



# NICOTINE POISONING



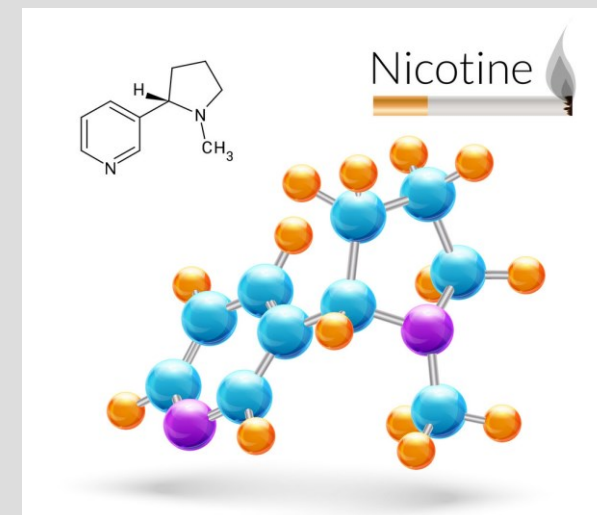
Toxicology Lab.  
4th Stage / 2nd semester  
(2020 – 2021)

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# INTRODUCTION:

- Nicotine is a water-soluble bioactive alkaloid with potent parasympathomimetic and addictive properties.
- Nicotine is obtained from the dried leaves and stems of tobacco plant *Nicotiana tabacum*, also found in tomatoes, potatoes, eggplant and green peppers
- Tobacco smoke contains more than 4700 toxic and carcinogenic compounds in addition to nicotine
- Nicotine was first isolated in (1828) by German chemists and named after (Jean Nicot) who introduced tobacco to French court



# PHARMACOKINETICS:

## **Absorption & Distribution:**

- Nicotine is well absorbed from all the body including:
  - Lungs (smoking)
  - Oral and nasal mucosa (cigarettes, chewing gum, nasal spray)
  - Skin (patches)
  - Gastrointestinal tract (ingestion and very uncommon)
- The most common way to get nicotine into your bloodstream is through inhalation
- Nicotine taken in by cigarette and takes only 10-15 seconds to reach the brain but has a direct effect on the body for only ~30 minutes
- Nicotine in smoke peaks in brain very rapidly, despite relatively slow increase in blood concentration
- A typical cigarette contains 20 mg of nicotine
- Half-life: ~ 2 hours
- 80-90% metabolized in liver

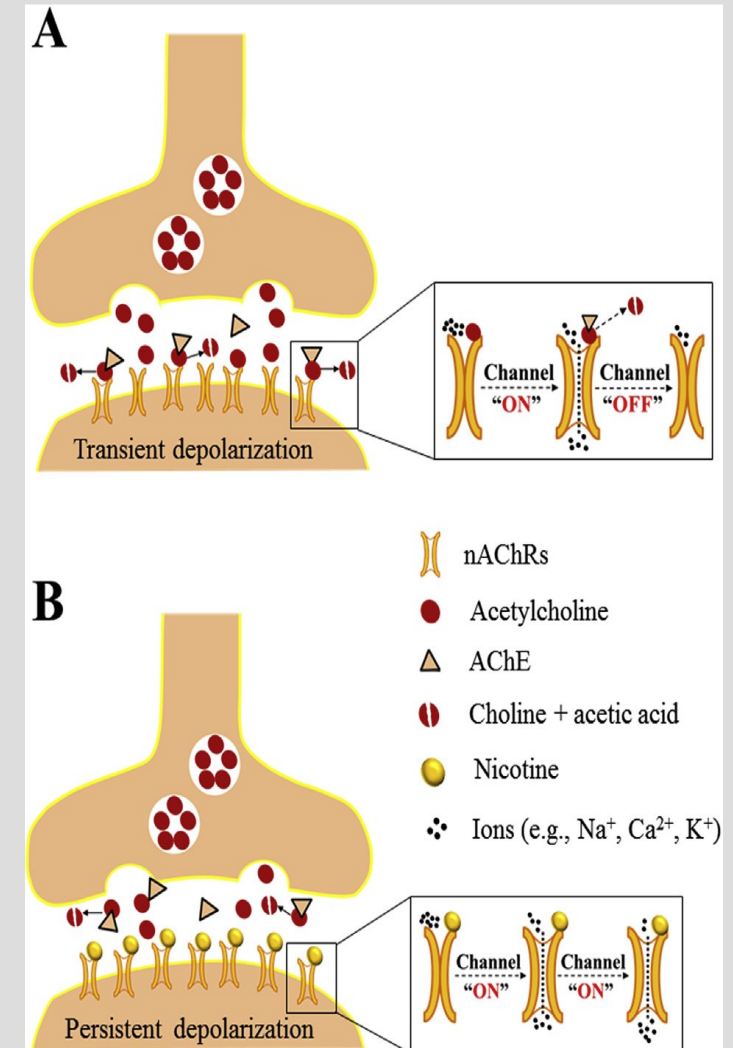
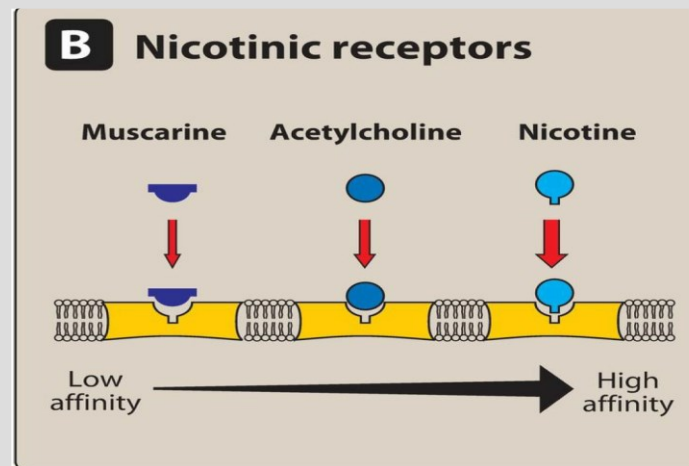
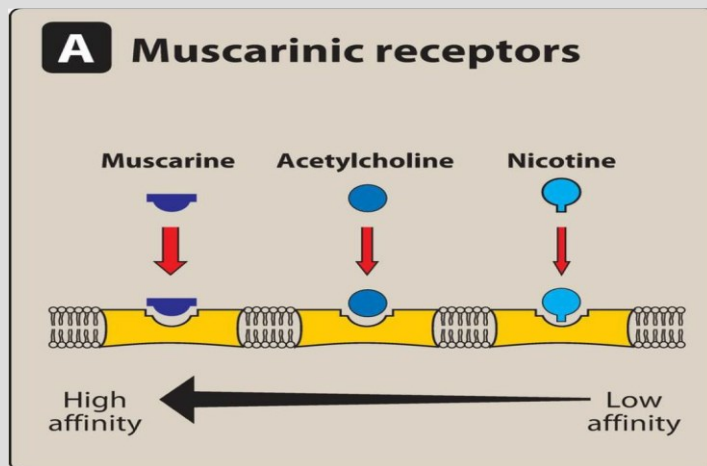
# PHARMACOKINETICS:

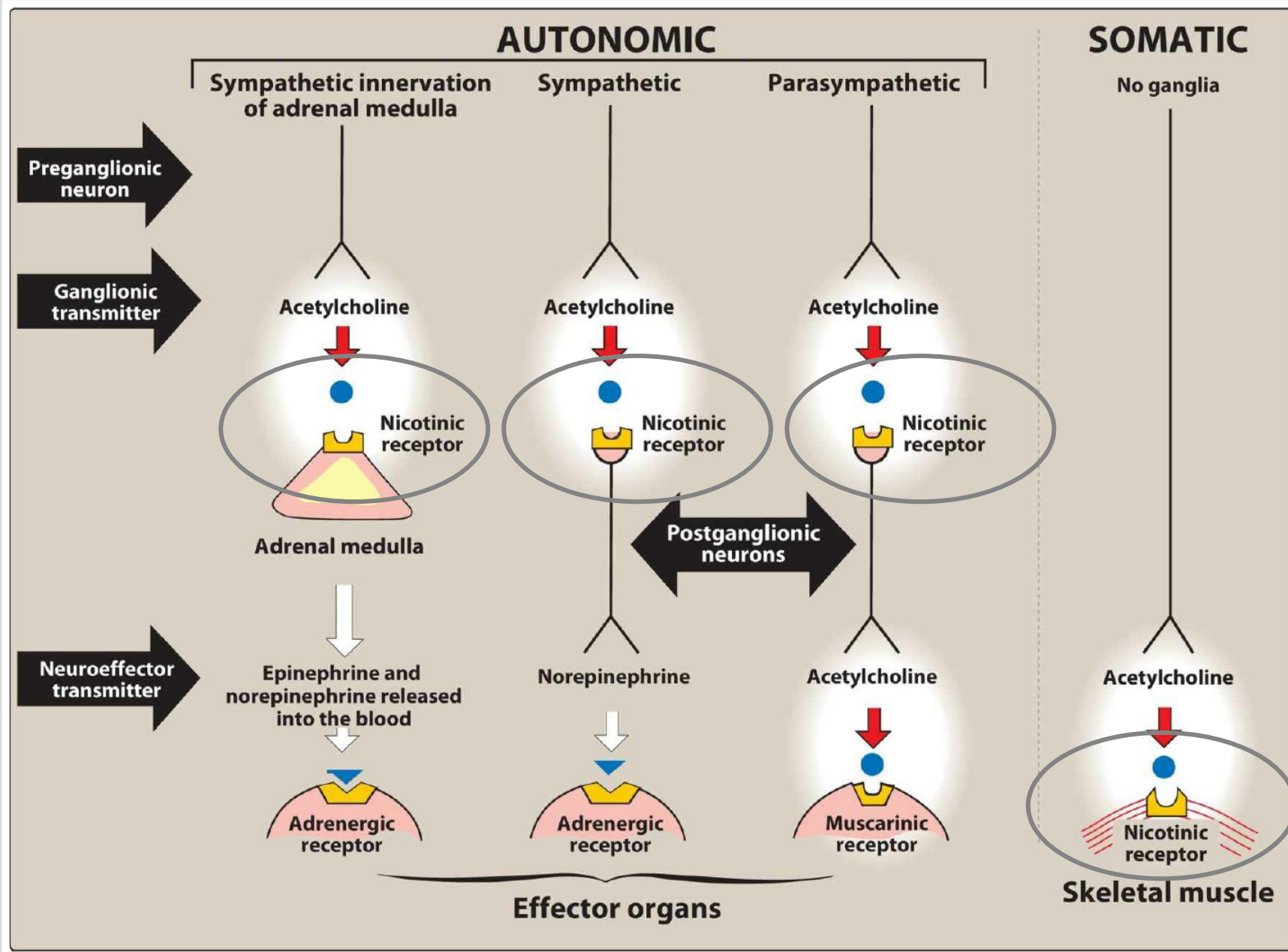
## **Metabolism & Elimination:**

- About 80% of the nicotine is metabolized by the liver through cytochrome P450 enzymes (specifically CYP2A6 and CYP2B6)
- Cotinine is the main metabolite of nicotine metabolism, the other two metabolites are (nornicotine and norcotinine)
- All the three metabolites can be found in varying concentrations in the lungs and the brain
- Cotinine and the remaining metabolites are filtered from the blood by the kidneys and excreted in the urine
- Nicotine and its metabolites can cross the placenta and appear in breast milk

# PHARMACODYNAMICS:

- Nicotine is a direct agonist on the nicotinic ACh receptors
- The nicotinic AChRs are transmembrane polypeptides with cation-selective ion channels which are permeable to  $\text{Ca}^{2+}$ ,  $\text{Na}^{+}$ , and  $\text{K}^{+}$ .
- The nicotinic AChRs are located on plasma membranes of the central nervous system (CNS) neurons, of postganglionic cells in all autonomic ganglia, and of muscles innervated by somatic motor fibers (NMJ), and the adrenal gland
- Binding of nicotine to its specific receptors resulting in the release of neurotransmitters (norepinephrine, dopamine, and ACh) and illicit a cellular response







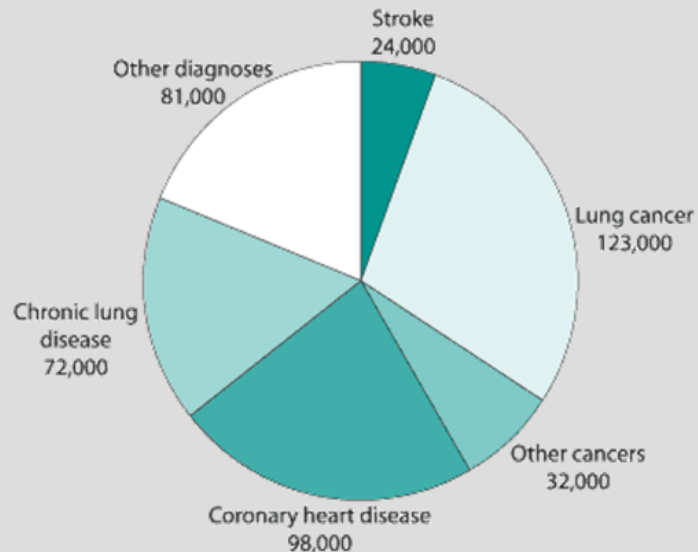
# PHARMACOLOGICAL EFFECTS:

- **Cardiovascular system:**
  - Increase in heart rate, stroke volume, heart oxygen consumption, hypertension
- **Central Nervous System (CNS):**
  - Stimulate dopamine release in the CNS which is responsible for the feeling of euphoria, and plays a significant role in nicotine addiction
  - Stimulate release of Ach neurotransmitter, which is important in memory function
  - Stimulate release of norepinephrine that plays a role in concentration, alertness and arousal and appetite suppression
  - Nicotine results in increased levels of beta-endorphin, which reduces anxiety.
- **Others:**
  - Stimulate the adrenal gland to release the hormone (epinephrine) which causes increase in glucose level, increase insulin resistance

# THE PROS & CONS OF USING NICOTINE

## POSITIVE EFFECTS

- Prevent Alzheimer disease
- Enhance cognitive function
- Improve symptoms of ADHD



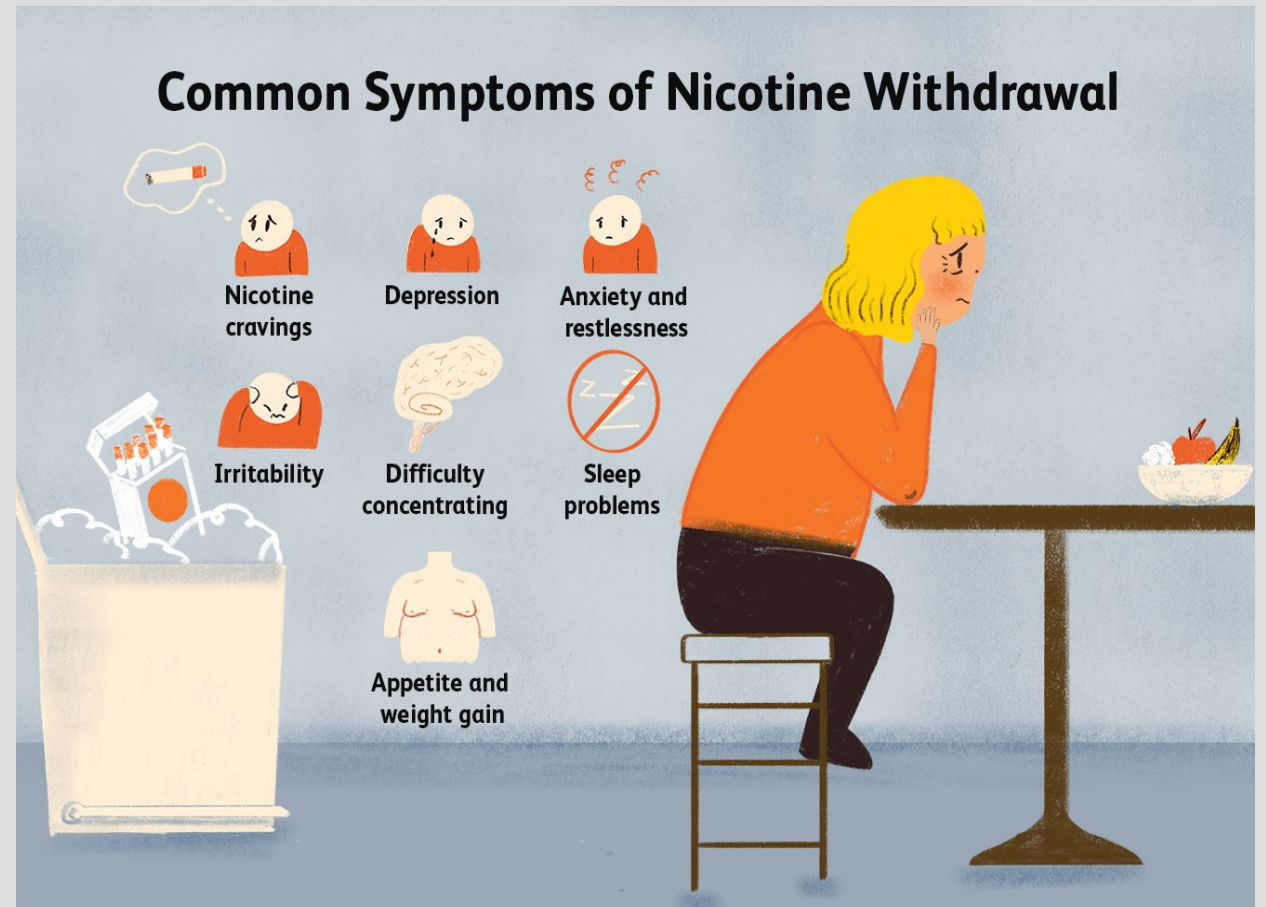
## NEGATIVE EFFECTS

- Cigarette smoking accounts for 90% of all cases of lung cancer and other types of cancers
- COPD (emphysema and chronic bronchitis)
- Coronary heart disorders
- GIT disorders (reflux esophagitis, gastritis)
- Abnormal fetal development
- Increase risk type 2 diabetes and insulin resistance
- Addiction (psychologically and physiologically). This effect was found to be mediated by NMDA receptors (N-methyl-D-aspartate) which control excitation, memory and learning



# NICOTINE IS HIGHLY ADDICTIVE:

- People who regularly consume nicotine and then suddenly stop experience withdrawal symptoms, which may include:
  - Craving
  - Anxiety
  - Depression
  - Irritability
  - Difficulty concentrating
  - Sleep disturbance
  - Increased appetite



# SMOKING CESSATION THERAPY:

- It aims to reduce the urges to consume nicotine as well as the associated risks and health problems.
- **The treatment for nicotine dependency include:**
  - **Nicotine replacement therapy (NRT):** a supply of nicotine in the form of (patches, nasal spray, gum, lozenges, and inhalers)
  - **Bupropion:**
    1. Anti-depressant that works by inhibiting the norepinephrine/dopamine re-uptake
    2. Used to reduce the craving and withdrawal symptoms of nicotine cessation
    3. For successful smoking cessation and prevention of relapse, it must be used for 3 – 6 months
  - **Varenicline (Chantix):**
    1. A nicotine receptor partial agonist, that stimulates nicotine activity but to lesser degree than nicotine itself, also acts on the dopamine system associated with nicotine addiction
    2. Reduces craving and withdrawal symptoms of nicotine cessation
    3. For successful results, it must be used for 3 – 6 months (usually this drug should be started 1 week before deciding quitting smoking)
  - **Other approaches:** (electronic cigarette, hypnosis, acupuncture. Yoga & meditation, and behavioral counseling)



# STRATEGIES FOR SMOKING CESSATION

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## Nicotine Replacement Therapy (NRT)

### LONG ACTING NRT

#### Patch

Wear for 24 hours at a time. Alternate sites to minimize skin irritation.

**Dose:**

If <10 cig/d, start with 14 mg/d

If >10 cig/d, start with 21 mg/d

Taper down with a regimen that is easiest for the patient

**Side Effects:**

vivid dreams, contact dermatitis

### SHORT ACTING NRTs. Combine with nicotine patch for best effect

#### Mini Lozenge

Allow to slowly dissolve. Do not chew or swallow lozenge.

**Dose:**

2mg/hr for patients who smoke their first cig >30 mins after awakening

4 mg/hr for patients who smoke their first cig <30 mins after awakening

**Frequency:** Every 1-2 hours. Try not to wait for cravings.

#### Gum

Chew minimally, "park" between teeth and cheek. Rechew when tingling is gone and rotate sites. Avoid use with acidic foods.

**Dose:**

2mg/hr for patients who smoke their 1st cig >30 mins after awakening

4 mg/hr for patients who smoke their 1st cig <30 mins after awakening

**Frequency:** Every 1-2 hours. Try not to wait for cravings.

**Side Effects:**

GI irritation when chewed

#### Nasal Spray

Can be used once to each nostril every 1-2 hours.

**Side Effects:**

can cause nostril irritation

#### Inhaler

Take short puffs but keep air in mouth. Do not inhale.

## Non-nicotine Replacement Therapy

### Varenicline (Chantix)

Nicotinic receptor partial agonist designed to decrease cravings, reduce withdrawal, and dampen nicotine-induced reward pathway.

**Dose:**

Take one week before quit date

0.5mg daily x 3d, 0.5mg BID x 3d

Then 1mg daily for 3-6 months

**Side Effects:**

nausea, vivid dreams

### Bupropion (Wellbutrin)

Nicotinic receptor antagonist and norepinephrine & dopamine reuptake inhibitor. Designed to reduce cravings and withdrawal.

**Dose:**

Take one week before quit date

150mg tablet once daily x 3 days.

Then 150mg tablet twice daily for 3-6 months

**Side Effects:**

lowers seizure threshold, insomnia, dry mouth

## Electronic Cigarettes

Reserve use until after FDA-approved treatments have failed.

Patients should avoid using traditional cigarettes with e-cigs (to minimize adding known harms to unknown harms).

Before prescribing e-cigs, discuss a plan for duration of use and when to stop.



# Nicotine Replacement Therapy Products

- Patch



- Mouth Spray



- Microtab



- Gum



- Inhalator



- Nasal Spray



- Lozenge



- Mouth Strips



# NICOTINE POISONING:

- Nicotine is poisonous and, though uncommon, an overdose still can result in serious toxic reactions, harmful symptoms or death.
- Vaping and liquid nicotine are the most common forms to cause nicotine poisoning in adults.
- Eating cigarettes or consuming liquid nicotine is the most common method of poisoning in children.
- The lethal dose of nicotine has been estimated to be 40–60 mg for adults and about 10 mg for children
- **The severity of nicotine intoxication is dependent on:**
  - dose,
  - dose duration and frequency,
  - route of exposure,
  - formulation of the nicotine product,
  - interpersonal variability

# SYMPTOMS OF NICOTINE POISONING:

- Symptoms of the toxic effects of nicotine occur following ingestion, inhalation, or skin contact.
- **Nicotine poisoning tends to occur in 2 stages:**
  - **1<sup>st</sup> Stage (the stimulation effects):**
    - ✓ Within the first 15 to 60 minutes following exposure, symptoms are related to the stimulatory effects of nicotine and include: (excessive salivation, nausea & vomiting, loss of appetite, tremor, anxiety, sweating, rapid breathing, increase heart rate and hypertension)
  - **2<sup>nd</sup> Stage (the depressor effects):**
    - ✓ The body begins to wind down. Nicotine's depressor effects appear within a few hours. These include: (low blood pressure, slow heart rate, shallow breathing, fatigue, diarrhea, weakness, pale skin)
    - ✓ In severe cases of poisoning / seizures, coma, difficulty breathing, respiratory failure)
    - ✓ Death occurs in rare cases

# MANAGEMENT OF NICOTINE POISONING:

Treatment of Nicotine Toxicity	
Clinical Manifestation	Intervention
Nausea, Vomiting Gastritis	Antiemetics Proton pump inhibitors
Tremor Seizures	Benzodiazepines
Hypotension Bradycardia	Fluid resuscitation, Vasopressors Atropine
Hypoventilation Hypersalivation	Intubation and mechanical ventilation Atropine, Glycopyrrolate
Nicotine Withdrawal	Nicotine replacement therapy

Clinical Effects of Nicotine Toxicity		
Organ System	Early phase (<1 hour after ingestion)	Late phase (>1 hour after ingestion)
Gastrointestinal	Hypersalivation Nausea and vomiting Abdominal pain	Diarrhea
Cardiovascular	Hypertension Arrhythmias Tachycardia	Arrhythmias Bradycardia Hypotension
Neurologic	Tremor Headache Ataxia Fasciculations Miosis	Hypotonia Seizures Coma
Respiratory	Bronchorrhea Tachypnea	Dyspnea Apnea Respiratory depression

**Note:** in case of ingested nicotine, then the first treatment option is **(induce vomiting with syrup of ipecac, gastric lavage, or administer activated charcoal)**



# EXPERIMENT REQUIREMENTS:

- Albino mice (male)
- Insulin syringes
- Smoking cigarettes
- The nicotine extract of cigarettes



## THE EXPERIMENT:

- 5 cigarettes are macerated in 50ml of hot DW overnight, then filtered by a filter paper
- 4 mice, each 2 mice are placed in a separate cage
- 2 mice will be given 20 IU nicotine extract IP, and the other 2 mice will be given 25 IU nicotine extract by oral gavage
- Observe the 2 stages of nicotine toxicity that should start with stimulation, then followed by depression and death if it occurs
- The LD50 of nicotine for mice is 3mg/kg

**Stop**  
Smoking



Start  
**Breathing**

