OMS – Sedation Study Review

Understanding Fear and Anxiety

Fear	**Physiological** process when threatened by danger - Sympathetic response -> Fight or Flight Dentistry: - > 1/3 Adult Canadians have some fear towards dentistry - 7.6% of ppl have missed, avoided, or canceled appointments b/c fear or anxiety - Women 2.5x ↑ of reporting anxiety
Anxiety	**Anticipation** of possible danger - Unable to control the thought of a possible negative event occurring Symptoms of Dysphoria and tension
Phobia	**Excessive** fear or anxiety related to **specific** object or situation -> Out of proportion for the actual danger - Spend an inordinate amount of time avoiding the thing they fear

Indications for GA/Sedation	- High anxious / phobic adults - Uncooperative children - Developmental disorders - Exaggerated gag reflex - Pt's w/ ineffective LA experience - To ↓ Stress and ↑ comfort
Types of Sedation	Inhalation - Volatile Gas - Nitrous Oxide + O_2 Oral (Enteral) Intramuscular Intravenous (IV)

Stages of Anesthesia

- Based on Ether

Stage 1	**Induction** - Period btwn initial administration and loss of consciousness
Stage 2	**Excitement** Stage - Period following LOC and marked by excited and delirious activity
Stage 3	**Surgical Anaesthesia**
Stage 4	**Overdose** - Coma/Death

Levels of Sedation

Minimal Sedation (Anxiolysis)	= *Minimal depressed level of consciousness* - Able to continuously maintain an airway - Able to respond normally to tactile stimulation - Able to respond to verbal command - Ventilatory and Cardio functions are unaffected **Methods**: - Inhalation (Nitrous + O_2) - Oral/Sublingual (+/- Nitrous)
Moderate Sedation (Conscious Sedation)	= *Depression of consciousness* - Able to respond purposely to verbal commands spontaneously or w/ light touch - Able to maintain airway - Cardio function is usually maintained **Methods**: - Oral with sedative drugs (+/- Nitrous) - Benzodiazepines (IV, IM, Subcutaneous, Submucosal, Intranasal) - Benzo + Narcotic (IV, IM, Subcutaneous, Submucosal, Intranasal)
Deep Sedation	= *Controlled unconsciousness* - Partial loss of protective reflexes -> Inability to respond purposefully to verbal command - Responds to painful stimuli - May need assistance to maintain airway -> Spontaneous ventilation may be inadequate - Cardiovascular function usually maintained **Methods**: - Hypnotic + Benzodiazepine +/- narcotics (IV +/- Nitrous) - Can add Ketamine (NMDA agonist) to the above

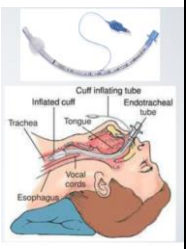
General Anesthesia

= *Drug-induced LOC*

- Pt's unarousable -> Even by painful stimulation
- Cannot maintain airway (depressed spontaneous ventilation, and neuromuscular function)
- Cardiovascular function may be impaired

Intubated GA:

- Hypnotic (Propofol)
- +/- benzodiazepine
- +/- Narcotic
- +/- Nitrous
- +/- Volatile gases
- **+/- paralytic**
  - If *< 30 yrs usually don't need paralytic*. Laryngeal muscles are not as tight or heavy. Easy to move tube around them
  - If *> 30 years use a paralytic* b/c larynx is too tight and large to navigate around



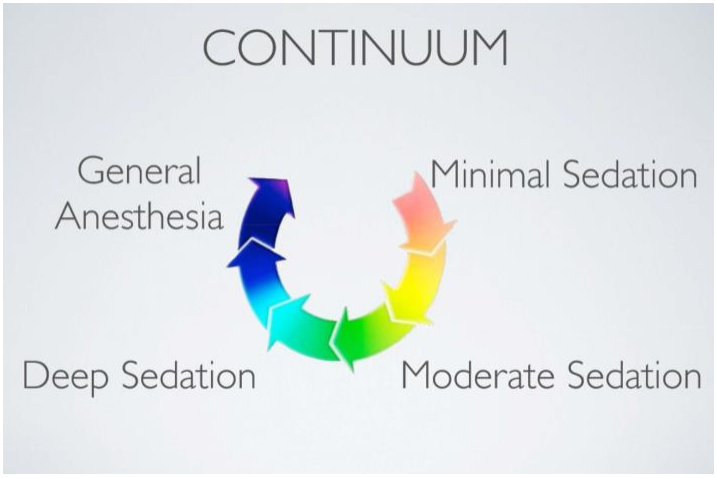
Non-intubated GA:

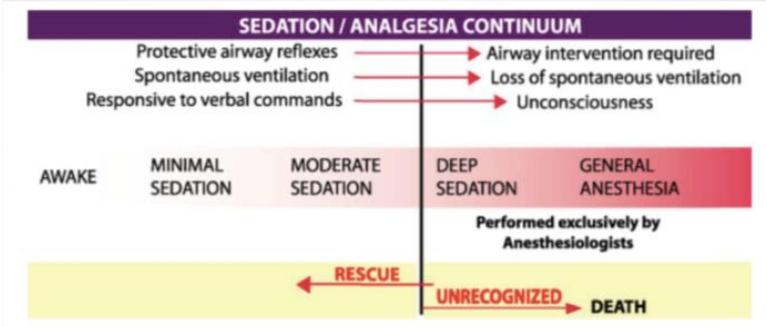
- Hypnotic (Propafol)
- +/- Benzo
- +/- Narcotic
- +/- Nitrous
- +/- Volatile gases

-> LMA (Laryngeal mask airway) with cuff inflated outer larynx

	Minimal Sedation (Anxiolysis)	Moderate Sedation (Conscious Sedation)	Deep Sedation	General Anesthetic
Responsiveness	Normal response to verbal+ Tactile stim	Purposeful response to verbal or tactile stimulation	Purposeful response following repeated or painful stimulation	Unarousable even w/ painful stim.
Airway	Unaffected	No intervention needed	Intervention *may* be needed	Intervention *often* needed
Spontaneous Ventilation	Unaffected	Adequate	*May* be needed	Frequently inadequate
Cardiovascular Function	Unaffected	Usually maintained	Usually maintained	May be impaired

*If only response is *reflexive* withdrawal from pain = Not min/moderate sedation





Not always possible to predict how an individual will respond to sedation.

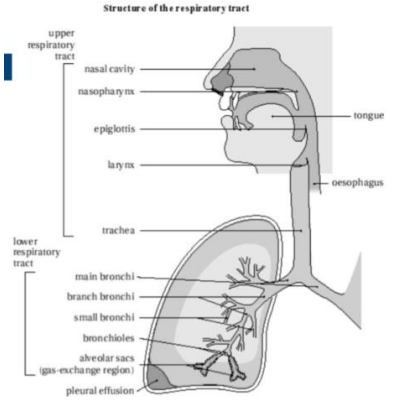
Rescue:

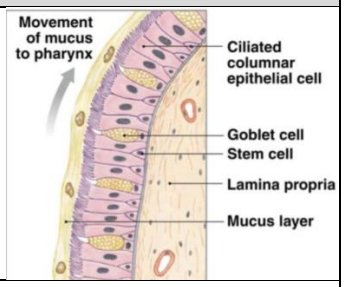
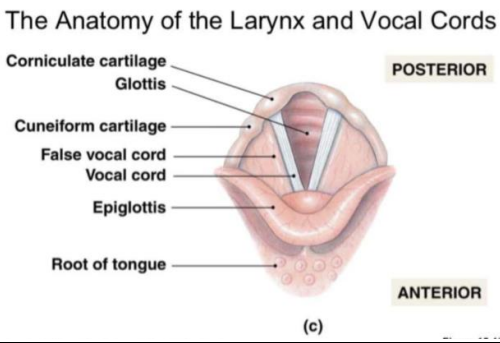
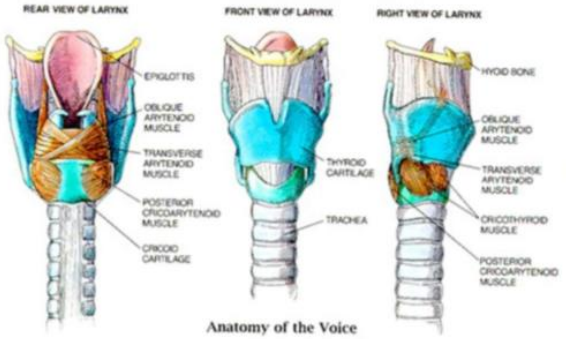
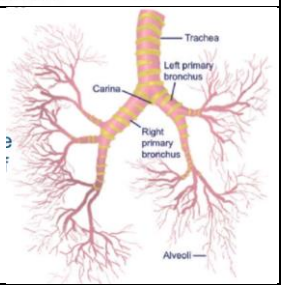
- Moderate -> Minimal
- Deep -> Moderate
- General -> Deep

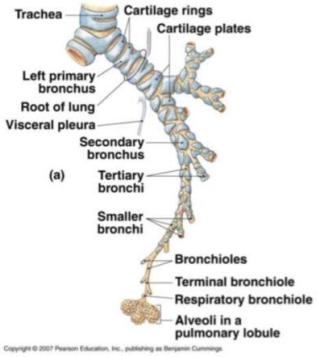
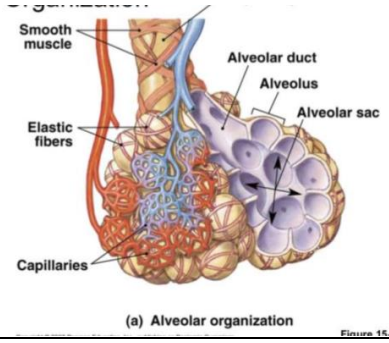
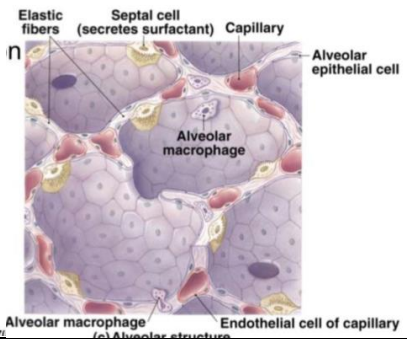
Respiratory Physiology

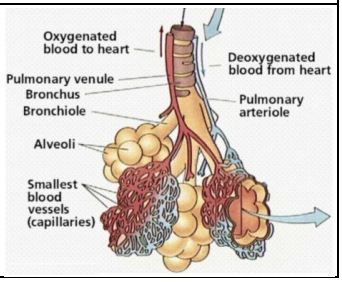
Function = Continuous gas exchange between inspired air and the blood in the pulmonary circulation

- Supply O_2 to the body
- Remove CO_2 from the body



Upper Airway Anatomy = Filter airborne particles, humidify and warm the inspired gases	
Respiratory Mucosa	= Respiratory epithelium + CT w/ mucous glands - Lines nasal cavity and most airways - Ciliated cells sweep mucous out of the airways and into the pharynx Goblet and Gland cells -> Secrete mucous - Mucous traps inhaled dirt, pathogens etc 
Larynx	Found at **C4-C6** **Components**: - Thyroid and cricoid cartilages - Arytenoid cartilages - Cuneiform and Corniculate cartilage -> Cuneiform is on the side and is smaller vs Corniculate - Epiglottis  
Trachea	Extends below cricoid cartilage to the carina (split of R and L Bronchi) - Most of the circumference is made up of C-shaped Cartilages - Posterior aspect of Trachea is made up on the trachealis muscle **If you cannot feel the cartilage rings passing when you pass the endotracheal tube -> Then you are probably in the esophagus…try again** 

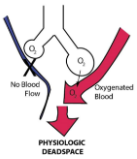
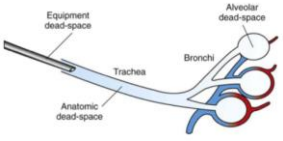
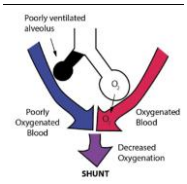
Lower Respiratory Tract	
Bronchi	R and L Primary bronchi - R Bronchus is more vertical off the trachea and is larger = Most aspiration occurs here Divides further into Secondary Bronchi -> Tertiary Bronchi -> Bronchioles -> Terminal Bronchiole -> Respiratory bronchioles 
Alveoli	Alveoli sacs in the respiratory bronchioles are responsible for the exchange of gases to and from the blood - 150,000,000 in the lungs -> HUGE surface area - *Elastic fibers* help expansion when they fill with gases - *Septal cells* -> Secrete surfactant that keep the surface tension high and prevent collapse  

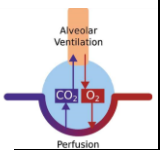
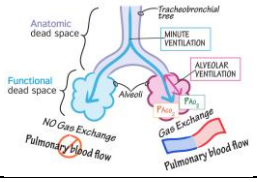
Blood Supply	Lungs have a double blood supply
	- ***Pulmonary Circulation*** -> gas exchange with the alveoli
	  - Arteries carry Deoxygenated blood
	  - Veins carry oxygenated blood
	- ***Bronchial Circulation*** -> supplies tissue of the lung itself
	  - Deoxygenated blood drains into the L side of the heart via the veins
	  - Considered part of the systemic circulation
	 

Ventilation

V/Q Ratio = Ventilation/Perfusion Ratio (https://www.youtube.com/watch?v=-mL_NQ3pKnA)

- Different Mismatches can occur

Hypoxemia Causes	
Dead Space (No Perfusion, Normal ventilation)	*Anatomic Dead Space* = Air that enters only the conducting airways *Alveolar Dead Space* = Air that reaches alveoli but doesn't exchange CO_2 or O_2 w/ capillary blood *Physiologic Dead Space* = Alveolar + Anatomic Dead Spaces Average Person = 150mL of dead space - Normal Tidal Volume is 500mL = 30% of air is wasted! V/Q ratio = ↓ ↓ ↓ *Q* (Perfusion) - ↑ V/Q Ratio causing higher O_2 in the alveoli and ↓ CO_2 (CO_2 retention in blood)  
Shunts (No Ventilation, Normal Perfusion)	**Causes** - Atelectasis (collapsed alveoli) - Pneumonia Capillaries running through areas of the lungs with damaged/blocked alveoli do not get ventilated with O_2. This ↓ O_2 in the blood mixes with the well O_2 blood in the Pulmonary Vein which causes an over all ↓ in the blood oxygenation - If we perfuse with 100% O_2 the, shunting still is unable to get that boosted O_2 into the blood. This means that it will not respond well -> This is the tell tale sign that its Shunting = ↓ V/Q Ratio = ↓ ↓ V causing decreased O_2 in the alveoli and ↑ CO_2 https://www.youtube.com/watch?v=pRIkwjlFRgo 

V/Q Mismatches (Most common cause of hypoxemia)	= Certain lung units that are high V/Q and others that are low V/Q, but it is not a 50:50 split so there is lack of compensation -> Responds well to 100% O_2 though - ↑ V/Q = Low Perfusion - ↓ V/Q = High Perfusion https://www.youtube.com/watch?v=RJ-H8_0-8wk
Ventilations	**Dead Space Ventilation**: = Part of ventilation that doesn't take part in gas exchange **Alveolar Ventilation (VA)**: = Volume of air breathed in per minute that: - Reaches the alveoli - Takes part in gas exchange  **Minute Ventilation** = the amount of air moved in or out of the lungs per minute - The sum of 2 types of ventilations (Alveolar and Dead Space) 

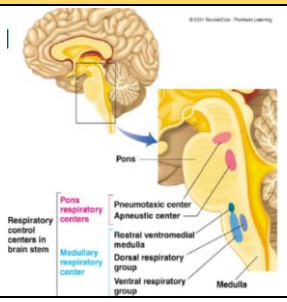
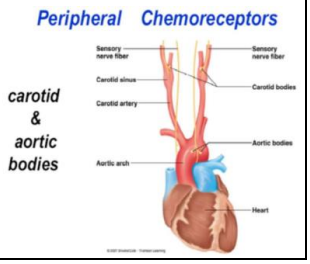
Mechanism of Breathing

Direction of airflow is largely determined by the difference in pressures from atmospheric pressure and lung pressure

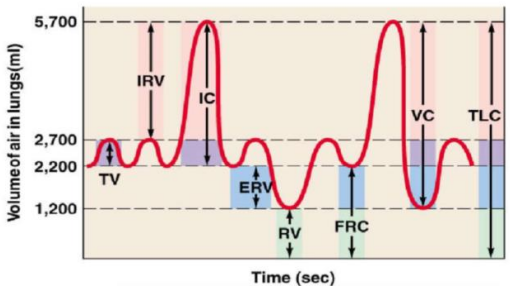
- Expand chest = ↓ pressure in the lungs, to allow air to flow down pressure gradient
- Contract chest = the opposite

Inhalation	Negative intrathoracic pressure produces inspiration - Volume increases, Pressure inside falls and air flows in **Phrenic nerves (C3, 4, 5, keep the body alive baby)** - Contract and move the diaphragm down -> Forcing abdomen contents down and out to make space for air in the lungs **Major Muscles of Inspiration**: - Diaphragm; - External Intercostals **Accessory Muscles of Inspiration**: - Sternomastoids; - Scalenes
Exhalation	Muscles relax during passive exhalation - Volume Decreases, Pressure inside rises so air flows out **Muscles of Active Exhalation**: - Internal intercostals; - Rectus abdominal muscles

Breathing Control

Chemoreceptors	
Central Control	Localised in the **Medulla** - Responds to CSF H^+ concentration, which is determined by CO_2 -> diffuses freely across Blood Brain barrier from arterial blood *Fast response and sensitive to small changes in $PaCO_2$ in arterial blood * 
Peripheral Control	**Not influential in normal circumstances -> like a fail safe** - Profound Hypoxia (<60mmHg) is required to produce significant activation - Also activated when CO_2 response is impaired (if $PaCO_2$ is chronically elevated, like in COPD patients) Located in the **Aortic Body and the Carotid Bodies** - ***Aortic***: Detects changes of CO_2 and O_2 (Not pH) - ***Carotid***: Detects CO_2, O_2, and pH 

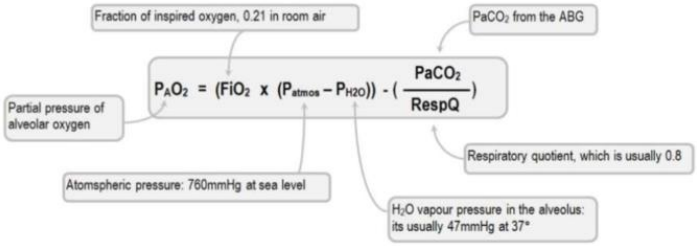
Lung Volumes



Tidal Volume (TV)	Air entering lungs at rest - Avg. 500mL
Inspiratory Reserve Volume (IRV)	Extra air inhaled above tidal with effort - Avg. 3000mL
Inspiratory Capacity (IC)	Combined TV + IRV - Avg. 3500mL
Expiratory Reserve Volume (ERV)	Max air exhaled after a TV inhaled - Avg. 1000mL
Residual Volume (RC)	Remaining air in lungs after a max exhale (This prevents lungs from collapsing) - Avg. 1,200mL
Functional Residual Capacity (FRC)	Volume of air in lungs after normal passive exhalation (Measure of how elastic your lungs are) - Avg. 2,200mL
Vital Capacity (VC)	Most air you can exhale after a maximum inhale (IC) - Avg. 4,500mL
Total Lung Capacity (TLC)	Most air the lungs can handle - Avg. 5,700mL

Alveolar Gas Equation

- Used to predict alveolar concentration of O_2 based on the alveolar concentration of CO_2



*For every 10% ↑ in FiO_2 the P_AO_2 will ↑ by 71-72 mmHg

Lets break it down:

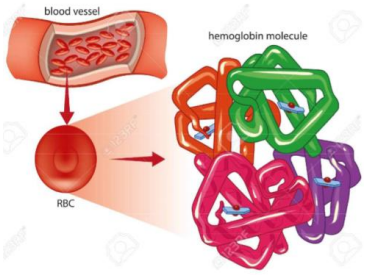
$P_AO_2 = (0.21 \times (760 - 47)) - (PaCO_2 \times 1.25)$

- $P_AO_2 = 149 - (PaCO_2 \times 1.25)$
- Pt w/ normal $PaCO_2$ (40): $P_AO_2 = 149 - 50$ -> Normal Person should have P_AO_2 of 99mmHg

Here is it explained clearly in video form (2 parts):

https://www.youtube.com/watch?v=zZX9jJqSlQs

https://www.youtube.com/watch?v=xH5Y3Kmx82w

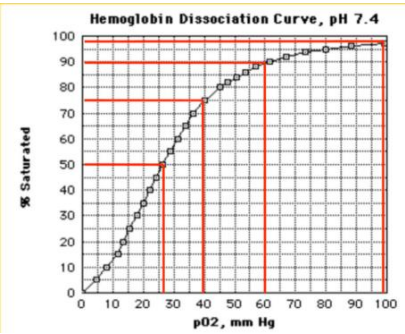


Hemoglobin

1 Hemoglobin molecule consists of 4 globin chains (2 pairs)

- Hb A = 2α and 2β chains -> This is 95% of the hemoglobin in a normal adult

O_2 reversibly binds to Hb to form Oxyhemoglobin -> Can get 4 molecules of O_2 in 1 hemoglobin molecule



-> When O_2 binds to hemoglobin the Hb chain shape changes and causes an ↑ affinity of binding further O_2

Taught form of Hb = ↑ binding of O_2 in high ppO_2 areas (Lungs)

Relaxed form of HB = ↓ binding of O_2 in low ppO_2 areas (Tissues)

Bohr Effect	Haldane Effect
↑ CO_2 = ↓ pH = Hb releases O_2	↓ O_2 (hypoxic) = Hb can carry more CO_2 to liberate it from the body (O_2 isnt taking the binding sites)

3% of O_2 in the blood is carried in a dissolved state in the plasma, 97% of O_2 is carried in the RBC's

- 7% of CO_2 is dissolved in plasma, 23% of CO_2 is bound to Hb (Carbaminohaemoglobin) in RBC's, 70% of CO_2 in blood is in HCO_3^- (Bicarbonate) form after conversion from H_2CO_3 (Carbonic Acid)

Lung Diseases

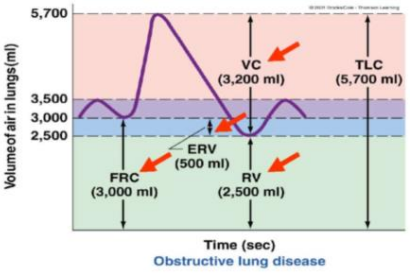
Obstructive Diseases
= Difficult to get air out of lungs

COPD

= Presence of airflow obstruction due to: Chronic Bronchitis (Large Airway) + Emphysema (Alveoli)

Affects the:

- Vital Capacity (↓),
- Residual Volume (↑),
- Expiratory Reserve Volume (↑)
- Functional Residual Capacity (↑)

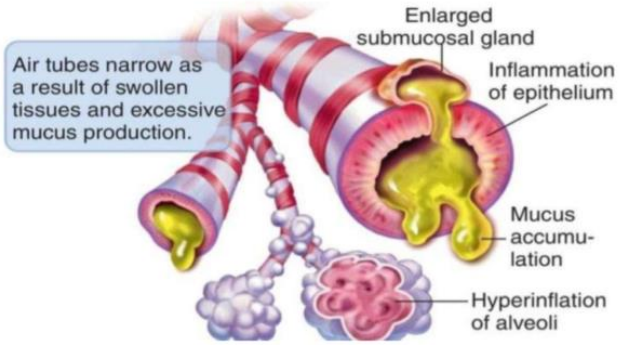


Chronic Bronchitis (Blue Bloaters)

- Air tubes narrow from swelling and ↑ mucous production = Heavy productive cough

Dx = Heavy productive cough for 3 months for 2 consecutive years

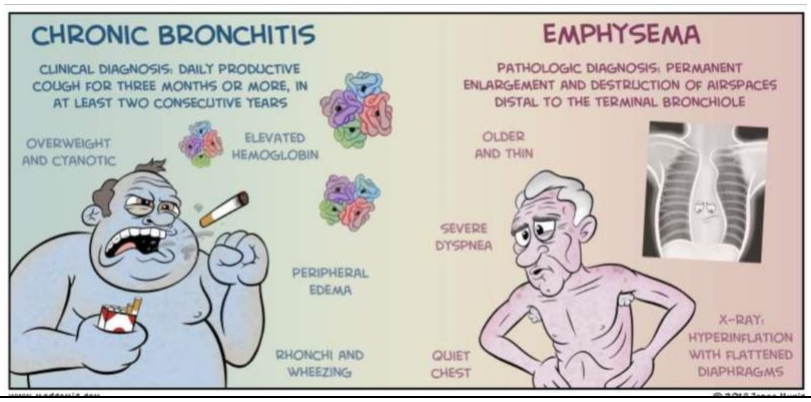
- ↓ ventilation and ↑ Cardiac Output (Central chemoreceptors become desensitized to ↑ CO_2)
  - *V/Q mismatch* = rapid circulation through a poorly ventilated lung (Hypoxemia and Polycythemia)
  - Low V/Q
- Hypercapnia and Respiratory Acidosis -> Pulmonary artery vasoconstriction and Cor Pulmonale
- Generalized edema + Cyanosis



Emphysema (Pink Puffers)

- Chronic progressive disease-causing enlargement of air spaces and destruction of alveolar walls by enzymes
  - Primary Cause = Smoking, or any continuous irritant (Coal dust etc)

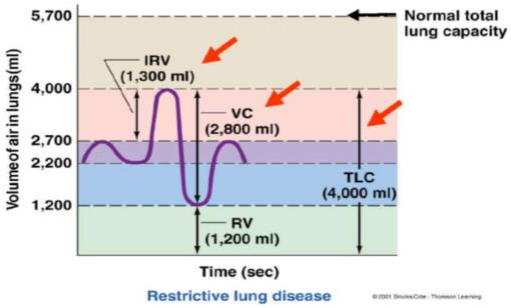
- ↓ lung recoil and weakened expiration = Lung remains partially expanded following expiration and traps air in chest -> Visible Barrel chest over time
- Gradual destruction of alveolar space and pulmonary capillary bed = ↓ ability to Oxygenate blood so body compensates by ↓ Cardiac Output and ↑ Hyperventilation
  - ↓ Cardiac Output = Tissue hypoxia, Muscle Wasting and Weight Loss
  - *V/Q Mismatch* = limited blood flow through well oxygenated lungs with normal blood gases and pressures in lungs
  - *High V/Q*



Restrictive Diseases
= Difficult to get air into lungs (tissues and chest wall are stiff)

Loss of lung compliance:
- Incomplete lung expansion
- ↑ lung stiffness
- Difficult to get air into the lungs

Affects the:
- Inspiratory Reserve Volume (↓)
- Vital Capacity (↓)
- Total Lung Capacity (↓)



Intrinsic Lung diseases (diseases of the lung parenchyma):
- Causes inflammation and scarring of the lung tissue (interstitial lung disease) or fills the air spaces with exudate and debris (Pneumonitis)
- Idiopathic fibrotic diseases, CT diseases, Drug induced diseases

Examples:
1. Sarcoidosis
2. Tuberculosis
3. Pneumonectomy (Loss of lung)
4. Pneumonia

Extrinsic Lung Diseases:
- Chest wall, pleura, and respiratory muscles have ↓ function

Examples:
1. Scoliosis, Kyphosis
2. Ankylosing Spondylitis
3. Pleural Effusion (fluid in the pleural cavity)
4. Pregnancy
5. Gross Obesity
6. Tumors
7. Ascites
8. Issues causing pain on inspiration (Rib fracture etc)

Pulmonary Function Tests

	Normal PTF Outcome	Mild Disease	Moderate Disease	Severe Disease
Values	>85% of predicted	>65% but <85%	> 50% but < 65%	<50%

Reading a PFT:

1. Forced Vital Capacity (FVC) -> is it WNL?
2. Forced expiratory volume in 1 sec (FEV1) -> is it WNL?
3. If both FVC + FEV1 are normal -> Pt is fine
4. If FVC and/or FEV1 are low -> There is likely a disease
    a. Check % Predicted for FEV1/FVC
        i. If % Predicted is 88-90% or more -> Pt has restricted lung disease (Pt can't get air in, but can get air out fine)
        ii. If % Predicted is <69% or lower -> Pt has obstructed lung disease (Pt can't get air out, but can get air in fine)

Obstructive Lung Disease

	Predicted Values	Measured Values	% Predicted
FVC	6.00 liters	4.00 liters	67 %
FEV1	5.00 liters	2.00 liters	40 %
FEV1/FVC	83 %	50 %	60 %

Restrictive Lung Disease

	Predicted Values	Measured Values	% Predicted
FVC	5.68 liters	4.43 liters	78 %
FEV1	4.90 liters	3.52 liters	72 %
FEV1/FVC	84 %	79 %	94 %

Oral Sedation in Dentistry

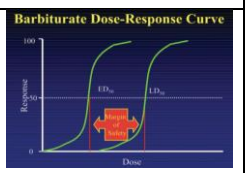
Advantages of Oral Sedation	Disadvantages of Oral Sedation
- Easy to administer - Relatively safe - Good patient acceptance	- Cannot titrate (can't just give another pill if it's not working) - Delayed, variable onset of action - Pt needs escort home - Limited success in young children - Excessive effects and duration in elderly

Oral Titration is done with/between each appointment -> NOT during the appointment

- Appointment #1 -> Give lowest effective dose, see how it works
  - Keep this appointment short and minimally invasive. Call Pt the next day and ask how the appointment went for them
- Appointment #2 -> Adjust your dose based on the effects in Appointment #1 (↑/↓)

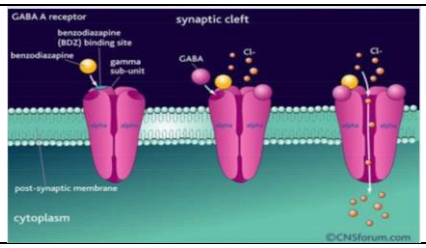
Drug Interactions:

Cytochrome P450 Inducers - ↓ duration of Benzo	*Antiepileptics* - Barbituates - Carbamazepine - Phenytoin - Primidone Smoking St. Johns Wort	Corticosteroids Antibiotics - Rifampin - Rifabutin
CP450 Inhibitors - ↑ duration of Benzo	Cardiovascular: - Quinidine - Amiodarone - Diltiazem - Verapamil - Propranolol - Nifedipine Antibiotics - Macrolides (Erythromycin) - Norploxacin	- Grapefruit Juice - Cimetidine - Quinine - Cyclosporine - Antiretrovirals

Old School Sedatives	
Chloral Hydrate	Discovered in 1832 *Onset of Action*: 10-15 mins (Fast) *Peak Plasma Levels*: 60mins *Active Metabolites*: Trichloroethanol (within 8 hrs for Adults, 10hrs for children) + Trichloroacetic Acid *Side Effects* - Daytime Drowsiness (hangover) **Narrow Therapeutic Index -> Leads to many pediatric deaths, OD is easy**
Barbituates - Sodium Thiopental - Amobarbital, - Phenobarbital	Strong sedative and sleep aid - Phenobarbital is used still as an epileptic medication  *Side Effects*: - Strong addiction potential - ↑ cardio and respiratory depression when taken with alcohol = ↑ risk of death - Small margin of safety

Benzodiazepines

MOA



GABA = inhibitory neurotransmitter
- GABA binds to receptor -> Influx of Cl^- = more –'ve intracellularly and further away from activation threshold

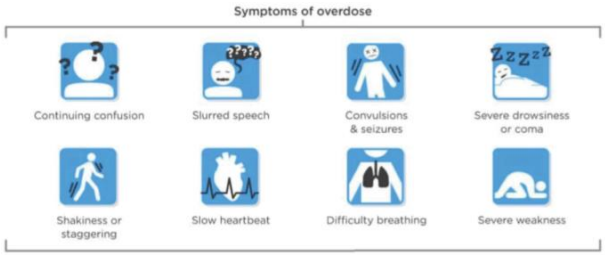
Benzo binds BZ receptor site on the GABA A complex (not the GABA receptor) -> Enhances Cl^-influx in response to GABA binding
- Only potentiates the action of GABA. Need GABA binding to work
- This is likely why its safer vs. barbituates which will open GABA receptor and send it independently of GABA

Effects
- Anxiolytic (Anti-anxiety) -> This is really the only effect we want it to have
- Sedative/Sleep inducing
- Anterograde amnesia
- Anti-convulsant
- Muscle relaxant

Negative Effects
- Mild anticholinergic effects (Dry mouth)
  - **Contraindicated if pt has Myasthenia Gravis**
- Respiratory depression
- Cardiovascular depression
- Disinhibition (Uninhibited behaviour, like being drunk)
- Dependence/Addiction
  - Legally we need to keep them in a safe and have a log book for when and how many we give out

Pregnancy:
- *Fetal Risk*: XM
  - **Fully contraindicated in women who are, or who may be pregnant**; Associated w/ Cleft lip +/- Palate development
- *Breast Feeding*: Not recommended
  - Recommended to "**Pump and Dump**": Pump milk out and throw it away for 24 hrs after taking benzo

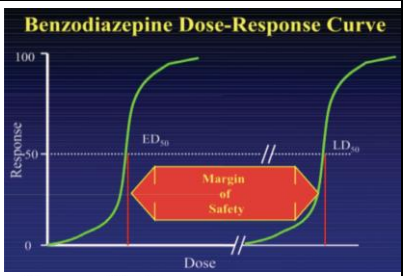
Overdose:



TX: -> **Flumazenil**
- Benzo receptor antagonist
- Short ½ life though (~1hr) -> Might have re-sedation if there is still benzo available in the body after Flumazenil is gone
- IM or IV administration
- ADJUNCT, not a substitute for proper management.

Pharmacokinetics and Dynamics

Wide Margin of Safety 😊



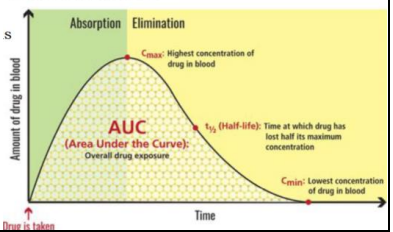
Lipid Soluble (very strongly bound to plasma proteins)

Duration of Actions
- Largely depends on how long the drug is in the brain (*Lipid Solubility*) + ½ Life
- Low Lipid solubility = ↑ duration of action, because it takes longer to redistribute away from the brain

Metabolism:
- Hepatic metabolism
- *Active metabolites -> lead to more prolonged action*
  - Phase 1 or 2 metabolites -> get conjugated by CP450 in liver
  - Liver disease will effect the ½ life, but not kidney disease
- P450 Inhibitors (amiodrone, cimetidine etc) = ↑ duration of action of Benzo's
- P450 Inducers (Dexamethazone, St. Johns Wort, Smoking) = ↓ duration of action of Benzo's

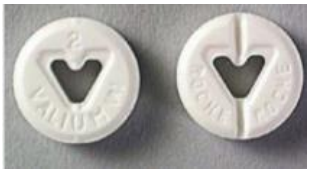
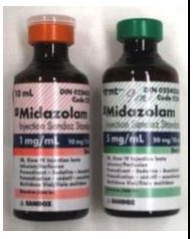
Excretion:
- Through Kidneys

Pharmacokinetics



Sensitivities

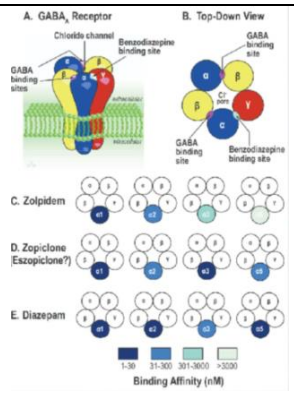
↑ Sensitivity	↓ Sensitivity
- Elderly - Liver Disease - CNS Depressants	- Smoking (induces liver enzymes) - Recent/Frequent use of: Benzo's, Alcohol, CNS Depressants

Diazepam (Valium)	*Onset*: - ~40 mins orally (Fast) -> Highly lipophilic *½ Life:* - 20-80hrs (long) - Active metabolites *Dose*: - 2-20mg *Side Effects:* - Daytime drowsiness - Anterograde amnesia 
Lorazepam (Ativan) **KNOW THIS ONE**	*Onset*: - 1-2 hrs (Intermediate) - Sublingual has faster onset *Duration of Action:* - ~ 6-8hrs *½ life:* - 10-20hrs - *Duration of action is longer than diazepam* though (even though ½ is less). ↓ lipid solubility so it stays in the brain longer - No Active metabolites *Dose*: - 0.5-4mg *Side Effects:* - Some anterograde Amnesia 
Alprazolam (Xanax)	*Onset*: - 60 mins (Fast) *Duration of Action:* - ~ 6hrs (Intermediate acting) *½ life:* - 11hrs - Minimal active metabolites *Dose*: - 0.25-1mg *Side Effects:* - Some anterograde amnesia - Antidepressant effects 
Triazolam (Halcion) **KNOW THIS ONE**	*Onset*: - 60 mins (Fast) - 40 mins w/ sublingual administration *Duration of Action:* - 1-2hrs *½ life:* - 1.5-5.5hrs (Short) - No active metabolites *Dose*: - 0.125-0.5mg - MAX Dose 0.5mg *Side Effects*: - Excellent anterograde amnesia 
Midazolam (Versed)	*Onset*: - 10-15mins as oral syrup (Very Fast) - Mixed w/ something sweet for oral administration (Tastes TERRIBLE) - 2-3 minutes w/ IV *Duration of Action* - ~1hr (as oral syrup) - 20 mins with IV -> Can titrate in more though if IV *½ Life:* - Short - Active metabolites *Dose*: - 0.25mg/kg - MAX 20mg - Choice med for Peds oral Sedation (For adults its no better than Triazelam though…) *Side Effects:* - Excellent Anterograde amnesia 

	Short to Medium Length Appointments	Long Appointments
Benzo of choice	- Midazolam - Triazolam	- Lorazepam - Diazepam - Alprazolam

	Diazepam	Lorazepam (Know)	Alprazolam	Triazolam (Know)	Midazolam
Onset	40 mins	1-2hrs (Faster if sublingual)	60 mins	60 mins (40min if sublingual)	10-15 mins (Syrup)
½ Life	20-80hrs	10-20hrs	11hrs	1.5-5.5hrs	Short
Duration	V. Long (Days)	6-8hrs	6hrs	1-2hrs	1hr (as syrup)
Dose	2-20mg	0.5-4mg	0.25-1mg	0.125-0.5mg	0.25mg/kg Max 20mg

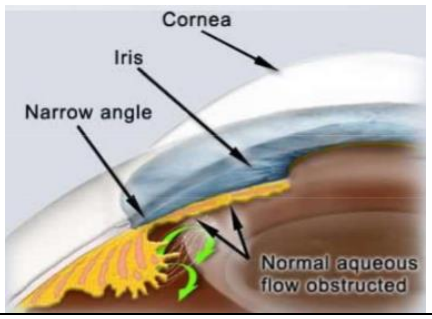
Non Benzo Sedatives

Zopiclone (Imaovane)	Binds GABA A Receptor Subunit I - Only non-benzo available in Canada - Better sleep aid than antianxiety med *Onset*: - 30 mins (Fast) *½ Life*: - 3-5 hrs (Short) - No active metabolites *Dose*: - 7.5-15mg *Side Effects*: - Some anterograde amnesia *Reversed by Flumazenil still* 
Zaleplon (Starnoc, Sonata)	Not available in Canada - Fast Onset - Short ½ life - No active metabolites - Reversed by Flumazenil
Zolpidem (Ambien)	Not Available in Canada - Fast Onset - Short ½ Life - No Active Metabolites - Reversed by Flumazenil
1st Gen Antihistamines	H1 Receptor Blockers - Allergic reactions - Anti-nausea - Sedation (Side effect) -> less effective than benzo *Diphendydramine (Benadryl):* 25-50mg *Hydroxyzine (Atarax)*: 50-100mg Promethazine (Phenergan): 25-50mg *Onset*: - Fast *½ Life*: - Short-intermediate *Side Effects*: - Anti-cholinergic effects

Oral Sedation Success

- Adults > Children
  - Adults understand the benefit of the procedure. Once you remove the anxiety, they become 100% cooperative b/c they know WHY it needs to be done
  - Kids just don't get it. When you remove the anxiety, they are still uncooperative because they don't understand why you are doing what you are doing. They might even get worse with the uninhibited behaviour sedatives produce
  - ONLY goal with kids is the Amnesia side effects -> They won't remember the procedure, so long term it will be ok
- Older Children > Younger Children

Health Considerations with Benzo's

Geriatric Patients	Physiological Decreases: - ↓ Cardiac Output - ↓ Cerebral Blood Flow - ↓ Renal and Hepatic blood flow - ↓ Pulmonary Function *Usually Benzo's will take longer to have effect, but when it hits it REALLY sedates* - Small dose of Midazolam (1-2mg IV) is a good dose
Cardiovascular Disease	Anxiety and Pain ↑ HR and BP - ↑ O_2 Coronary Artery Disease -> Angina (because the increased O_2 demand is not being met) Arrythmias **Sedation and pain control is beneficial for these patients** - Always use supplemental O_2 in these patients, even in mild sedation
Renal Disease	Single Doses are ok - No dose adjustment needed ***Avoid Chloral Hydrate*** - Very dependent on renal clearance
Hepatic Disease	Single Dose is ok - Consider ↓ the dosage depending on the stage of the disease. ↓ enzymes = ↑ duration of action
Epilepsy	Single dose is OK Benzo's have anticonvulant effect - Some anti-epileptics are P450 inducers though (↓ duration of action)
OSA	Pt unable to keep airways open during sleep - ↑ CO_2 leads to pulmonary vascular resistance -> Right Ventricular Hypertrophy, Cor Pulmonale, R. Heart Failure Very sensitive to CNS depressants -> ↑ risk of Upper Airway constriction - Be cautious and use supplemental O_2
Acute Narrow/Closed Angle Glaucoma	Benzo's Contraindicated  **Signs/Symptoms**: - Pain, Blurred vision, Nausea, Vomiting, Blindness (if not treated fast) - Fluid in the eye drains at the angle between the cornea and the pupil… -> Shortening this angle ↓ drainage - Anticholinergics close this angle = bad *Open Angle Glaucoma* -> Tx w/ eyes drops (this is your clue) = Benzo's ok *Closed Angle Glaucoma* -> Tx w/ laser = Benzo's not ok

Considerations

Giving Sedation at home

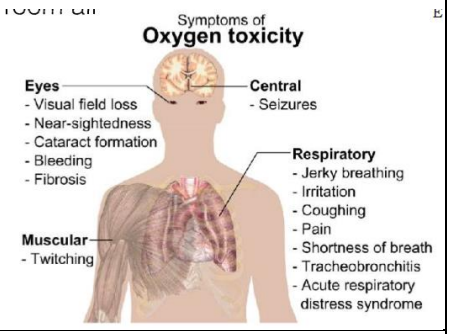
- Give sedative the night before (Lowest dose and never for the 1st appointment) -> Only if they can't sleep because of anxiety
- The morning of the appointment

After the Appointment

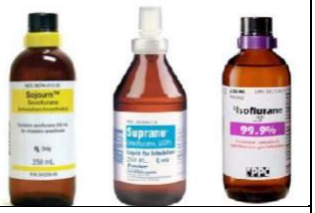
- No driving for 24 hrs
- No heavy machinery for 24hrs
- Must be escorted home (and to the office if they took the pill in the AM or night before)
- Signed consent for the Tx before sedative administration
- No important or legal decisions made within 24hrs
- No alcohol or other CNS depressants for 24 hrs

Nitrous Oxide and Oxygen

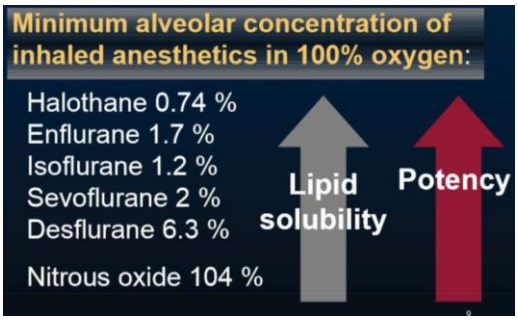
- Nitrous can be used for minimal, Moderate and Deep Sedation -> It just depends on how much you titrate

Oxygen	Non Flammable - Supports combustion though! -> Without O_2 the fuel will be unable to burn in a fire Fire needs: - Fuel (or combustible material) - Ignition or heat source - Oxygen Atmospheric Air = 21% O_2 *Excessive O_2 supplementation (>60% O_2) can cause Oxygen Toxicity*: -> Evidence of injury can be found w/i 24hrs *Stay away from the O_2 bars in Vegas…and PDC* 
Nitrous Oxide	Colorless non-flammable gas at room temperature - Sweet odor and taste…yummmmmyyyy It's a greenhouse gas ☹ - Contributes 7% of all emissions - 10x worse than methane for the atmosphere, and 250x worse than CO_2 -> HOWEVER its such a small percentage overall that it doesn't add thhhhaaaatttt much bad to the atmosphere

Inhalation Anesthetics effects on the body

CNS Effects	= Non-selective CNS Depressant - Mechanism for ↓ perception of sensation and unconsciousness is unknown **<u>Effects are:</u>** - Dose Dependent (each patient is different) - Titratable to effect - Dependant on pt being conscious and responsive *<u>Examples</u>*: - Desflurane -> Very Potent (6.3%) - Sevoflurane -> Very Potent (2%) - Isoflurane -> Very potent (1.2%) - Nitrous Oxide -> This is the wimpiest, least potent (104%) 
Respiratory	Respiratory Depressants - Affects the Hypoxemic/Hypercapnic Drive -> Contraindicated in COPD patients - Concentrations of ½ MAC have a minimal effect on hypercapnic drive but response ↑ big time when you titrate to higher concentration: Apnea at 1.5 MAC Nitrous Oxide is the only one that doesn't ↓net ventilation - All other ↓ tidal volume
Cardiovascular	Dose Dependent ↓ in mean arterial pressure and cardiac output Nitrous oxide is the only one that doesn't ↓ BP, and only mildly ↓ cardiac contractility (Cardiac Output is maintained though) - Nitrous ↑ venous tone = ↑ venous return to the heart, this offsets the ↓ cardiac output that inhaled anesthetics typically produce - Opioids ↓ sympathetic outflow lots though -> so when combined with N_2O the sympathetic masking nitrous typically does is decreased and we can get ↓ C.O.
Skeletal Muscle Effects	Most provide muscle relaxation - This creates a risk for Malignant Hyperthermia - NOT nitrous though! No effect on skeletal muscle for this boi
GI Effects	↑ Concentration and ↑ Duration can cause nausea and vomiting - Slowly induce to ↓ the risk - Nitrous alone has a fairly ↓ risk, but when we mix it with other things with IV then the risk ↑

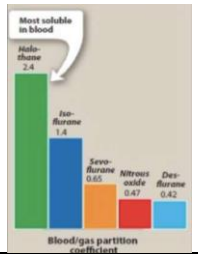
<table>
<tr><th colspan="2">Pharmacology</th></tr>
<tr><td><u>Minimum Alveolar Concentration (MAC)</u>
(Potency)</td><td>= % at 1atm that causes anesthesia in 50% of the patients
- Amount of drug that inhibits movement in 50% of people when painful stimulus is applied (GENERAL ANESTHESIA)

↑ Potency = less % you need to use

<table>
<tr><th>Factors that ↑ MAC</th><th>Factors that ↓ MAC</th></tr>
<tr><td>- Fever
- CNS Stimulants (Cocaine, Amphetamines)
- ↓ Age
- Chronic alcoholism</td><td>- Hypothermia
- CNS Depressants (Cannabis, Alcohol)
- ↑ Age
- Hypercapnia
- Hypoxemia
- Anemia</td></tr>
</table></td></tr>
<tr><td><u>Blood-Gas Partition Coefficient (Solubility in Blood)</u>

(Onset and Elimination)</td><td>$\frac{Conc.\ of\ anesthetic\ in\ blood}{Conc.\ of\ anesthetic\ in\ gas}$
-> Low = Rapid induction.
- Means gas is not soluble in the blood, so it wants to leave ASAP. Goes in from alveoli and jumps out at the brain fast and vice versa. Hops out of the blood and into the alveoli fast to exhale

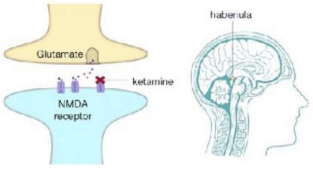
 

Ether = 12
Sevofluorane = 0.65
Nitrous = 0.47</td></tr>
<tr><td><u>Metabolism</u></td><td>Reductive metabolism in the GI tract
- Elimination through expiration</td></tr>
</table>

How Nitrous Works

<table>
<tr><td>Analgesia Effects
Without Loss of Consciousness</td><td>At subanesthetic doses -> has analgesia effects

Useful in:
- Obstetrics
- Cancer
- Colonoscopies
- IV Drug administration
- ER

<u>Theories as to why:</u>
<table>
<tr><td>Opioid Hypothesis</td><td>Naloxone blocked the analgesia
Specific subtype though depends on the stimulus, species and area of the brain stimulated</td></tr>
<tr><td>GABA Receptor Hypothesis</td><td>Nitrous is sensitive to Flumazenil antagonism
- Those tolerant to benzo’s can also be tolerant to nitrous</td></tr>
<tr><td>NMDA Hypothesis</td><td>Nitrous is thought to ↑ binding to NMDA in cortex (similar to ketamine)
- Inhibits the excitatory action of NMDA
- Causes Dissociative anesthetic
 
</td></tr>
</table></td></tr>
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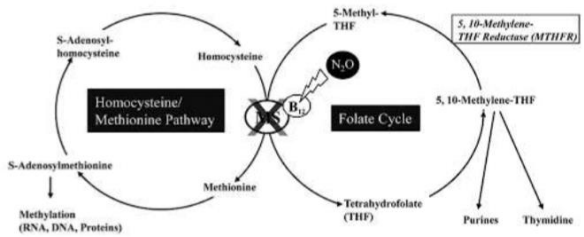
Chronic Exposure Effects

- This pertains to Dentists and staff around the stuff all day

Psychomotor Performance	Old studies showed that with 50ppm inhaled over 2hrs there was impairment in audiovisual performance as well as possible perceptual, cognitive and motor skill ↓ - This was then debunked by the very same people who did the first study
Biochemical Disturbances	Nitrous Oxidizes cobalt in the reduced form of vitamin B12 -> Inactivates - This prevents Vit. B12 from acting as the coenzyme for methionine synthase, an important cycle for the production of Myelin Sheath - Pt's with dietary deficiency of B12, or that have Pernicious Anemia are at ↑ ↑ risk  Studies showed reproductive toxicity effects in dental assistants w/ N_2O exposure levels of 3-5 hrs per week in offices **WITHOUT** scavenging - There is no risk though if there is sufficient scavenging (which ↓ levels to < 50ppm)
Exposure Levels	There is no official max N_2O as dictated by the ADA - Worksafe BC though has dictated a maximum of 50ppm Minimum threshold for biologic effects in humans is >100ppm N_2O for 8hr a day and 400ppm per single administration - 8hr day level is mostly of concern for Peds clinics - 400ppm level is more for the general dentist doing 1 or 2 nitrous cases a day *Two most common causes of nitrous contamination in the office are from:* 1. Patients talking 2. Patients mouth breathing *Rubber dam prevents these*

Pressure/Volume Effects

- Blood:Gas coefficient of nitrous oxide is 0.46 -> 34x greater than nitrogen (0.014)
- When inspired gas mixture is switched from air (78% nitrogen) to nitrous mix (50% nitrogen) -> Nitrous oxide will enter gas-filled spaces >30x faster than nitrogen can exit = ↑ volume or pressure
  - Big issues w/ obstructed bowel, pneumothorax, or ear infection
- Ask Pt if they have had any ocular procedures or surgeries within 3 months
  - They might have an intraocular gas bubble -> N_2O can diffuse into the bubble, ↑ pressure and cause vision loss

Nitrous Advantages and Disadvantages

Advantages	- Rapid onset - Ease of titration (dose control) - Limited physiologic effects - Analgesic - Suppression of gag reflex
Disadvantages	- Weak - Lack of patient acceptance? - Inconvenient when working on Maxillary anterior teeth - Potential chronic toxicity - Potential abuse - Necessary equipment is needed and services annually
Contraindications	- Uncooperative patients (mental disability, Claustrophobic) - Nasopharyngeal Obstruction - Conditions w/ closed tissue spaces (COPD) - Vitreoretinal surgery within 3 months - Recent bleomycin chemo within 1 year

Nitrous Equipment and Techniques

There are 3 types of machines that will mix the gases for us (N_2O and O_2):

1. Fully Portable
   - Tanks and everything on a single cart
2. Semi-Portable
   - Doesn't carry the tanks -> its mostly just a gas mixer. Gas outlets are built into the operatory and the mixer plugs in
3. Stationary
   - Everything is built in centrally

Components

Common to all systems

- Gas Cylinders
- Reducing Valves (Regulator)
- Flowmeters (For both N_2O and O_2)
- Reservoir bag
- Conducting tubing (From the mixing unit to the nasal hood)
- Nasal Hood

Color Coding

Standardized everywhere (Except the US) -> Hoses, Tanks Valves

Nitrous Oxide = Blue
Oxygen = White/Green (in the US)

Compressed Gas Cylinders

Different Sizes (A, B, D, E, M, G, H, HH)

cylinder	dimension (inches)	weight (empty-lbs)
A	3.0 x 10	2.75
B	3.5 x 17	8
D	4.24 x 20	12
E	4.5 x 29.5	21
M	7.12 x 46	74
G	8.5 x 55	130
H	9.0 x 55	130
HH	9.25 x 59	136

- **Size E** is what is mostly found on the portable units
  - *21lbs*, easy to haul around
- Sizes **G and H** are mostly what you find in the Centralized, Stationary Systems
  - *130lb*, harder to haul around

	Oxygen Cylinders		Nitrous Oxide Cylinders	
Size	**E**	**H**	**E**	**G**
Dimensions	4.5"x29.5"	9"x55"	4.5"x29.5"	8.5"x55"
Color	White/Green	White/Green	Blue	Blue
PSI – Full	**2000**	**2200**	**750-800**	**750-800**
PSI – ½ Full	1000	1100	750-800	750-800
Capacity (Liters)	**660**	**6909**	**1590**	**13839**
Physical state of the contents	**Gas**	**Gas**	**Liquid/gas**	**Liquid/gas**

Very important to know PSI's and tank capacities -> Allows us to know how long our tank will last

- If we have 1000PSI O_2 then we have about 330 liters left in an E cylinder. If we run at 6L/min…then we have about 55mins left

Regulators (Reducing Valves)

-> Lowers the gas pressure from 2000 PSI -> 50 PSI so you don't explode a persons lungs

- If cylinders are opened too fast, the rapid change in pressure can cause significant ↑ in temps and possible fire (1500-2000 °F)

Yoke

-> Holds the cylinder to the mixing unit

- Keep minimum of 2x O_2 units and 1x N_2O unit -> Never really know when you will run out, so have a backup

Continuous Flow Unit

2 Pressure systems:

High Pressure System	Low Pressure System
- Compressed Gas Cylinders - Yoke - Reducing Valve/Regulator	- Reducing Value/Regulator (The other side of it) - Flowmeters - Reservoir Bag - Nasal Hood

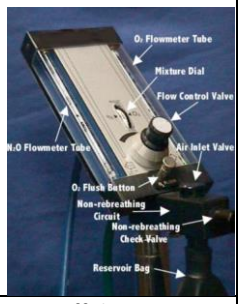
Flowmeters

- These are really the only way to differentiate between a newer and older unit
  - **Old system**: Tells you the L/min and you calculate the %
    - Eg: O_2 at 2L/min and N_2O at 4L/min = running at 33% O_2, 66% N_2O at 6L/min
  - **New System**: Tells you the % already

3 Types:

- Rotameter
- Ball
- Rod

O_2 is always on the Right
N_2O is always on the Left



Emergency Air intake Value

= Allows air to enter if the unit is not operating, so if machine turns off the patient can still get air through the mask

- Closed when gas is flowing so as to not dilute the mixture

Rubber Goods

Reservoir Bag

= Provides extra gas for deep ventilation

- Also allows us to monitor respiration. Can visually see how much the bag is inflating/deflating with each breath

Adult: 5L
Child: 3L

Conducting Tubes

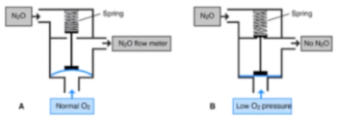
Connects sedation machine to the breathing apparatus

- Ribbed tubing to prevent kinks or obstructions….also for your pleasure 😉

Breathing Apparatus

Full Face Mask	Nasal Cannula	Scavenging Nasal Hood
- Allows ventilation through nose + mouth - Obviously impractical for dentistry…used for emergencies when need ↑ $F_i O_2$	- Good for claustrophobic patients - LOTS of leakage though - Needs ↑ N_2O L/min and % to get the same F_i to the lungs - No scavenging possible	- Delivers fresh gases from sedation unit - Vents exhaled gases away from the operator, prevents exhaled gases going into open air
		

Safety Features	

Safety Features	- *Pin Index Safety System*
	- *Diameter Index Safety System*
	  - N_2O and O_2 valves have different diameters, so you can't plug one into the wrong hose
	- *Minimum Oxygen Flow*
	 
	- As O_2 ↓ too much –> N_2O valve closes, and you cant get either
	- *Minimum Oxygen Percentage*
	- *Oxygen Fail Safe*
	- *Emergency Air Inlet*
	- *Oxygen flush button*
	  - Press and hold to bypass the nitrous and blow 100% O_2 to fill reservoir bag and give Pt O_2
	- *Color Coding*

Signs of N_2O-O_2 Sedation

Early -> Ideal	- Light headedness - Tingling or numbness of hands and feet or lips - Wave of warmth - Feeling of vibration throughout the body - Euphoria - Feeling of floating in air, or sinking deep into the cushion - Lightness or heaviness of extremities
Deep -> Mild Over Sedation	- Hearing distant sounds, More acute hearing - Visual images and become confused - Seeing dark stars - Sleepiness - Diaphoresis (Sweating) - Dreaming - Laughing, Crying (Lacrimation) - Nausea - ↑ Movement - ↑ Respiration rate **Signs**: - Nausea; - ↓ responsiveness **Symptoms**: - Vomiting; - Loss of consciousness
Over sedation	= Most likely to occur during lulls in Tx when there is no verbal visual or physical stimulation **Signs**: - Persistent closing of the mouth (Lack of cooperation) - Spontaneous mouth breathing - Patient states effects are too intense - Complaints of Nausea - Pt fails to respond rationally or is sluggish - States they are about to fall asleep - Incoherent - Appears to be dreaming - Laughing, crying, overly giddy - Uncoordinated movements **Tx**: - ↓ N_2O by 0.5-1 L/min - ↑ O_2 by the same L/min

Stopping N_2O-O_2

1. ↑ O_2 flow to the original L/min
2. ↓ N_2O to 0 L/min
3. Administer 100% O_2 for 3-5 minutes (This prevents room contamination from excess N_2O, as well as Diffusion hypoxia)
    a. Longer if necessary, until ALL Sign/Symptoms of sedation remain

Theoretical Diffusion Hypoxia

- After N_2O is stopped -> the concentration in the blood is ↑ vs the alveoli
- Nitrous diffuses into the alveoli -> Fills w/ N_2O and displaces the O_2

*Breathing room air during this time can cause alveolar hypoxia -> So give 100% O_2 for 3-4 mins at end of appointment to allow residual nitrous to be capture by the reservoir bag and scavenged

Discharging Patient

- Assess the patient response, looking for signs of continued sedation
- Monitor Vitals:
  - BP -> Ideally we want within 10% of the patients baseline when they leave
  - HR
  - RR
- Make your Notes
- Titrate for next appointment:
  - If Pt was 50% at one appointment, at the next start at 35-40% and move up to 50%

Record Keeping

"Nitrous Oxide/Oxygen was titrated to effect. Patient received ____% N_2O and ____% O_2 at a total liter flow of ____L/Min. The Procedure lasted approximately ___Mins. At the termination of the procedure the patient received 100% O_2 for ____min at a flow of ___L/Min. The patient tolerated the procedure well and was dismissed from the office in good condition

Cleaning the Equipment

1. Wash Nasal hood w/ soap + water -> Then place in glutaraldehyde for 10 minutes
2. Rinse with tap water
3. Hang to dry
4. Gas sterilize

Complications

Excessive Perspiration	
Behavioral Problems	- Claustrophobia - Vivid dreaming - Talkative
Shivering	N_2O Vasodilates - Useful when you are looking for an IV site actually - Causes body heat loss Usually occurs at the end of the procedure when N_2O stops and the body tries to rewarm itsef *Give blankets and reassure the patient
Nausea	*Causes*: - ↑ sedation depth - ↑ sedation length - Patient emotional status - Inherent tendency to become nauseated - Presence of food in stomach -> Light meal only >2hrs before nitrous to ↓ risk *Management*: - ↓ N_2O by 10% and reassess
Vomiting	*Management*: - Turn N_2O completely off + administer 100% O_2 - Remove nasal hood if they start to puke - Remove rubber dam - Turn Pt head away from you + High volume suction airway - After vomiting, replace nasal hood with 100% O_2
Sexual Phenomenon	There is an ↑ risk of complaints of sexual assault following N_2O Administration - ALWAYS have an assistant present (preferably the same gender as the patient)

Contamination Concerns

N_2O can come from:

- Perimeter of a poorly fitting mask
- Mouth breathing patient
- Talking or Laughing patient
- Worn hose connectors
- Loose/Defective gaskets and seals
- Worn/defective bags and breathing tubes
- Loosely assembled slip joints and threaded connections

Detection

Daily	-	Assess rubber goods for leaks or cracks -> Can use soapy water and look for bubble formation
Monthly	-	Assess hard connections
Quarterly	-	Measure ambient N_2O levels (IR Analyzer)

Techniques

Method 1 (Constant L Flow technique)

1. Prepare unit
2. Establish 5-6 L/min O_2 flow
3. Secure nasal mask
4. Determine adequate flow of gases (w/ O_2)
5. Titrate initial N_2O
6. ↑ 1 L/min N_2O and ↓ 1L/min O_2 -> Maintain constant flow
   - Determine CNS response after 1 min
7. ↑ 0.5L/min N_2O and ↓ 0.5 L/min O_2
   - Repeat until you are where you want to be
8. At end: give pt 100% O_2 for 3-5 minutes
   - Determine level of recovery prior to dismissal

$$\text{Percentage of N20} = \frac{\text{lpm N20}}{\text{lpm O2} + \text{lpm N20}}$$

% N20
Constant liter flow technique

O2 LPM	N20 LPM	% N20
6	0	0
5	1	16.6
4.5	1.5	25
4	2	33.3
3.5	2.5	41.7
3	3	50
2.5	3.5	58.3

Method 2 (Titrate by Percentage)

i. Prepare unit
ii. Establish 5-6L/min O_2 (100%)
iii. Secure nasal hood
iv. Determine adequate flow of gas
v. Titrate initial N_2O
   - 90% O_2; 10% N_2O
   - Determine CNS Response after 1-2 mins
vi. Adjust percentage of O_2 to 85% (↓ 5%)
   - Reassess after 1-2 mins
   - Repeat until desired sedation is reached
vii. At End: give 100% O_2 for 3-5 minutes