Mental Dental – Pharmacology

Local Anesthetics

Categories and Calculations

Amides	Esters
Metabolism: Liver LA's: - Lidocaine 2% - Bupivicaine 0.5% - Mepivicaine 2% and 3% - Articaine 4% - Prilocaine 4% *All have an "I" before the "-caine" *Facts*: - Lidocaine -> Safest to for children - Bupivicaine -> Most dangerous for children -> Longest lasting - Mepivicaine -> ↓ about of vasodilation - Articaine -> Has 1 ester chain (and an amide) -> Metabolized in both liver and plasma -> Shortest acting - Prilocaine -> Can cause methemoglobinemia	***Metabolism***: Plasma via pseudocholinesterase LA's: - Procaine - Cocaine - Tetracaine - Benzocaine *↑ Toxic, ↑ Allergic -> B/c Methylparaben (food preservative) interacts with esters* *Facts*: - Cocaine -> Vasoconstricts (all other LA's are dilators) - Benzocaine -> Common topical anesthetic

Vasoconstrictor is added (Epinepherine) to:

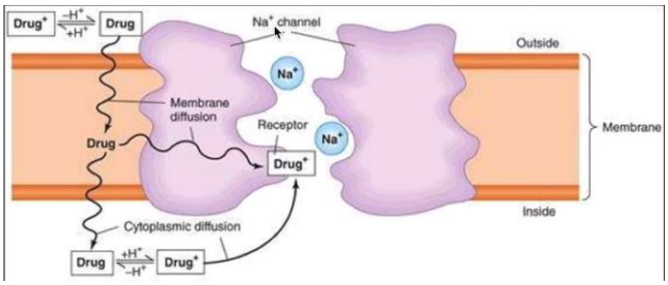
1. Prolong numbness
2. ↓ Toxicity
3. Promote hemostasis

Toxicity Values:

- Max Epinepherine for ASA I patient = 0.2mg
- Max Epinepherine for Cardiac Patient (MI or arrythmia) = 0.04mg
- Max Lidocaine w/o vasoconstrictor = 4.4mg/kg
- Max Lidocaine w/ vasoconstrictor = 7mg/kg

Pharmacodynamics

= Na^+ channel blockers



- Only the non-ionized (free-base) form can penetrate the neuronal membrane.
- **Inflamed tissue is acidic (↓ pH)** = ↓ the non-ionized form of LA available -> ↓ effectiveness of LA in infected/inflamed tissue
- **Critical Length**: 3 consecutive nodes of Ranvier needs to be blocked for profound anesthesia

Pharmacokinetics

Blood Flow	↑ blood flow = ↓ duration of action
Lipid Solubility/Hydrophobicity	↑ lipid solubility = More potent (more can cross the membrane) = Longer Duration
Protein Binding	↑ Protein Binding = ↑ Duration of action (↑ attraction to receptor sites)

pKa	↓ pKa = Faster onset - (Stronger acid = gives up proton easier -> non-ionized form easier to achieve) **#'s** - Mepivacaine: 7.6 - Closer to pH of inflamed tissue = ↑ effectiveness vs others in acidic tissues - Lidocaine, Prilocaine, Articaine: 7.8 - Bupivacaine: 8.1

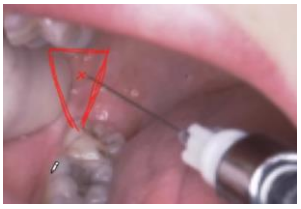
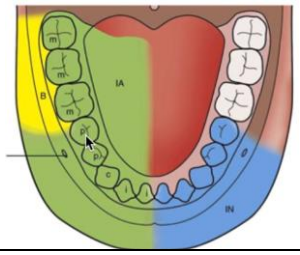
Calculations

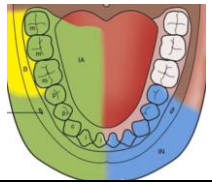
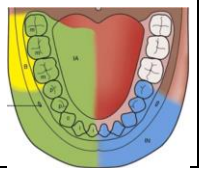
Anesthetic	Epinepherine
1mL of liquid at sea level weight 1g -> 1.8mL of cartridge = 1.8g (1800mg) for 100% solution - For 1% LA = 1800mg x 0.01 = 18mg - For 2% Lidocaine = 1800mg x 0.02 = 36mg - For 4% Articaine = 1800mg x 0.04 = 72mg	1:100,000 = 1/1000 of a % - 18mg X 0.001% epi = 0.018mg Epi - Move the decimal over 3 places

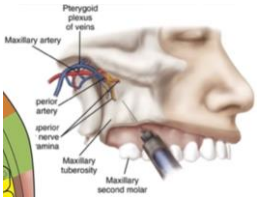
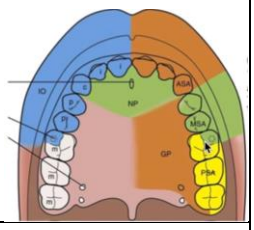
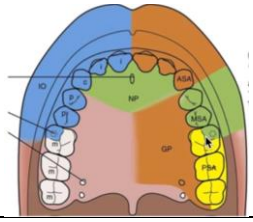
Injections and Techniques

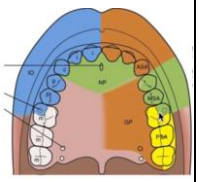
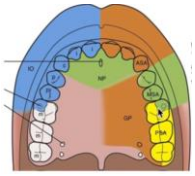
Delivery	*Slow Injections are best* -> 1 carpule per minute - Most uncomfortable part of the injection is the pressure from the volume of liquid being deposited

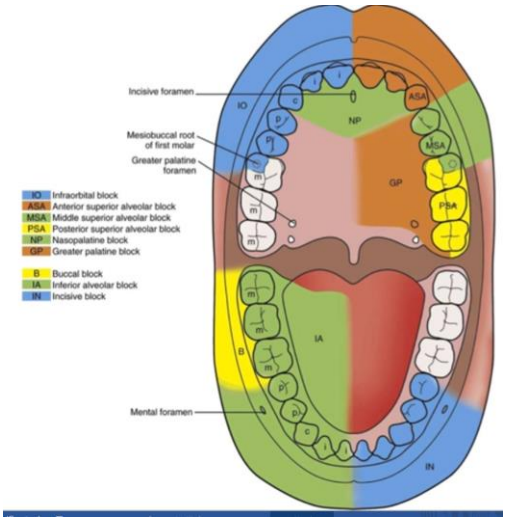
Needles	
Length	*Short*: 20mm *Long*: 32mm
Diameter	*30 Gauge (Blue)* = 0.3mm - Too thin! ↑ risk of breakage *27 Gauge (Yellow)* = 0.4mm *25 Gauge (Red)*= 0.5mm **Larger gauge Pro's:** - ↓ deflection - ↓ breakage - Easier aspiration

Mandibular Injections	
Inferior Alveolar Nerve Block (+ Lingual Nerve)	*Amount*: ¾ carpule - Triangle formed between Coronoid Notch and Pterygomandibular Raphe - Approach from contralateral premolars, aim 1.5cm above mandibular occlusal plane (Center of the triangle - Contact bone about ¾ of the long needle **  **Highest Failure Rate** - Halstead method -> Classic - Gow-Gates -> Open mouth, aiming for condyle - Akinosi -> Closed mouth *Numbs*: - All Mandibular teeth in that quadrant - Lips and gingiva of anterior teeth + Premolars of that quad 

Long Buccal Nerve Block	*Amount*: ¼ carpule - Insert along occlusal plane just buccal to the teeth (only like 1-2mm into mucosa) *Numbs*: - Buccal soft tissue of mandibular molars 
Mental Nerve Block	*Amount*: 1/3 carpule - Locate the rubbery bundle of nerve fibers with fingers (near the apices of the 2nd premolars) *Numbs*: - Soft tissue of the mandibular anterior + Premolars 
Incisive Nerve Block	*Amount*: 1/3 carpule - Technique is same as mental nerve block -> but you hold pressure over the foramen for 2 minutes to force LA into the mental foramen and bathe the incisive nerve *Numbs*: - Anterior teeth and premolars 

Maxillary Injections	
Posterior Superior Alveolar Block	*Amount*: ½ Carpule - Injecting at the height of the buccal vestibule just posterior to the 2nd molar -> 45° in, up, and back - Insert 16mm (1/2 long needle) ** High Hematoma Risk due to proximity to neurovascular bundle**   *Numbs*: - Maxillary Molars (Except the MB Root of the 1st molar 75% of the time!) 
Infraorbital Block	*Amount*: ½ carpule - Aiming for the infraorbital foramen  *Numbs*: - Maxillary Anteriors + Premolars (hits both ASA and MSA) 
Greater Palatine Nerve Block	*Amount*: ¼ Carpule - Aiming for greater palatine foramen (1/2 way between gingival margin of 2nd molar and the midline of the palate) 

	- Search for it using cotton tip applicator where the alveolar ridge meets the hard palate -> Looking for spongey tissue - Apply pressure with the cotton tip -> pressure anesthesia <u>Numbs</u>: - Posterior Hard Palate from premolar posteriorly 
Nasopalatine Block	<u>Amount</u>: ¼ carpule - Inject at the palatal papilla   **Most Painful** <u>Numbs</u>: - Hard palate from canine to canine
Local Infiltration	<u>Amount</u>: ½ carpule - Enter at the height of vestibule aiming for the root apex -> Want the LA to diffuse through the bone - Works best in the anteriors (cortical plate is thinner) - Articaine has the best bone penetration 



Antibiotics

Never mix Bacteriostatic + Bacteriocidal

Sulfonamides	= Bacteriostatic <u>MOA</u>: - **Folate synthesis inhibitor** (competes w/ PABA) <u>Drugs:</u> - **Sulfa**diazine - **Sulfa**methoxazole
Fluoroquinolones	= Bactericidal <u>MOA</u>: - DNA Synthesis inhibitors <u>Drugs</u>: - Cipro**floxacin** - Levo**floxacin**

Penicillins	= Bactericidal *MOA*: - Cell wall synthesis inhibitor, β Lactam ring - ***Cross-allergenic w/ *cephalosporins* b/c chemically related** *Drugs*: - Penicillin G (IV, more sensitive to acid degradation) - Penicillin V (Oral) - Amoxicillin (Broad Spectrum) - Augmentin (Amox + Clavulanic Acid) -> **β-lactamase resistant** - Methicillin (β lactamase resistant) - Dicloxacillin (β lactamase resistant) - Ampicillin (Best/broadest spectrum Gram –'ve) - Carbenicillin (Used specifically against pseudemonas)
Cephalosporins	= Bactericidal *MOA*: - Cell wall synthesis inhibitors , β lactam also *Drugs:* - 1st Gen: **Ceph**alexin (Keflex) - 2nd Gen: **Cef**uroxime - 3rd Gen: **Cef**triazone - 4th Gen: **Cef**epime - 5th Gen : **Cef**taroline
Monobactams	= Bactericidal *MOA*: - Cell wall synthesis inhibitors, β Lactam *Drugs*: - Aztreon**am**
Carbapenems	= Bactericidal *MOA*: - Cell wall synthesis inhibitor, β lactam *Drugs*: - Imipe**nem**
Tetracyclines	= Bacteriostatic *MOA*: - Protein synthesis inhibitor (30S ribosomal subunit) - Broadest antimicrobial spectrum of all antibiotics *Drugs*: - Tetracycline - Doxycycline - Minocycline
Macrolides	= Bacteriostatic *MOA*: - Protein synthesis inhibitors (50S ribosomal subunit) *Drugs*: - Ery**thromycin** - Clari**thromycin** - Azi**thromycin** *Mac likes to Throw Mice*
Lincosamides	= Bacteriostatic *MOA*: - Protein synthesis inhibitors (50S ribosomal subunit) *Drugs*: - Clinda**mycin** - Linco**mycin** *Link Likes to hide Mice*

Side Effects	**Pseudomonas colitis** - Clindamycin **Superinfection** - Broad Spectrum Antibiotics (Tetracycline) **Aplastic Anemia** - Chloramphenicol **Liver Damage** - Tetracycline **Allergic Cholestatic Hepatitis** - Erythromycin
Drug Interactions	- -Cidal + -Static Cancel each other out - **Penicillin + Probenecid (Gout drug)** - ↓ renal clearance of penicillin - **Tetracycline + Antacids/Dairy** - Tetracycline chelates Ca^{+} and ↓ absorption - **Broad spectrums + Anticoagulants** - ↑ action of anticoagulants by ↓ Vit K producing bacteria - **Antibiotics + oral contraceptives** - ↓ normal GI flora and their recycling of steroid hormones - **Macrolides + Seldane/Digoxin**
Drug Concentrating	Clindamycin -> Concentrates in Bone Tetracycline -> Concentrates in Gingival Crevicular Fluid

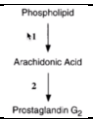
Antibiotic Prophylaxis

Antibiotic Prophylaxis Recommendations	**Cardiovascular Conditions** - Prosthetic heart valve - Hx of endocarditis - Heart transplant w/ valvulopathy/valve dysfunction - Congenital heart problems **Compromised immunity** - Organ transplant - Neutropenia - Cancer therapy
NO Antibiotic Prophylaxis	**Cardiovascular** - Pacemaker - Rheumatic fever w/o valvular dysfunction - Mitral valve prolapse **w/o** valvular regurgitation
Rx for Infective Endocarditis Prophylaxis	Amoxicillin 2g, 1hr before Tx - Kids: Amoxicillin 50mg/kg, 1hr before Tx **Penicillin allergy:** Clindamycin 600mg, 1hr before Tx - Kids: Clindamycin 20mg/kg, 1hr before Tx **Non-Oral** Ampicillin (IV) 2g, 30 mins before Tx - Kids: Ampicillin 50mg/kg, 30min before Tx
Rx for Prosthetic Joint Prophylaxis *Not needed in Canada*	Cephalexin 2g 1hr before Tx

Antivirals + Antifungals

Antivirals	Used for Herpes infections - Acyclovir - Valcyclovir
Antifungals	Used for Candidiasis - Fluconazole - Ketoconazole - Nystatin - Clotrimazole (Troche)

Analgesics

NSAIDs	
Drugs	**Aspirin (ASA)** - COX 1 and 2 Blocker - Irreversible - Impacts GI system (Upset stomach) **Ibuprofen** - COX 1 and 2 Blocker - Reversible - Hard on the **Kidney** **Naproxen** - COX 1 and 2 Blocker - Reversible **Ketorolac** - COX 1 and 2 Blocker - Reversible - Available IV, IM, Oral **Indomethacin** - COX 1 and 2 Blocker - Reversible **Phenylbutazone** - COX 1 and 2 Blocker - Reversible **Diflunisal** - COX 1 and 2 Blocker - Reversible - ↑ half life **Celecoxib** - COX 2 selective blocker **Meloxicam** - COX 2 Selective Blocker - Used for Arthritis
Therapeutic Effects (MOA) of Aspirin	**Analgesic** -> Inhibits COX 1 and COX 2 (↓ Prostaglandin synthesis) **Anti-inflammatory** -> See above **Antipyretic** -> Inhibits PG synthesis in the Hypothalamus (Temp regulation center) **Bleeding Time** -> ↓ TXA2 synthesis = inhibits platelet aggregation 
Toxic Effects of Aspirin	- Occult bleeding from GI - Tinnitis - Nausea and vomiting - Metabolic acidosis - ↓ tubular resorption of uric acid - Salicylism - Delerium - Hyperventilation
Acetaminophen	
Facts	**Not an NSAID** - Drug of choice for feverish child -> Aspirin can cause Reye's Syndrome ****Hard on the Liver**** *MOA*: - Not fully understood - Inhibits pain in the CNS
Max Doses	***Ibuprofen: 3200mg/day*** ***Acetaminophen: 4000mg/day*** ***Aspirin: 4000mg/day***
Corticosteroids	
Drugs	- Prednis**one** - Hydrocortis**one** - Triamcinol**one** - Dexamethas**one**
Therapeutic Effects	**Analgesic** -> Inhibits Phospholipase A2 (Arachidonic Acid Synthesis) -> A step upstream from NSAIDS **Anti-inflammatory** -> Same
Side Effects	- Gastric Ulcers - Immunosuppression - **Acute Adrenal Insufficiency** - Rule of 2: Adrenal suppression risk if Pt takes **20mg Cortisone (or equivalent), for 2 weeks, within 2 years of dental Tx** - Osteoporosis - Hyperglycemia - Redistribution of body fat

Narcotics/Opiods	

Drugs	- Morphine
	- Hydrocodone
	- Oxycodone
	- Oxycontin -> Controlled release
	- Codeine -> Cough suppression, in cough syrup
	- Tramadol -> Similar to Codeine
	- Heroin
	- Fentanyl
	- Sufentanyl
	- Carfentanyl
	- Meperidine (Demerol) -> Lethal if combined with MAOI
	
	Combination Narcotics:
	- Vicodine
	  - Hydrocodone + APAP
	- Percocet
	  - Oxycodone + APAP
	- Percodan
	  - Oxycodone + ASA
	- Tylenol 1
	  - 300mg APAP + 8mg Codeine
	- Tylenol 2
	  - 300mg APAP + 15mg Codeine
	- Tylenol 3
	  - 300mg APAP + 30mg Codeine
	- Tylenol 4
	  - 300mg APAP + 60mg Codeine

MOA	Mu-opioid Receptor Agonists (in the CNS)
Therapeutic and Side Effects	**M** – Miosis (Pupil dilation) **O** – Out of it **R** – Respiratory Depression (Effects in medulla) **P** - Pneumonia **H** - Hypotension **I** – Infrequency (urinary retention and constipation) **N** – Nausea and Vomiting (effects in medulla) **E** – Euphoria and dysphoria
Overdose and Addiction	Naloxone - Inverse agonist, Emergency Tx Naltrexone - Antagonist, used for Addiction Tx Methadone - Addiction Tx Pentazocine, Nalbuphine, Buprenorphine - Mixed agonist-antagonist
Nitrous Oxide	
Facts	*MAC*: 105% Nitrous Tank is always Blue - O_2 is either Green or White Sensation before onset -> Tingling Side Effects -> Nausea Long term exposure -> Peripheral Neuropathy Keep Pt on O_2 100% for 5 minutes after nitrous use to avoid Diffusion Hypoxia

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Pharmacokinetics

= What the body does to the drug

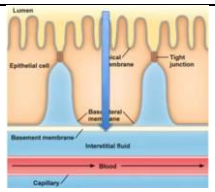
Administration -> Absorption -> Distribution -> Metabolism -> Elimination

Administration

Oral -> Ingestion through mouth
Sublingual -> Dissolved under the tongue
Subcutaneous -> Injected under the skin
IM (**intramuscular**) -> Injected into muscle
IV (**Intravenous**) -> Injected into vein
Inhalation -> Breathed in
Topical -> Applied to skin or mucous membrane

Absorption

Drugs cross epithelial +/- endothelial cell layers to enter the body



Local Drugs: Effect at the site of administration
Systemic drugs: Need to enter the blood stream to work systemically

Passive Diffusion
- Drugs need to be non-ionized to pass through the cell membrane passively

Facilitated Diffusion
Active Transport

pH Considerations
- Acid/Base properties of drug + pH of the environment affect the charge state of a drug and therefore its absorption
- For Weak Acids: Want pH < pKa
- For Weak Bases: Want pH > pKa

	Acid Drug	Base Drug
Acid Environment	Non-ionized	Ionized
Base Environment	Ionized	Non-ionized

Distribution

How does drug get to the target site?
- Most must reach the blood to get distributed evenly -> Once at the target site, it needs to leave the blood and then enter the tissue

First Pass Effect:
- Oral drugs undergo this effect -> 1st Absorbed into the GI, sent through the hepatic portal system and into the Liver.
- In the liver it gets metabolized (1st pass) = ↓ the bioavailability of oral drug before it enters the systemic circulation

Volume of Distribution:
= distribution of drug across the 3 body water compartments
- Plasma (4%)
- Interstitial fluid (16%)
- Intracellular (40%)

Women, obese, and older patients have ↓ body water (Adipose has the lowest H_2O content ; Brain and muscle having the highest)
- Should be given ↓ dose because of the ↓ body fluids to distribute

Serum protein binding (Albumin) ↓ Volume distribution and traps drugs in the blood as hydrophilic molecules

Metabolism

How is a drug molecule chemically altered by the body?

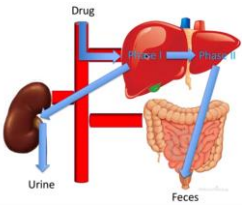
Drug ---------Phase I--------> Metabolite -----Phase II---------->Inactive Drug

Phase I:
- Functionalization (Oxidation, reduction, hydrolysis)
- Cytochrome P450 in liver

Phase II:
- Conjugation (Glucouronide, glutathione, glycine)
- UDP-glucouronosyltransferase

Drug-Drug Interactions:
- Induction: Drug #1 induces CP450 = ↑ in metabolism and ↓ effect of Drug #2
- Inhibition: Drug #2 competes for CP450 or inhibits = ↓ metabolism and ↑ effect/toxicity of drug #2

Dental Drug	Interacting Drug	Effect
Diazepam	Clarithromycin	Increased sedation because of reduced metabolism of benzodiazepine
Tetracyclines	Oral antacids (TUMS)	Reduced absorption of tetracyclines
Aspirin	Anticoagulants	Increased bleeding tendency
Aspirin	Probenecid	Decreased effect of probenecid
Aspirin	Methotrexate	Increased methotrexate toxicity
Acetaminophen	Alcohol	Increased risk of liver toxicity in chronic alcoholics
Local anesthetics	Acetylcholinesterase inhibitors	Reduced effectiveness of acetylcholinesterase inhibitor

Elimination	**<u>How is a drug eliminated from the body?</u>** - Mostly the kidneys, but not always  Phase I makes drugs more ionized -> typically eliminated in urine Phase II makes drugs ionized + larger -> Eliminated in the feces **<u>1st Order Kinetics</u>** - Constant **fraction** of drug is eliminated proportionally per unit time (%/hour) - More common **<u>0 Order Kinetics</u>** - Constant **amount** of drug is eliminated per unit time (mg/hr) - Less common - Higher risk of drug accumulation

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Pharmacodynamics

= What the drug does to the body

Almost all drug targets are **proteins**

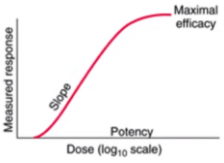
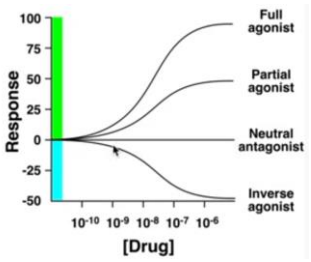
- Receptors
- Ion channels
- Enzymes
- Carriers

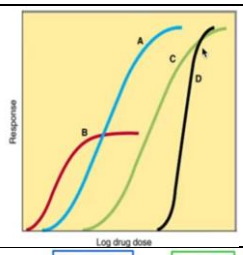
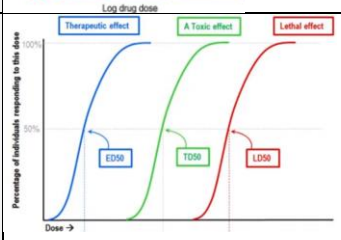
How a drug interacts w/ its target to produce its effects

- Agonist
- Antagonist
- Inverse Agonist

Agonist	= Mimics the effects of an endogenous molecule - Full Agonist = produces 100% of the effect - Partial Agonist = Produces less than 100% of effect 
Antagonist	= Inhibits normal function of endogenous molecule - Competitive Antagonist = Competes w/ agonist for the same binding site - Non-Competitive antagonist = binds to a different non-overlapping site
Inverse Agonist	= Inhibits the basal activity of a receptor in the absence of normal agonist - Binds to a special kind of receptor that is active at rest to inhibit its basal activity

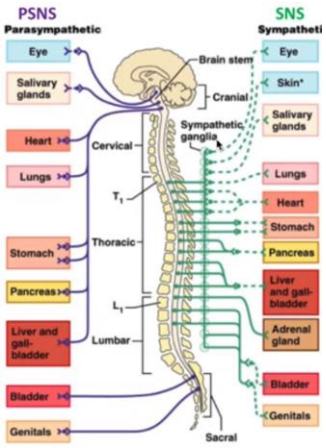
<u>Dose Response Curves</u>

Type I Dose Response	 X-Axis: Dose of the drug Y-Axis: Response/efficacy of drug - Can be hyperbolic or Sigmoid/Log  **<u>Intrinsic Activity</u>** = Maximum effect (E_{max}) of the drug - Full Agonist = Intrinsic activity of 1 - Partial Agonist = between 0-1 - Antagonist = Intrinsic activity of 0 **<u>Definitions</u>**: - *<u>Efficacy</u>* = Effect of a drug as a function of binding - *<u>Affinity</u>* = Attractiveness of a drug to its receptor - ↓ dissociation constant (Kd) = ↑ Affinity - *<u>Potency</u>* = Power of a drug at a specific concentration - Measured by the effective concentration (EC_{50}) -> 50% of maximum response

	 A: Agonist curve C + D: Competitive antagonist -> Shifts curve to the right (↑ drug needed to produce same response) B: Non-competitive antagonist -> Shifts curve down (↓ max effect of the drug)
Type II Dose Response Curves	 **X-Axis**: Dose of the Drug **Y-Axis**: Number of subjects responding to the drug (not the efficacy) - Gives us a holistic view that shows lethal dose, toxic dose, and therapeutic dose (3 separate curves) **ED_{50}**: Effective dose (50% of population treated effectively) **TD_{50}**: Dose where 50% of population gets toxic side effects **LD_{50}**: Does where 50% of population died **Toxic Index: TI_{50}/ED_{50}** - Therapeutic window = Top of the ED and bottom of the TD

Autonomic Nervous System

- In general, the PSNS (Parasympathetic) and the SNS (Sympathetic) control the same organs, but have the opposite effects
  - SNS: Fight or Flight
  - PSNS: Rest and Digest
- All nerves originate from the CNS (Brain + Spinal Cord)
  - 12 Cranial
  - 0 Cervical
  - 12 Thoracic
  - 5 Lumbar
  - 5 Sacral

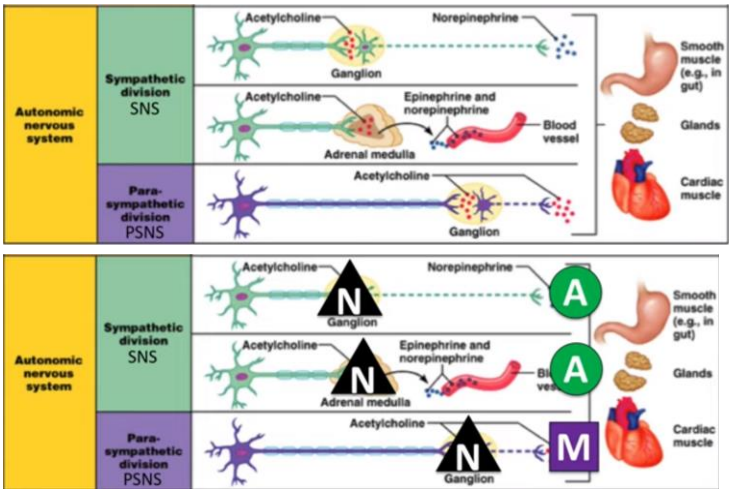


PSNS	SNS
Eyes: - Pupil Constriction **Mouth**: - Stimulated saliva **Cardiovascular**: - ↓ HR **Respiratory**: - Airway constriction **GI**: - Stimulated Digestion **Bladder**: - Bladder constriction	**Eyes**: - Pupil Dilation **Mouth**: - Dry Mouth **Cardiovascular**: - ↑ HR **Respiratory**: - Dilated/relaxed airway **GI**: - Slowed Digestion **Bladder**: - Bladder relaxation

Receptors in ANS

- Ionotropic = ion channels
- Metabotropic = G-protein coupled Receptor

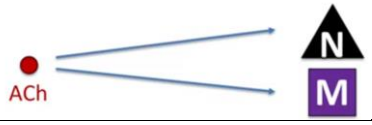
Cholinergic Receptors	= Binds Acetylcholine Nicotinic: - Binds Ach + Nicotine - Ionotropic (Ion channel) Muscarinic - Binds Ach + Muscarine - Metabotropic (G-protein coupled)
Adrenergic	= Binds Epinephrine/Norepinephrine - Metabotropic



**All Ganglionic and Medulla Receptors are Nicotinic (ionotropic)

- Post Ganglionic Parasympathetic = Muscarinic
- Post Ganglionic Sympathetic = Adrenergic

Cholinergic

Synthesis of Acetylcholine	Acetyl CoA + Choline = Acetylcholine - Catalyzed by choline acetyltransferase - Reversed by Acetycholinesterase  -Activates both Nicotinic and Muscarinic
Muscarinic Receptors	**Post Ganglionic Receptor Types:** M_1: CNS M_2: Heart - Bradycardia (↓ HR), and ↓ electrical conduction -> Rest and Digest M_3: Smooth Muscle - Smooth Muscle Relaxation - **SLUDS**: Salivation, Lachrymation, Urination, Defecation, Sweating - **BAM**: Bronchoconstriction, Abdominal Cramps, Miosis M_4: CNS M_5: CNS
M Agonists	= Non-selective for muscarinic receptors (Affects all M_{1-5}) - Don't use systemically if: Peptic Ulcers, Asthma/COPD, CHF

Direct Acting	Directs acts on M receptor
Pilocarpine	= Stimulates Saliva, or eye drops to constrict pupils
Methacholine	
Indirect Acting	**Non-competitively inhibits acetylcholinesterase**
Neostigmine **Physostigmine** **Endophonium**	= Reversibly inhibits cholinesterase
Organophosphate Insecticides **Nerve Gases**	= Irreversibly inhibits cholinesterase - Poison! Tx w/ Pralidoxime

Muscarinic Antagonists	Block M Receptors and compete w/ Ach - ↓ Saliva - Emergency drug to treat bradycardia *Drugs*: - Atropine - Scopolamine - Propantheline

Nicotinic Antagonists

Ganglionic Blockers

Non-depolarizing	Blocks N receptors at allosteric site
Mecamylamine Hexamethonium	Used as antihypertensive
Depolarizing	**Binds N receptor, but cannot be removed**
Nicotine	= Addictive substance found in tobacco products

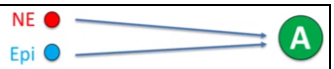
Neuromuscular Blockers

Non-depolarizing	Blocks N receptor at active site
Tubocurarine	= Arrow poison
Depolarizing	**Binds to N receptor, but cannot be removed**
Succinylcholine	= Prevents laryngospasms, acts as muscle relaxant during surgery

Adrenergics

Synthesis of Epinephrine and Norepinephrine

Tyrosine -> L-DOPA -> Dopamine -> NE -> Epinephrine



- *Catecholamines* = Dopamine, NE, Epi
- *Monoamines* = Dopamine, NE, Epi, Serotonin (5-HT), Histamine

Adrenergic Receptors

α_1: **Smooth muscle of Vasculature**
- Vasoconstriction
- Urinary retention
- Pupil Dilation (Mydriasis)

α_2: **Smooth Muscle of Vasculature**
- Vasoconstriction

β_1: **Heart**
- SA and AV nodes: ↑ HR and ↑ electrical conduction, ↑ Strength of contraction
- M_2 is the opposite receptor
- ↑ renin release from the kidneys

β_2: **Smooth Muscle of the lungs**
- Bronchodilation
- Vasodilation
- ↓ Peristalsis

1 Heart, 2 lungs

Adrenergic Agonists

Isoproterenol
- Activates all β receptors

Norepinephrine
- Activates all α and β_1 receptors

Epinephrine
- Activates all α and β receptors

Phenylphedrine (*Sudafed*)
- Activates α_1 receptors
- ↓ swelling via vasoconstriction

Dobutamine
- Activates β_1 receptors
- Kickstarts the heart

Albuterol
- Activates β_2 receptors
- Bronchodilator used as an emergency inhaler

Adrenergic Antagonists

Prozosin
- Blocks α_1

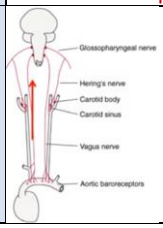
Chlorpromazine
- Blocks α_1 and D2 Receptor

Metoprolol + Atenolol -> β Blockers
- Blocks β_1 receptor (Cardioselective)

Propranolol
- Blocks all β Receptors
- Prolongs lidocaine duration

Carvedilol
- Blocks all β receptors and α_1

Phentolamine + Phenoxybenzamine
- Blocks all α receptors

Sympathomimetics	= Don't actually bind to α or β receptors, but **mimics the effects of an agonist** *Amphetamine, Tyramine, Ephedrine* - Stimulates release of stored NE *Cocaine* - Inhibits reuptake and NE and dopamine *Methylphenidate* - Inhibits psychostimulants -> for ADHD *TCA's* - Inhibits reuptake of Serotonin + NE *MAOI* - Blocks enzymatic degradation of monoamines (NE, E, Dopamine, 5-HT, Histamine)
Sympatholytics	= Don't bind to receptors, but **mimic the effects of a sympathetic antagonists** *Guanethidine* - Inhibits release of NE *Reserpine* - ↓ NE stores to inhibit release *Clonidine + Methyldopa* - α_2 agonists which actually blocks SNS - Wierd
Epinephrine Reversal	= Vasoconstrictor effect of epinephrine is converted into a vasodilator effect in the presence of an α blocker -> β_2 vasodilator effect becomes the major vascular response - Basically, α-blocker cancels out the epinephrine's α activation effects and it ony activates the β receptors
Vasovagal Reflex	 = NE can activate baroreceptors, which stimulate the vagal reflex to ↓ HR -> Leads to opposite response to what NE usually does - Atropine blocks this reflex

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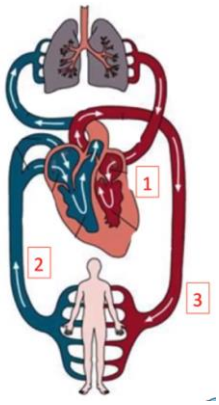
Cardiovascular Drugs



3 Factors contributing to Blood Pressure

Pump = Cardiac Output

Tubing = Peripheral Resistance (PR)

Fluid = Blood Volume (SV)

BP = CO x PR

CO = SV x HR

BP = SV x HR x PR

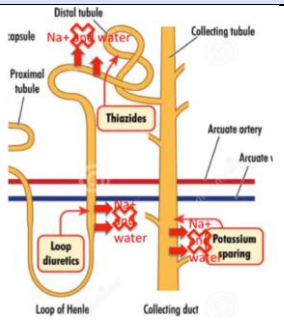
Systole: Pressure in the arteries when the heart ***Contracts***

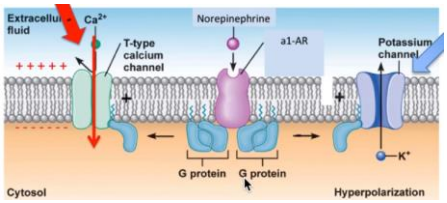
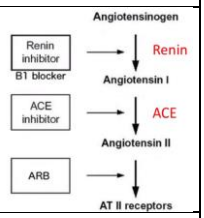
Diastole: Pressure in the arteries when the heart ***relaxes***

Preload: Pressure in the Ventricles before the heard contracts

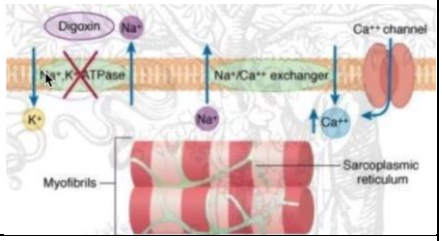
Afterload: Pressure in arteries against which the ventricles must pump

Antihypertensives	

Diuretics	= ↓ renal re-absorption of Na^+ = net fluid loss and ↓ in blood pressure
	
	Drugs:
	- **Furosemide** = Loop Diuretic
	  - Acts in the Loop of Henle
	- **Hydrochlorothiazide (HCTZ)** = Thiazide Diuretic
	  - Acts in the Distal Tubule
	  - Caution: Hypokalemia
	- **Spironolactone** = K^+ Sparing
	  - Acts in the Collecting Duct
	  - Caution: Hyperkalemia
	
	 

Vasodilators	= Opens K^+ channels to cause vasodilation - Hyperpolarize the vascular smooth muscle to cause dilation *Drugs*: - Hydralazine
Calcium Channel Blockers (CCB)	= Block Ca^+ influx to cause vasodilation - Again, hyperpolarizes the cell causing smooth muscle relaxation - May cause gingival hyperplasia *Drugs*: - Verapamil - Diltiazem - Amlodipine - Nifedipine 
ACE Inhibitors	= Blocks the Angiotensin Converting Enzyme (Converts Angiotensin I into Angiotensin II) -> AG II is a potent vasoconstrictor Drugs: - "-prils" 
Angiotensin II Receptor Blockers	= Competitive antagonist at angiotensin II receptor -> blocks the potent vasoconstrictor Drugs: - "-sartan"

Anti-Anginals	
- Angina = chest pain caused by insufficient O_2 to cardiac muscle M - Morphine O - Oxygen N - Nitroglycerine A - Aspirin	
Nitroglycerine	= Vasodilation of smooth muscle in coronary arteries to ↑ O_2 Supply
Propanolol	= ↓ O_2 demand by relaxing the heart
CCB	= ↓ O2 demand by reducing peripheral resistance via vasodilation

Anti-CHF Drugs = Failure of heart to pump enough blood (usually result of a weakened heart)	
Cardiac Glycosides	= Blocks Na/K ATPase to ↑ Ca^+ influx and promote positive inotropy (Strength of contraction) in the cardiac muscle only *Drugs*: - Digoxin - Digitalis *Digitalis can also be used for arrhythmias* - A. fib, paroxysmal tachycardia 
ACE Inhibitors	See above

Anti-Arrhythmic = Used for irregular heartbeats	
Type I	= Na^+ channel blockers for cardiac muscle only - *1A* = Lengthens refractory period to ↓ HR - *1B* = Shortens refractory period to ↑ HR *Drugs*: - Quinidine (1A) -> A. Fib, Supraventricular tachyarrhythmia - Procainamide -> Same as Quinidine - Lidocaine (1B) -> Ventricular arrythmia
Type II	β Blockers - 2nd letter in the alphabet = Type II *Drugs*: - Propranolol -> Paroxysmal tachycardia
Type III	K^+ channel blockers - K has 3 lines in it = Type III
Type IV	Ca^{++} channel blockers (CCB) *Drugs*: - Verapamil -> A. fib, paroxysmal tachycardia, supraventricular tachyarrhythmia

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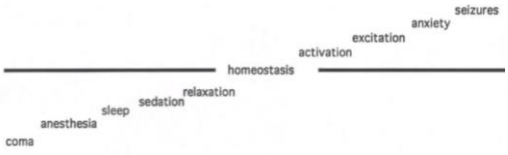
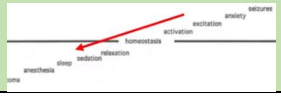
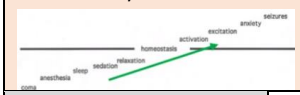
Central Nervous System



Antipsychotics = Calming the brain down 	
1st Gen	= D2 Blocker (Dopamine) *Drugs*: - Haloperidol - Side Effects: Tardive Dyskinesia, Anticholinergic effects - Phenothiazines - Side Effects: Tardive Dyskinesia, Anticholinergic effects
2nd Gen	= D and 5-HT blocker (Dopamine and Serotonin) *Drugs*: - Clozapine - ↓ side effects 😊
Antidepressants = Stimulate/Excite the CNS 	
SSRI	= Selective serotonin re-uptake inhibitors - ↑ serotonin in the synapse *Drugs*: - Fluoxetine - Citalopram - Trazodone -

SNRI/TCA	Serotonin and NE re-uptake inhibitor *Drugs*: - Amitriptyline - Imipramine
MAOI	= Monoamine Oxidase inhibitors - Don't use Levonordephrine! ↑ BP too much *Drugs*: - Phenelzine - Tranylcypromine
Lithium	= Used to Tx manic depression in bipolar disorder
	**Anxiolytics/Sedatives**
Benzodiazepines	= ↑ GABA binding and Cl^- ion influx to slow down the CNS - Ideal drug for oral sedation in dentistry - Propylene glycol can induce thrombophlebitis in large veins *Drugs*: - Diazepam (Valium) -> 2-10mg 1hr before appointment - Triazolam (Halcion) - Chlordiazepoxide *Vs Barbiturates:* - ↑ Therapeutic Window - ↓ Respiratory depression - Safer - ↓ Addiction potential
Barbiturates	= Same MOA as Benzo's *Contraindications*: - Intermittent porphyria - Overdose cause respiratory depression *Drugs*: - Thiopental - Quick onset, short duration of action
General Anesthetics = The more soluble the agent in the blood, the more you need to reach critical tension in the brain *Drug*: - Halothane (Caution with hepatotoxicity)	
Stage I	Analgesia
Stage II	Delirium
Stage III	Surgical Anesthesia
Stage IV	Medullary Paralysis

Parkinson's Disease

What Causes?	= Dopamine deficiency in the brain - Substantia nigra to striatum is the main pathway
Tx	**Injected **dopamine** cannot cross the BBB….but it's precursor **Levodopa** (L-Dopa) can - **Carbidopa** block at the DOPA decarboxylase -> allows the L-DOPA to cross the BBB, where it can then be converted to **dopamine** in the brain *Tx*: - Levodopa + Carbidopa combination - L-DOPA is a sympathomimetic = Sympathetic stimulation in the periphery