DNA damage
- nitrosamines
- aldehydes
- epoxides
- aza-arenes
- trace metals

→ a smoker’s lung is black while a normal person’s lung is yellow → black colour is a result of tissue damage

- **Dr. Alton Ochsner** linked cancer to smoking 1919
- lung cancer then and now:
 - 1919: only 400 cases in North America (chimney sweeps)
 - 2004: 190,000 cases in North America (smokers)

Tobacco Advertising

- Tobacco advertising emphasized glamour
- tobacco companies advertise the image that men should smoke to attract women
- tobacco companies paid stars to smoke in movies
- cigarettes were provided free to soldiers

- tobacco advertising targeted women in 1950s
- women started smoking to stay slim
 - urban myth
 - when smokers STOP smoking, they tend to gain weight because of the lack of dopamine-reward pathway

- smoking causes wrinkles
- smoking damages skin for two reasons:
 - 1) smoke contains CO, which is a potent vasoconstrictor, therefore it decreases blood supply to skin cells
 - 2) chemicals in smoke can destroy both collagen and elastin. Elastin, in particular, is very important to maintain elasticity in skin, therefore lack of elastin results in wrinkles

→ Ads target children

→ Second hand smoke is harmful

→ Emphysema significant cause of death

→ Smoking during pregnancy linked to low birth weight

Cigarettes are highly engineered drug delivery device

→ Use of reconstituted tobacco

- recon

- paper made from tobacco
- cut into small strips
- can use the whole tobacco plant
- cheaper
- can blend tobacco
- cut costs by mixing small amounts of high quality tobacco with cheap tobacco
- easy to introduce additives
- flavour (chocolate, vanilla, titanium dioxide), burn rate
- control nicotine content

→ Paper is specially designed

- Many chemical additives to control burning
- even burn rate
- titanium dioxide keeps the paper lit
- burn rings regulate combustion
- thin areas burn quickly when smoker draws
- thick areas burn slowly between puffs

→ Filter is decoration

- doesn't do anything
- 99% of all chemicals goes through the filter

→ cigarettes are engineered to deliver nicotine

- addition of ammonia shifts the solid-liquid equilibrium to liquid, resulting in greater consumption of nicotine which has to be in gas form to be consumed
- combustion makes acids

→ light cigarettes are just as dangerous as regular

- light cigarettes contain holes
- as a result, government tests cigarette smoke using a vacuum, the concentration of nicotine and other chemical substances is artificially reduced
- smoking machine collects fixed amounts of smoke
- vent holes placed at top of filter
- holes placed outside machine connection
- light cigarettes are not safer because
- to get 2 mg dose of nicotine
- people draw more deeply on light cigarettes
- people smoke more light cigarettes
- people cover the holes with fingers and lips

→ tobacco companies suppress information

→ Rose Cipolione vs Philip Morris 1988

- no one has ever won a case against tobacco companies with the exception of Rose
- no one wins a case because the tobacco companies employ "delay tactics" (wait until person dies)

→ Less cancerous cigarettes are Eclipse and Accord

→ Florida sues big tobacco in 1998

- Florida was one of the first states to win a legal case against a tobacco company

→ Companies always claimed tobacco not addictive

- dependence
- withdrawal
- tolerance
- intoxication

→ does not “intoxicate” a person so not addictive according to the companies

→ warning labels on cigarettes

To stop smoking

→ nicotine gum to stop smoking

- gum and patch work the same way – contain nicotine to reduce desire to smoke
- patch is safer because it is delivered over a long period of time

→ nicotine inhaler to stop smoking

- shape of cigarette to make you feel like you’re smoking

→ Chantix to stop smoking

- partial nicotine agonist

→ Plants in the Faboideae family contain cytisine

- partial nicotine agonist
- cytisine is difficult to make synthetically
- cytisine is similar to morphine
 - use morphine to make varenicline (similar)

→ Cold turkey works best!!