Minimal sedation – understanding fear and anxiety

- Fear
  - Physiological process that occurs when the body is threatened by danger
  - Sympathetic system that prepares for the fight or flight response
- Anxiety
  - Anticipation of the possibility of danger
  - Unable to control the thought of a possible negative event occurring → leads to dysphoria and tension
- Prevalence of dental fear in the American population
  - 36% - some level of fear towards dentistry
  - 18.1% - would visit the dentist more if given a drug to reduce nervousness
  - 2.8% - currently receive IV sedation of GA for dentistry
  - 8.6% - would prefer IV sedation or GA if available
  - 7.6% - have missed, cancelled, or avoided a dental appointment because of fear or anxiety
    - In the low/no fear of dentistry group, only 5.2% of patients missed, cancelled, or avoided an appointment
    - In the high fear group, 49.2% missed, cancelled, or avoided an appointment
  - Women are 2.5x more likely to report themselves as high dental fear
  - No difference between age and dental fear/anxiety
  - No difference between education level and dental fear/anxiety
  - >400,000 have not been to the dentist in 1+ year due to fear or anxiety
  - >1.5 million have missed, cancelled, or avoided a dental appointment due to fear of anxiety
  - >800,000 are so terrified they will not go to a dentist even when in severe pain
- Public's interest in sedation
  - 12.4% are definitely interested. Of this group, 11.4% are in the low fear group and 31.1% are high fear
  - 42.3% are interested depending on cost. Of this group, 42.3% are in low fear, and 54.1% are in high fear
  - 12.4% of people are interested in sedation for dental treatment, 42.3% are depending on cost, and 44% are not
  - 12.7% of people in the high risk group will avoid RCT's, but went down to 5.4% if sedation was proposed
  - 2.5 million are definitely interested in sedation or GA for dentistry, 8.5 million are interested depending on cost
- Indications for GA/sedation
  - Highly anxious and/or phobic patients
  - Uncooperative children
  - Patients with developmental disorders
  - Patients who have an exaggerated gag reflex
  - Patients who experience ineffective local anesthetics
  - Patients who elect to undergo sedation/GA to reduce stress and increase comfort
- Types of anesthesia
  - Inhalation: mixture of nitrous oxide and oxygen
  - Oral/enteral
  - Intramuscular
  - Intravenous
- History of nitrous oxide
  - 1772 – Joseph Priestley discovered nitrous oxide and oxygen
  - 1796 – Humphry Davy discovered that breathing the gas helped with toothaches
  - Mid 1800's – Nitrous used as a source of entertainment and amusement (laughing gas)
  - 1844 – Nitrous used on Sam Cooley as a show, had leg injured on stage without batting an eyelid
- Other sedative uses
  - Horace Wells – experimented with chloroform, became addicted to it, and committed suicide while on it
  - William Morton – first one to perform an extraction using ether
- Benefits of sedation
  - Relaxation and partial amnesia → good for mild~moderate levels of fear/anxiety
  - General anesthesia → good for even the most phobic dental patient
  - Dentist can complete care rather than delay care due to anxiety and fear
  - Improved dental care when patient's apprehension and movements are reduced
  - Lengthy procedures can be completed comfortably

Guidelines for anesthesia use in a dental office

- Stages of anesthesia

Stage 1	Induction	-Period between initial administration and starting to lose consciousness
Stage 2	Excitement stage	-Excitement and delirious activity, patient moves around and needs to be restrained
Stage 3	Surgical anesthesia	-No sensation
Stage 4	Overdose	-Coma

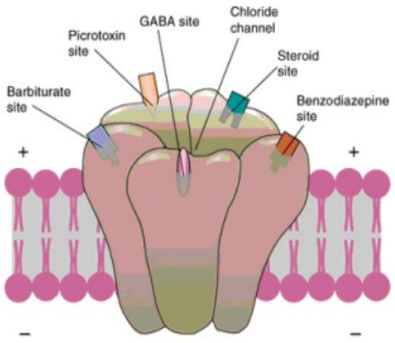
  - These stages were discovered based on using ether as a sedative agent
  - Nowadays, sedatives work much quicker so the early stages are less evident
  - Stage 1 is quicker, stage 2 is only around 10 seconds (as opposed to 8~10 mins with ether)
- Components needed for GA
  - Intubated GA: benzodiazepine, narcotic, hypnotic, paralytic (to relax vocal chords)
  - Non intubated GA: benzodiazepine, narcotic, hypnotic
- Pediatric oral sedation
  - For children <12, refer to American Academy of Pediatrics for guidelines
  - "Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures"
- Levels of sedation

	Minimal sedation (anxiolysis)	**Moderate sedation (conscious sedation)**	**Deep sedation**	**General anesthesia**
Responsiveness	-Normal response to verbal and tactile stimuli	-Purposeful response to verbal or tactile stimuli (they look at you when you tap them on the shoulder)	-Purposeful response following repeated or painful stimuli	-Unarousable even with painful stimulus
Airway	-Unaffected	-No intervention required	-Intervention may be required	-Intervention frequently required
Spontaneous ventilation	-Unaffected	-Adequate	-May be inadequate	-Frequently inadequate
Cardiovascular function	-Unaffected	-Usually maintained	-Usually maintained	-May be impaired

  - Is not discrete, but a continuum
  - A patient can drift between different levels depending on painfulness of a procedure
  - A patient whose only response is reflex withdrawal from a painful stimulus is not considered min/moderate sedation
  - When the goal is minimal or moderate sedation, the drug and/or technique should have a safety margin wide enough such that there is never unintended loss of consciousness
- Dosing for minimal sedation using oral drugs
  - Dose should be no more than the maximum recommended dose (MRD) that's allowed for unmonitored use
  - Titrating is not possible
  - Time should be given for the drug to absorb
- Dosing for intravenous and inhalational drugs
  - Titration (giving incremental doses of a drug until desired effect is reached)
  - Repeating a dose before the previous dose has reached its full effect may cause greater sedation than intended
  - Therefore, it is important to know the drug's time of onset, peak, and duration of action
  - One must know whether the previous dose has taken full effect before giving another dose
- Rescue
  - Practitioners should be able to diagnose and manage patients who become sedated more than intended
  - Proper training, skills, drugs, and equipment must be present
  - Minimal sedation procedure = practitioner should know how to rescue from moderate sedation
  - Moderate sedation procedure = practitioner should know how to rescue from deep sedation
  - Deep sedation procedure = practitioner should know how to rescue from general anesthesia
- Maintaining airway
  - Tilt the head, and lift the chin – make sure it is held high and aggressive enough
  - Avoid GA in patients with hypoplastic mandibles (Treacher-Collin syndrome, Golden-Harr syndrome) as the airway may not be maintainable if they go into unintentional loss of consciousness

- Recovery
    - Patients may be at risk of complications after sedation, assume no medial supervision once the patient leaves
    - Decreased procedural stimulation, delayed drug absorption, slow drug elimination may lead to residual sedation that can manifest as cardio-respiratory depression
    - During the procedure, the patient's anxiety may have been fighting against the sedation. Once the procedure ends, they are relaxed and that sedative in their system could go to its full effect

Oral sedation



- The GABA receptor
    - Channel that opens when the GABA molecule attaches to it
    - Allows chloride ions to go into cells, hyperpolarizing them and making these cells harder to depolarize → cell is inhibited
    - The GABA receptor mediates how much a cell is inhibited
    - Inhibitory drugs (like barbiturates and benzodiazepines) bind to the GABA receptor on a unique binding site
    - These drugs allow GABA to attach easier → more likely that channel is open → more likely that cells are inhibited
    - Important note: the drugs don't open the channels themselves, they just make GABA bind to the channel easier
- Classes of oral sedatives

	Chloral hydrate	Barbiturates	Antihistamines	Benzodiazepines
Types and date of discovery	-Discovered in 1832	-1860's: barbituric acid -1903: barbital -Newer: thiopental, amo/seco/pheno barbital	-Diphenhydramine -Hydroxyzine -Promethazine -Only first gen, as second gen does not cross BBB → no sedative effect	-1954: chlordiazepoxide -1963: diazepam -1965: nitrazepam -1969: temazepam
Pharmaco-kinetics and dynamics	-Onset: 10~15m -Peak: ~60m -Duration: ~8h in adults, ~10h in children		Promethazine: -Fast onset -Short~med ½ life	-Excretion: hepatic and renal -<u>Increased effect</u>: elderly, patients with liver disease, or patients on other CNS depressants -<u>Decreased effect</u>: smokers (↑ liver enzymes), frequent user of BDZ, EtOH, other CNS depressants
Therapeutic window	-Very narrow	-Narrow	-Wide	-Wide
Mechanism and effects	-Is a pro drug -Active metabolites are tricholoro-ethanol and trichloroacetic acid	-Binds to GABA receptor complex	-Blocks histamine receptors -Anti-nauseant, with sedation as a side effect	-Binds to GABA receptor complex -Anticonvulsant, ↓ muscle tonus -Sedative, anxiolytic
Cautions	-Daytime drowsiness (hangover) -Doesn't get rid of anxiety, just makes patient drunk -Basically works just like alcohol	-Can cause death if taken with alcohol -Addictive	-Anticholinergic side effects	**Side effects:** -Anterograde amnesia (lapses in memory) -Mild anticholinergic effects -Disinhibition -Dependence/addiction **Overdose:** -Drowsiness, hypotonia, confusion, hypotension, impaired coordination, respiratory depression, CV depression, slurred speech, lethargy, death **See next page for BDZ use in medically compromised**

- Benzodiazepines rescue agent – Flumazenil
    - Benzodiazepine receptor antagonist
    - Has a short half life (will last about 45 minutes), after which the patient will return to prior level of sedation
    - Given IV (10~15 second onset) or IM (5~15 minute onset)
    - Could predispose patients to seizures
    - Not meant for routine use, only use as a last effort when EMS has not arrived and patient's O_2 is dropping
- Types of benzodiazepines

	Type	Dose + route	Onset	Active metabolite	Effects	Etc info
Long acting	Chlordiazepoxide (Librium)		-Intermed.	-Yes	-Daytime drowsiness	
	Diazepam (Valium)	-5~20mg PO/IV	-Fast	-Yes	-Daytime drowsiness -Anterograde amnesia	-$T_{1/2}$ increases with age
Intermediate acting	Lorazepam (Ativan)	-0.5~4mg PO/SL/IM	-Intermed.	-No	-Some anterograde amnesia	-IM: for seizures -IV: avoid -SL: most common
	Alprazolam (Xanax)	-0.25~1mg	-Intermed.	-Yes	-Some anterograde amnesia	-Anti-depressant effects
Short acting	Triazolam (Halcion)	-0.125~0.5mg SL	-Fast	-No	-Excellent anterograde amnesia	
	Midazolam PO (Versed)	Peds: 0.5mg/kg, 20mg max Adult (rarely used): 0.25mg/kg, 20mg max	-Fast (10~15m)	-Yes	-Excellent anterograde amnesia	-Can be used as premed before GA -1/10 children have a paradoxical effect
	Midazolam IV		-Seconds			-For adults (mod sed'n)
	Zopiclone (Imovane)	-7.5~15mg	-Fast	-Yes	-Some anterograde amnesia	-Not a BZD -Only produces sedation, not anxiolytic
	Zaleplon (Starnoc, Sonata)		-Fast	-No		-Not in Canada
	Zolpidem (Ambien)		-Fast	-No		-Not in Canada

- Benzodiazepine use in medically compromised

Condition	Modification required	Reason
Pregnancy	-Avoid	-Teratogenic
Breastfeeding	-Not recommended	-Could "pump and dump" accumulated drug in mother's body into the baby
Geriatric	-Reduce dose -Use shorter acting agents	-↓ CO, cerebral/renal/hepatic blood flow, pulmonary function -Comorbidities like heart disease, HTN, arthritis, diabetes
Cardiovascular disease	-Ensure adequate pain control and sedation	-These pts already have an increased oxygen demand -Anxiety + pain could ↑ HR, ↑ BP, and lead to angina and arrhythmias
Renal disease	-Avoid chloral hydrate -Single doses acceptable -No dose adjustments needed	
Diabetes	-No dose adjustments needed -Ensure [glucose] is stable -Schedule for short morning appt	-Maintain caloric intake pre/post op OR adjust dose of diabetes meds -Hypoglycemia and mimic over-sedation, so take extra caution ensuring patient does not become hypoglycemic
Hepatic disease	-Single doses acceptable -Consider decreasing dose	
Respiratory disease	-Usual doses acceptable -Consider antihistamines	-Note that stress can trigger asthma attacks
Epilepsy	-Usual doses acceptable, but may have a reduced effect	-Some anti-epileptics are hepatic enzyme inducers
Acute narrow (closed) angle glaucoma	-Avoid in patient experiencing ACAG (fortunately, they will rarely go to the dental clinic if they have this) -Caution in patients with Hx of ACAG **If pt doesn't know what kind of glaucoma they have:** -"Taking eyedrops" → open angle -"Needing lasers" → closed angle	-Symptoms of closed angle glaucoma: pain, blurred vision, nausea, vomiting, possible loss of vision -Closed angle refers to the angle between the iris and the cornea -When the iris is close to the cornea, it blocks a drainage spot for the fluid in the eye -Blocking the drainage spot means pressure in the eye accumulates and can cause problems -BDZ's have an anticholinergic effect → pupils dilate → angle closes even more → worsens condition
Obstructive sleep apnea	-Contraindicated	-BDZ will reduce muscle tone → obstruction of airway -May be obstructed even with jaw thrust

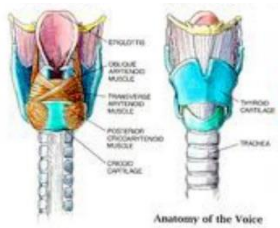
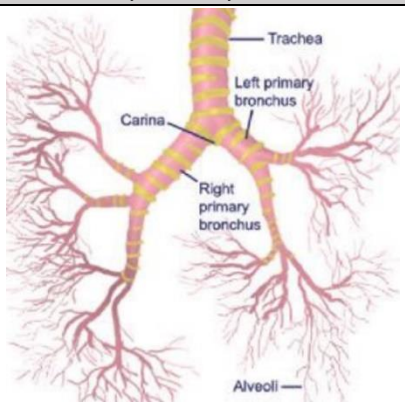
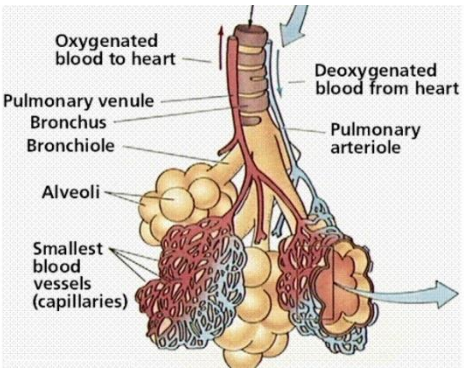
- Inform patients to avoid taking food before the appointment
    - This is because oral dosing is much more predictable on an empty stomach
    - If you were putting the patient in deep sedation, you also want to avoid food because any regurgitation could cause aspiration pneumatitis (however, unlikely with oral BDZ)
- Benzodiazepine interactions (don't need to know)
    - Pharmacodynamic interactions: ethanol and other CNS depressants can increase sedative effect
    - Pharmacokinetic interactions: CYP3A4 drugs can affect levels of midazolam, triazolam, and diazepam
        - 3A4 inducers (↓ [BDZ]): antiepileptics, corticosteroids, rifampin, rifabutin
        - 3A4 inhibitors (↑ [BDZ]): grapefruits, cimetidine, quinine, cyclosporine, antiretrovirals, macrolides, norfloxacin, cardiovascular medications
- Titration of oral sedatives
    - The long onset time of oral administration makes titration slower and more unpredictable
    - In the scope of dental practice, titrating doses should be done per appointment, not within an appointment
    - Appointment #1: administer <u>lowest</u> effective dose and assess response. Don't give any more
    - Appointment #2: give a higher or lower dose, based on previous response
- Agents to use in the dental setting
    - Short~medium length appointment (1~4h): midazolam, triazolam
    - Long appointment (4~6h): lorazepam, diazepam
    - Appt length should be based on drug of choice and med Hx, <u>not based on how much dentistry needs to be done</u>
- Adult oral sedation scenario

Pre-op preparation	**Patient education** -"Sleeping pill" will make patient extremely comfortable, but will not make patient pass out -Not to be confused with general anesthesia, which will put you fully asleep -Patient may fall in/out of asleep, but would wake up if their name was called -Tell patient to take it 1 hour before the appointment, so it reaches an effective dose -Tell patient not to eat before the appointment and taking the drug **Dosing cautions** -"Go low, start slow" – start with the lowest dose and least invasive procedures on first visit -Make sure patient will have someone else drive them home and monitor them the rest of the day
Day of appointment	**Pre-sedation checklist (ROADS)** -R: reversal agent (flumazenil) ready on the counter with a needle and syringe -O: oxygen tank -A: ambubag capable of delivering positive pressure -D: drugs (check medical emergency drugs) -S: suction ready **Example of timing (assuming 9am start)** -8:00 → patient shows up 1 hour prior to appointment <u>with someone else to take them home</u> -8:05 → bring patient to operatory, review med Hx, check NPO status, and sign informed consent -8:05 → the <u>dentist</u> administers 0.25mg triazolam sublingually (SL faster onset, higher peak) -8:50 → check on patient to see how they are feeling -9:00~9:15 → good time to begin treatment. Give topical LA, then injectable LA. Ensure LA is profound -11:30~12:00 → treatment is complete and triazolam begins to wear off -Since the patient is unstimulated, they could fall into a deeper level of sedation -If the patient is capable of sitting and being awake while unstimulated, they can be released -If the patient continues to doze off, then keep patient in chair and wait -Have a staff member walk the patient to their car -11:30~12:00 → treatment is <u>not complete</u> and triazolam begins to wear off -Nitrous oxide and oxygen can be given to titrating effect
Things to keep in mind	-Minimal sedation pts don't need constant monitoring, but always have a female staff member with you -This is due to accusations of inappropriate misconduct while the patient is sedated -Tell all staff to be empathetic to the patient so they feel like they are in a comfortable environment -The goal should be minimal sedation: the patient should be responsive to you calling their name -If the patient enters deep sedation -Maintain airway/breathing/circulation and monitor vitals -Cannot continue doing dentistry as this is not what we are licensed for -Rescue from moderate sedation is far easier than rescue from deep sedation -If using nitrous + oxygen + BDZ combo, then turn off the nitrous

- Oral sedation success
    - Success rate: adults > older children > younger children
    - Size of the patient doesn't fully determine how they will respond to a dose
    - Anxiety level has a greater effect than weight or dose, and counteract the sedative effect of the BDZ
    - Social history can also play a role (smoking, drinking, on other medications)
    - If 0.25mg of triazolam was not enough the first appointment, the next appointment can be 0.375mg
    - Success rate is about 70~85% with a moderate level of anxiety
    - Follow up next day to see if patient was happy with level of sedation achieved
- Patients with cardiac disease
    - Limit the length of the dental appointment to multiple short appointments, not one all day appointment
    - Do not let the dentistry dictate the length of the appointment
    - Anxiety may raise the patient's blood pressure on day of the appointment

Respiratory physiology

- Airway anatomy

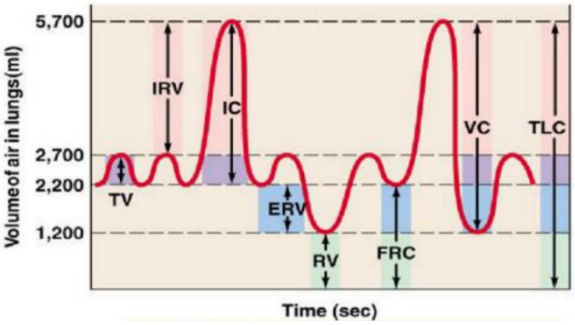
Larynx	Trachea, bronchi, bronchioles	Alveoli
		
-C4 to C6 -Main components are: thyroid and cricoid cartilages, arytenoid cartilages, and the epiglottis	-There are 23 airway divisions between trachea and alveoli -Trachea: below the cricoid cartilage to the carina -Bronchi: below the carina -Trachea and bronchi are supported by C shaped rings of cartilage -Trachealis muscle runs vertically on the posterior surface of the trachea	-End of the airway pathway -Where gas exchange happens **Dual blood supply** -<u>Pulmonary circulation</u>: facilitates gas exchange in the alveoli -<u>Bronchial circulation</u>: supplies gas exchange to the lung parenchyma itself -Blood from bronchial circulation drains to left atrium via pulmonary veins

- Mechanism of respiration
    - **Inspiration muscles**: diaphragm (major), SCM (accessory), scalenus (accessory)
        - Diaphragm is innervated by the phrenic nerve (C3~C5) and contracts downwards, expanding the lung
    - **Expiration muscles**: internal intercostal muscles, abdominal muscles
        - Expiration is usually passive, but muscles are used for forced expiration
    - **Central chemoreceptors**: area in the medulla that detects [H] in CSF
        - CO_2 in blood crosses the blood brain barrier and changes [H] which is then detected
    - **Peripheral chemoreceptors**: area in the carotid that detects [O_2]
        - Not influential in normal circumstances
        - Kicks in when there is profound hypoxia (<60mmHg) and forces breathing
        - If $PaCO_2$ is chronically high (seen in some diseases), then the CO_2 response in the brain becomes impaired, and breathing becomes reliant on the peripheral chemoreceptors
- Lung anatomy
    - <u>Right lung</u>: upper, middle, and lower lobes
    - <u>Left lung</u>: upper and lower lobes
    - Bronchi of the right lung is more vertical, which is where a tube is likely to get stuck if pushed too far
    - 50~100 m^2 of surface area for gas exchange

- Lung physiology terms

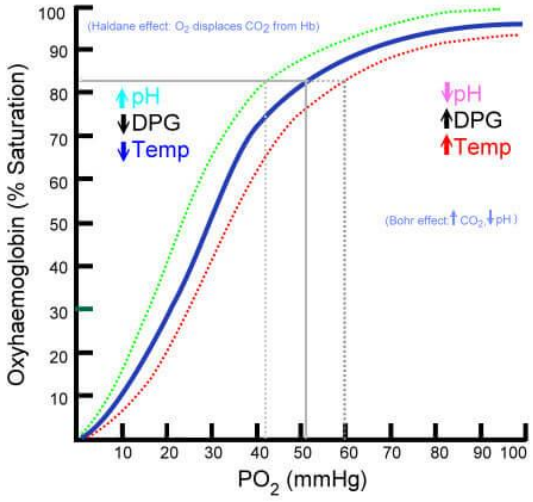
V	-Ventilation of air
Q	-Perfusion of blood
Anatomic dead space	-Air enters airway, but not to the areas where gas exchange occurs
Alveolar/physiologic dead space	-Air enters alveoli, but no gas exchange happens (Q ≈ 0)
Shunt	-Blood is flowing, but there is no air (V ≈ 0) -Seen in atelectasis (collapsed alveoli) or pneumonia
Minute ventilation	-Amount of air moved in or out of the lungs per minute -Minute ventilation = alveolar ventilation + dead space ventilation
Alveolar ventilation	-Volume of air that reaches the alveoli and exchanges gas every minute
Dead space ventilation	-Volume of air that is inspired but does not exchange gas every minute

- Lung volumes

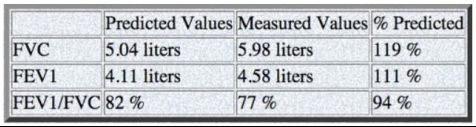
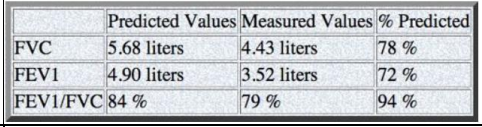
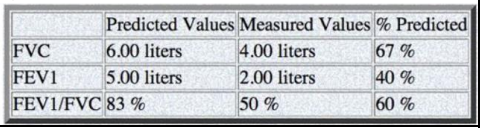


TV = Tidal volume (500 ml)
IRV = Inspiratory reserve volume (3,000 ml)
IC = Inspiratory capacity (3,500 ml)
ERV = Expiratory reserve volume (1,000 ml)
RV = Residual volume (1,200 ml)
FRC = Functional residual capacity (2,200 ml)
VC = Vital capacity (4,500 ml)
TLC = Total lung capacity (5,700 ml)

- Oxy-hemoglobin dissociation curve
  - There is about 100 mmHg PO_2 in the blood, which means blood is almost 100% saturated with oxygen
  - **Oxygen transport**: 97% in RBC, 3% dissolved
  - **CO_2 transport**: 23% RBC, 7% dissolved, 70% in HCO_3^-
  - Haldane effect
    - When the body is hypoxic, hemoglobin has the ability to carry more CO_2, as the hemoglobin binding sites are not occupied by O_2



- Pulse oximeters
  - Placed on patient's finger and reads % of oxyhemoglobin
  - Should be close to or at 100%
  - However, there is a 30 second delay
  - If the patient is visibly struggling to breathe or is obstructed, the 100% will drop quickly after some delay
- Pulmonary function tests
  - There are a set of predicted values
    - Normal PFT: >85% of predicted values
    - Mild disease: 65~85%
    - Moderate disease: 50~65%
    - Severe disease: <50%
  - Interpreting PFT's
    - First, look at FVC (forced vital capacity) and FEV1 (forced expiratory volume in 1 second)
    - If FVC and FEV1 are normal, patient is normal
    - If FVC and/or FEV1 are low, then there is disease. If this is the case, go to the % predicted for FEV1/FVC
      - If % predicted for FEV1/FVC is >88%, then the patient has a <u>restrictive lung disease</u>
      - If % predicted for FEV1/FVC is <69%, then the patient has an <u>obstructive lung disease</u>

Normal	Restrictive	Obstructive
		
FVC and FEV1 are normal	FVC and FEV1 are low FEV1/FVC is normal	FVC and FEV1 are low FEV1/FVC is low

- Lung diseases

<table>
<tr><th colspan="2">Obstructive</th><th colspan="2">Restrictive</th></tr>
<tr><td colspan="2">-Difficult to get air out of lungs</td><td colspan="2">-Difficult to get air into lungs</td></tr>
<tr><td colspan="2">-Chronic obstructive pulmonary disorder (COPD)
-COPD is further classified into 2 etiologies: chronic bronchitis and emphysema
-Heavy productive, persistent cough for at least 3 months in 2 consecutive years</td><td colspan="2">-Further divided into intrinsic and extrinsic diseases
-Incomplete lung expansion, increased stiffness, and general difficulty getting air into lungs
-Reduced inspiratory reserve volume, total lung capacity, and vital capacity</td></tr>
<tr><td>Chronic bronchitis (blue bloaters)
-Chronic exposure to irritants like smoking
-Inflammation, hypersecretion, and <u>enlargement</u> of bronchi
-Body responds by ↓ ventilation (V), ↑ cardiac output (Q) → V/Q mismatch
-<u>Oxygen</u>: hypoxemia and polycythemia (body trying to get more oxygen by ↑ Hgb) → patient appears blue-ish
-<u>CO_2:</u> hypercapnia and respiratory acidosis
-Right heart pushes against a constricted pulmonary artery → right heart can fail due to stress (cor pulmonale)
-Generalized edema and cyanosis → blue bloater</td><td>Emphysema (pink puffers)
-Chronic exposure to irritants like smoking or coal
-Destruction of alveoli: many small sacs become few big sacs due to enzyme mediated destruction
-Sacs lose their recoil and become stiff
-Weakens expiration, lung always remains partially expanded and traps stagnant air
-“Barrel chest” appearance
-Destruction of alveoli and capillaries → ↓ oxygenation of blood
-Body compensates by ↓ cardiac output and hyperventilation
-V/Q mismatch → low perfusion in a well ventilated lung
-Tissue hypoxia, muscle wasting, weight loss</td><td>Intrinsic lung disease
-Inflammation, scarring of lung tissue, or filling of air spaces with exudate/debris
-Includes idiopathic fibrotic diseases, CT diseases, drug induced lung disease, and primary lung diseases
<u>Examples:</u>
-Sarcoidosis
-Tuberculosis
-Pneumonectomy (loss of a lung)
-Pneumonia</td><td>Extrinsic lung disease
-Disease affecting chest wall, pleura, or respiratory muscles
<u>Examples:</u>
-Scoliosis, kyphosis
-Ankylosing spondylitis
-Pleural effusion
-Pregnancy
-Gross obesity
-Tumors
-Ascites
-Pain on inspiration (pleurisy, rib fractures)</td></tr>
</table>

Nitrous oxide and oxygen

- Oxygen
  - Non flammable gas which is involved in combustion (one of the 3 requirements for fire: air, heat, fuel)
  - 21% of room air
  - Too much oxygen can lead to pulmonary fibrosis (restrictive disease) or retinopathy of prematurity
- Nitrous oxide
  - Colourless, non flammable gas with a sweet odour and taste
  - Made by heating ammonium nitrate (NH_4NO_3 → $2H_2O + N_2O$)
  - Accounts for 6% of greenhouse gases (30% of which are from humans, 70% from oceans and soil)
- Nitrous oxide in the scope of medicine
  - Non selective depressant of the CNS (like all other inhalational GA’s, hypnotics, and ethyl alcohol)
  - Nitrous oxide is the “wimp” of general anesthetics
  - Minimum alveolar concentration (% needed to inhibit movement to a painful stimulus in 50% of patients)
    - Sevoflurane (general anesthetic) = 2%
    - Nitrous oxide = 104% → basically impossible in 50% of people
  - Blood-gas partition coefficient (how soluble it is in blood)
    - Sevoflurane = 0.65
    - Nitrous oxide = 0.47 → barely soluble → rapid induction, but also rapid elimination
  - Metabolism: undergoes reductive metabolism in the GI tract to an extent of 0.004%
  - Reduces pain (anti-nociceptive) and reduces anxiety (anxiolytic)
  - No maximum dose has been determined yet

- Mechanism of action
    - The specific mechanism of losing sensation and consciousness is not known
    - May interfere with physiological functioning of nerve cells via an action at the lipid matrix of the membrane
    - Opioid hypothesis
        - Naloxone, an opioid antagonist, blocks the analgesic effect of nitrous
        - There are many subtypes of the opioid receptor
        - The specific subtype that nitrous is involved with depends on stimulus, species, and area of the brain
    - BDZ/GABA receptor hypothesis
        - Flumazenil, a BDZ antagonist, blocks the anxiolytic effects of nitrous
        - Those tolerant to BDZ's are also tolerant to the anxiolytic effects of nitrous
    - NMDA hypothesis
        - Nitrous is thought to block NMDA channel activation non-competitively
        - Inhibition of an excitatory neurotransmitting pathway
        - Similar to ketamine (dissociative anesthetic, giving an "out of body" experience)
- Adverse effects
    - High concentration and greater duration of use → ↑ nausea + vomiting
    - Psychomotor performance
        - Worry was that long term nitrous exposure would affect psychomotor, perceptual, and cognitive function
        - Study found >50 ppm for >2 hours leads to ↓ audiovisual performance
        - Although this study was biased and has not been reproduced, 25ppm is now the maximum in the workplace
    - Biochemical disturbance and its implications on reproduction
        - Mechanism
            - Homocysteine → methionine is performed by methionine synthase and Vit B12 as a co-factor
            - Nitrous oxidizes cobalt in Vit B12 → Vit B12 inactivates → cannot be used as a co-factor
            - Homocysteine accumulates as methionine cannot be made
            - Affects DNA synthesis, which is bad in pregnancy
            - Populations particularly susceptible are: vit B12 deficient patients and pernicious anemia patients
        - Real life studies
            - Affects reproduction if concentration is high and exposure is prolonged (>24h)
            - **Study 1**: link found between reproductive toxicity in CDA's to nitrous exposure of more than 3~5 hours per week in offices without scavenging
                - Scavenging: leftover nitrous gas that was not inhaled by the patient is suctioned away
                - This link was NOT found in offices that used scavenging
            - **Study 2**: found chronic exposure to 1800 ppm did not exert any detectable effect in humans, so 400 ppm was set as an arbitrary value, far below the biologic threshold
            - **Study 3**: No link between operating room (exposed to anesthetic gases) and miscarriage/congenital malformation
            - **Study 4**: no controlled prospective study has found evidence for reduced fertility
        - Conclusion/take home messages
            - Clinical use of nitrous in pregnancy = <u>no increased risk to fetus</u> over other pain control methods
            - Reproductive health = <u>no causal relationship</u> in scavenged low levels of nitrous
    - Sensory neuropathy
        - Seen in chronic use/abuse
- Exposure levels
    - Minimum threshold to see biologic effects: <u>100ppm average over 8h</u> or <u>400ppm average over 1 appointment</u>
    - Use of a scavenging system can reduce nitrous to 50ppm
    - Patient <u>talking and mouth breathing</u> are the most common sources of nitrous contamination
    - Infrared analyzer can be used to detect [N_2O] in the office from 1 to 2000 ppm

- Contraindications to use
    - Uncooperative patients (cognitive impairment, claustrophobic)
    - Nasopharyngeal obstruction (like obstructive sleep apnea)
    - Conditions with closed tissue spaces
    - Vitreoretinal surgery within 3 months
    - Recent bleomycin chemotherapy within the past year
- ENIGMA trial studies
    - ENIGMA 1
        - [70% N_2O + 30% O_2] vs [20% N_2 + 80% O_2] in 2050 randomized patients
        - Looked at incidence of MI and death within 30 days
        - 3.5 years later, found that N_2O did not increase risk of death
        - However, found hyperhomocysteinemia in large proportion of patients with MI
        - Suggested that high [homocysteine] is atherogenic and thrombogenic
        - Problems: patient selection wasn't directed at CV events, O_2 concentrations varied widely, and followup was 3.5 years (too long)
        - **Conclusion: N_2O did not increase risk of death**
    - ENIGMA 2
        - [70% N_2O + 30% O_2] vs [70% N_2 + 30% O_2] in 7112 randomized patients at risk of perioperative CV events
        - Looked at 30 day incidence of major CV event or 1 year secondary outcome (death, disability, MI, etc)
        - **Conclusion: N_2O did not increase the risk of death, disability, MI, or stroke**

Nitrous equipment

- Pathway from compressed cylinder to patient
    - Cylinder → yoke → reducing valve → flowmeter → reservoir bag → tubing → nasal hood/cannula/mask
- Which components are under pressure?
    - High pressure: gas cylinders, yoke, and the reducing valve
    - Low pressure: reducing valve, flowmeters, reservoir bag, and nasal hood
- Gas cylinders

Colour	-Nitrous oxide containers are blue -Oxygen containers are white (green in US)
Size	-Size E (portable): 4.5 x 29.5 inches, 21lbs -Size H (large storage): 9.0 x 55 inches, 130 lbs -Size G (large storage): 8.5 x 55 inches, 130 lbs
Storage of gas	-Amount of oxygen stored is linear with pressure (if you double amount of O_2, the pressure doubles) -Amount of NO_2 stored is not linear because it turns into a liquid under pressure. If you reach a certain pressure, adding more N_2O will maintain the same pressure because the excess N_2O will turn into liquid

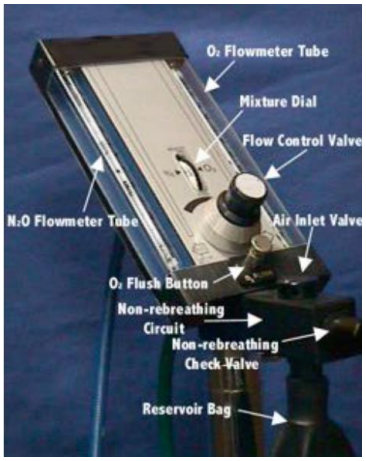
	O_2 in size E	**O_2 in size H**	**N_2O in size E**	**N_2O in size G**
PSI @ full	2000	2200	800	800
PSI @ ½	1000	1100	800	800
Capacity	660L	6909L	1590L	13839L
State	Gas	Gas	Gas/liquid	Gas/liquid

-In practice, we use size E's. As seen in the table, O_2 tanks only have a 660L capacity whereas N_2O tanks have a 1590L capacity (since liquid storage is possible)
-You will be changing O_2 tanks far more frequently than N_2O tanks
-N_2O tanks are only replaced when the pressure starts dropping. This indicates there is no more liquid and the tank only has gas left, which will run out soon
-It is OK to run out of N_2O but never OK to run out of O_2
-A nitrous delivery unit has 2 of each tank. Only open <u>one of each at a time</u>

- Yoke
  - Holds cylinders to the unit
  - Each yoke has holes and pins oriented such that the wrong gas can't be attached to the wrong yoke
  - Minimum of 2 O_2 cylinders and 1 N_2O cylinder

- Reducing valves (AKA regulators)
  - Lowers pressure of gas to 50 PSI, but also generates tremendous heat in the process
  - If the cylinders are opened rapidly, the regulator can reach 1500~2000F
  - Never grease connections/valves on the nitrous delivery unit, as this high temp can ignite the oil and start a fire
  - Also, always open a tank slowly

- Flowmeters
  - Overall purpose: allows precise delivery of gases
    - Measured in litres per minute
    - 3 types: rotameter, ball, and rod
    - Stay away from electronic ones because they can fail
  - Sub-components in a flowmeter
    - **Non-rebreathing check valve**: makes sure air only goes one way, so you don't need to sterilize the reservoir bag
    - **Flush button:** flushes oxygen through reservoir bag
    - **Air inlet valve:** emergency air vent if the patient is trying to breathe but the reservoir bag is empty. This is closed when gas flows
    - **Flow control:** controls the overall flow (nitrous + O_2)
    - **Flowmeter tubes:** the actual component that shows the flow rate of O_2 (right) and N_2O (left)



- Reservoir bag
  - The gas cylinder releases a <u>constant</u> flow of gas (we set it to 6L/min, or 100mL/sec)
  - The patient consumes 6L/min, but it is <u>not constant</u>. The patient takes ~500mL breaths every few seconds
  - This means that during a 1 second breath, they will only breathe in 100mL of the gas from the cylinders and the other 400mL will be just room air → dilutes the nitrous
  - Therefore, a reservoir bag is used to accumulate the gas before the patient breathes it in
  - This way, all 500mL of inspired air is from the bag and none from room air
  - Adult reservoir bags at 5L, pediatric bags are 3L
  - Also has a secondary function of being able to monitor the patient's respiration (watching bag deflate/inflate)

- Conducting tube
  - **Thick black ribbed tube** (͡° ͜ʖ ͡°): carries the mixed N_2O and O_2 from the reservoir bag to the patient
  - Cannot be obstructed
- Delivery method to patient

	Advantages	Disadvantages
Full face mask	-Patient can breathe through mouth and nose -Important in emergency care	-Impractical in dentistry
Nasal cannula	-Good for claustrophobic patients	-Leakage -Requires ↑ N_2O rate and % (no reservoir bag)
Scavenging nasal hood	-Delivers fresh gas with no room air mixing in -Exhaled gases are scavenged away	

- Safety features
  - **Pin index safety system:** nitrogen and oxygen cylinders will not attach to the wrong yoke due to pin patterns
  - **Diameter index safety system:** nitrogen and oxygen tubing diameters are different, can't plug in wrong way
  - **Minimum oxygen flow/percentage, oxygen fail safe:** decline in O_2 pressure will cause nitrous pressure to lower as well, so you can never deliver 100% nitrous to a patient unknowingly
    - Activates when oxygen is at 30% capacity
    - If oxygen goes down while nitrous goes up, then it is not working. Discard that machine
  - **Others:** emergency air inlet, oxygen flush button, reservoir bag, colour coding

Nitrous delivery

- Signs and symptoms

Early sedation ~ ideal sedation	Deeper sedation ~ mild oversedation	Oversedation
-Lightheadedness -Tingling, numbness of hand and feet -Wave of warmth -Feeling of vibration throughout body -Euphoria -Lightheadedness or heaviness of extremities	-Hearing, especially distant sounds, more acute -Visual images become confused -Sleepiness -Diaphoresis -Dreaming -Laughing, crying -Nausea -Increased movement -Increased ventilation	-Nausea/vomiting -Lack of responsiveness/unconsciousness -Laughing, crying, becoming giddy -Persistent closing of mouth -Spontaneous mouth breathing -Patient says effects are too intense -Fails to respond rationally or responds sluggishly -Patient states they are about to fall asleep -Incoherent speech and movement

- Oversedation
    - When a patient is overdosing, don't raise them up. Raising them up could cause their head to suddenly lower, cause obstruction, and death
    - 3 ways to treat oversedation
        - Taper down: decrease N_2O by 0.5~1.0 L/min and increase O_2 by corresponding amount
        - Give O_2: shut off N_2O and give 100% O_2 to full 6L/min for 3~5 minutes or longer PRN
        - Give room air: remove nasal hood and give room air
    - Oversedation is more likely to occur during lulls in treatment when there is no verbal/visual/physical stimulation
    - Observe the patient and inhalation unit during the procedure
- Diffusion hypoxia
    - N_2O discontinued → cleared form alveoli, but still some remaining in alveoli → nitrous diffuses into alveoli → displaces oxygen in the alveoli → breathing room air can cause alveolar hypoxia, so patient must be given 100% O_2 immediately after nitrous procedure
    - **This belief is not true – it is theoretical, and not a real thing**
    - The reason 100% O_2 is recommended it because we don't want the patient exhaling nitrous and contaminating the operator's air space. Keeping the nasal hood on will scavenge the remaining nitrous in the patient's blood
- Complications
    - Excessive perspiration
    - Behavioural problems: claustrophobia, vivid dreaming, talkativeness
    - Shivering
        - Body trying to warm itself after all the heat loss from vasodilation
        - Reassure patient and give blankets
    - Nausea
        - Could be due to depth/length of sedation, patient's emotional status, inherent tendency to become nauseated, or presence of food in stomach
        - Decrease N_2O by 5~10%
    - Vomiting
        - Immediately turn off N_2O and give 100% O_2
        - If vomiting begins, remove nasal hood and rubber dam if present
        - Turn patient's head to side and suction airway
        - After incident, replace nasal hood and administer 100% O_2
- Criteria for discharge
    - Patient responsive
    - Vitals stable (BP, HR, RR)
- Record keeping
    - Vital signs (baseline before nitrous, and recovery before discharge)
    - "Nitrous oxide/Oygen was titrated to effect. Patient received _____ % N2O and ____% O2 at a total liter flow of _____ lpm. The procedure lasted approximately ____ minutes. At the termination of the procedure the patient received 100% O2 for _____ minutes at a flow of _____ lpm. The patient tolerated the procedure well and was dismissed from the office in good condition."

- Cleaning nasal hood
  - Wash with soap+water → place in glutaraldehyde for 10 mins → rinse in tap water → hang to dry → gas sterilize
- Repeated appointments
  - Always titrate up to a working dose, never go straight into the last appointment's working dose
  - For example, if a patient was comfortable at 30% nitrous, don't start at 30% the next appointment. Titrate up to it
- N_2O exposure to the operator
  - N_2O can leak out in many places
    - **From the patient**: mouth breathing, talking, laughing, around the mask
    - **From a high pressure source**: worn wall connecters, loose/cracked hose connections
    - **From a low pressure source**: loose/defective gaskets and seals, worn bags/tubes, loosely assembled joints/connections
  - Eliminating N_2O
    - Test equipment for leaks, vent waste gases, scavenging nasal hoods, minimize patient talking, monitor air
    - Check rubber goods daily
    - Check hard connections monthly
    - Measure ambient N_2O (IR analyzer method) quarterly
- Sexual phenomenon with N_2O
  - 105 cases of sexual accusations with inhalation sedation
  - All complaints were towards male doctors from female patients
  - No patient discussed the experience with the doctor after recovery, but commented later about how shocked or stunned they were
  - Several were unable to think clearly until the next day
  - No patient gave indication of distress during treatment
  - Male doctors were alone with the female patient in these cases
  - Vast majority of these cases had >50% concentrations of N_2O
  - Never sedate any patient (inhalational, IV, oral) without an assistant present in the room
- Nitrous sedation scenario

Prior to administration	-Have patient visit restroom -Review medical history and take vital baseline -Place patient into supine position and bring the inhalation sedation unit -Giving the patient realistic expectations of N_2O is a huge part of success – tell them it will only take the edge off, not cause complete sedation
Administering N_2O	-Reservoir bag should be partially inflated, not empty or overfilled -When checking to see if patient is properly sedated, don't ask them if they feel tingling (or any specific symptom) -This is because they patient may never feel that symptoms, despite being oversedated -Rather, tell the patient to describe their symptoms to you **Technique 1 (titrate by volume)** -Establish 5~6 L/min O_2 flow -Place the nasal hood on the patient -Determine if 5~6L/min flow is adequate -Patients will often say it is not enough, but have them relax and get used to it -Increase N_2O by 1L/min while decreasing O_2 by 1L/min -Determine CNS response 1 minute later -Increase N_2O by 0.5 and decrease O_2 by 0.5 repeatedly until level of sedation reached **Technique 2 (titrate by percentage)** -% N_2O = [L/min of N_2O] / [L/min of N_2O + L/min of O_2] -Follow steps in technique 1 -Titrate N_2O from 0% → 10% → 15% → 20%... etc
End of dental treatment	-Permit patient to inhale 100% O_2 for 3~5 minutes -Determine level of recovery prior to dismissal

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

- Converting PSI on gas cylinder to remaining time
  - Assume 6L/min flow → 360L of gas used in 1 hour
  - E sized O_2 gas cylinder has a 660L capacity at 2000 PSI
  - So, 2000 PSI will last almost 2 hours and 1000 PSI will last about 1 hour