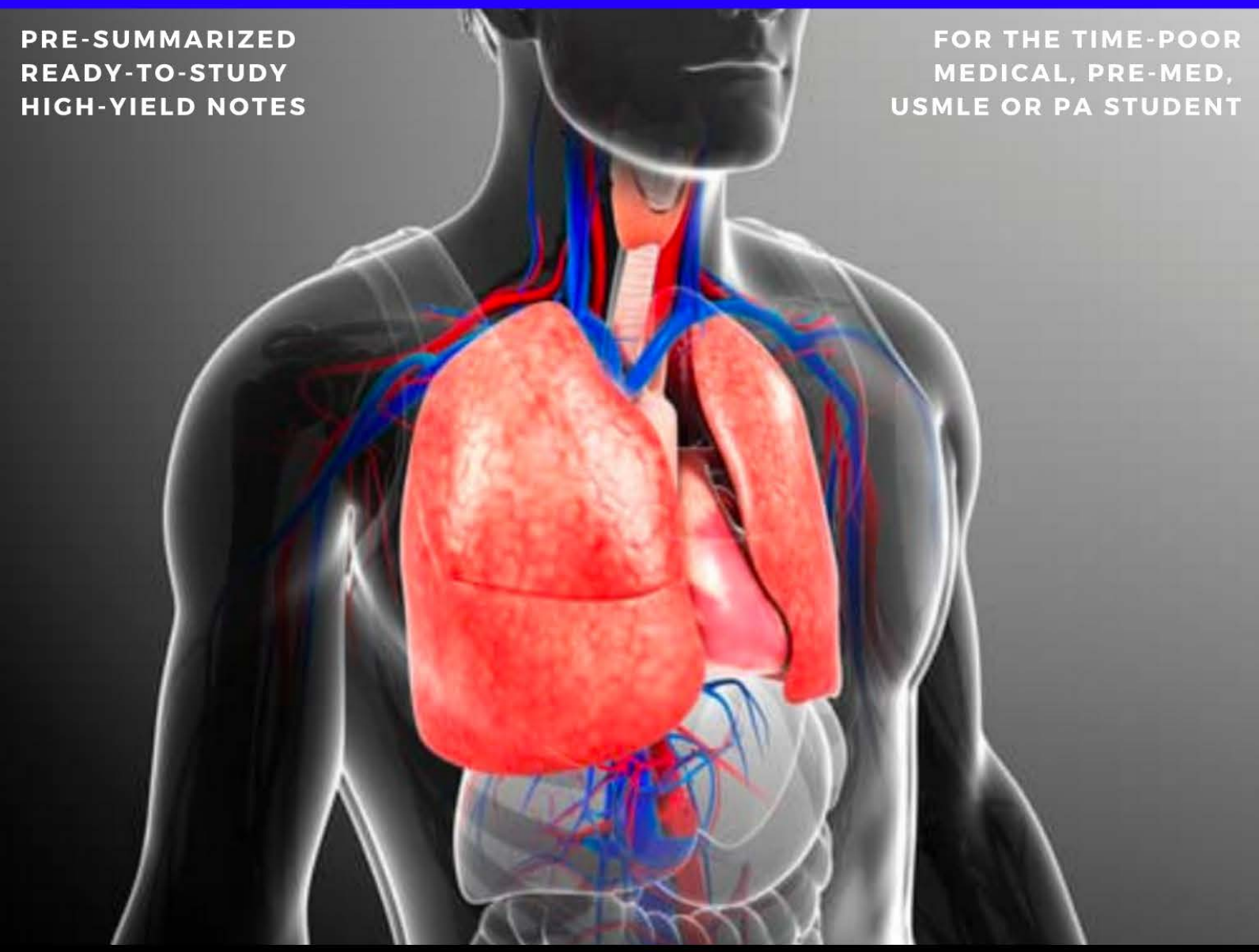
ANATOMY, PHYSIOLOGY & PATHOLOGY NOTES OF THE

RESPIRATORY SYSTEM

PRE-SUMMARIZED
READY-TO-STUDY
HIGH-YIELD NOTES

FOR THE TIME-POOR
MEDICAL, PRE-MED,
USMLE OR PA STUDENT



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What's included: Ready-to-study anatomy, physiology and pathology notes of the respiratory system presented in succinct, intuitive and richly illustrated downloadable PDF documents. Once downloaded, you may choose to either print and bind them, or make annotations digitally on your ipad or tablet PC.

Free Bonus: 'Respirology' and 'Otolaryngology' chapters of Toronto Notes for reference and further detailed reading.

File List:

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- TORONTO - Respiratory
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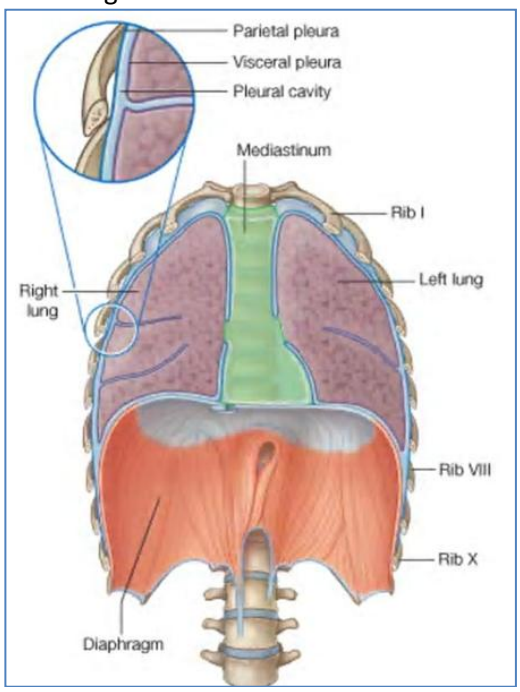
System: Respiratory

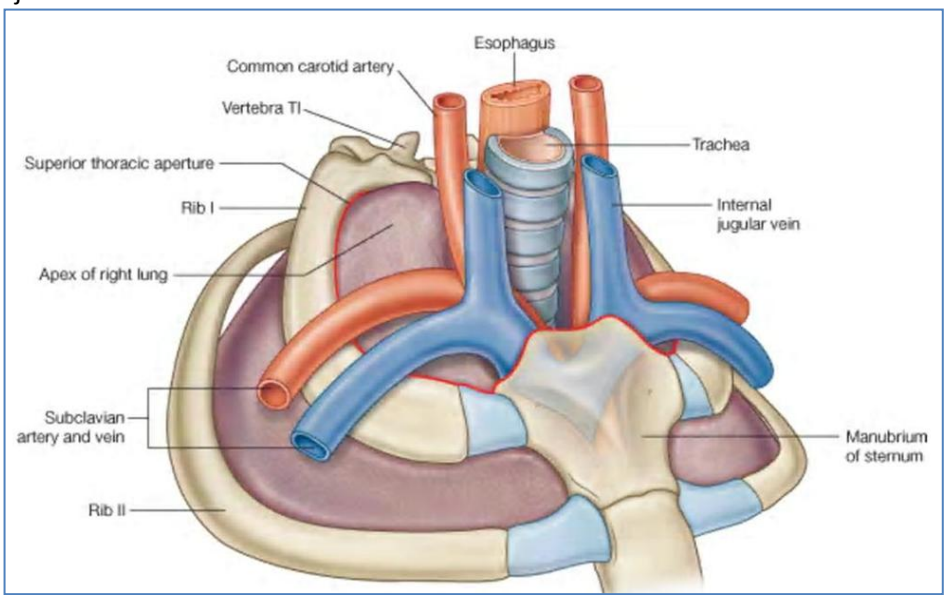
Thoracic Overview:

- **3 Parts:**
  - Thoracic Cage (skeletal components)
  - Thoracic Wall (muscular components)
  - Thoracic Cavity (internal area
- **3 Internal Compartments:**
  - **Central Mediastinum**
    - Containing the Heart/oesophagus/trachea/nerves/vessels
  - **Left Pleural Cavity**
    - Containing the L-Lung
  - **Right Pleural Cavity**
    - Containing the R-Lung

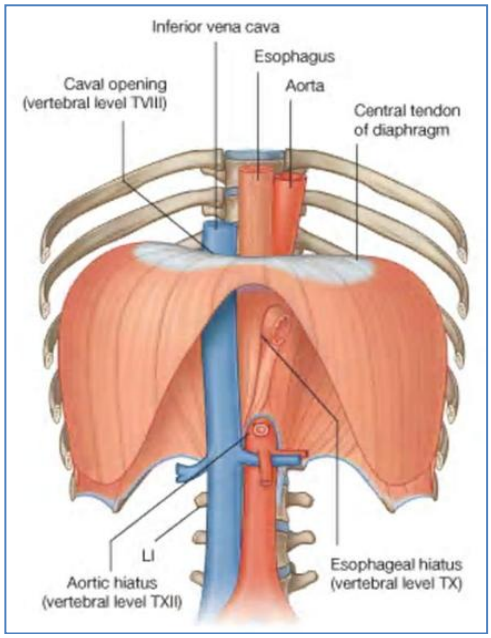


Relationship to Other Regions:

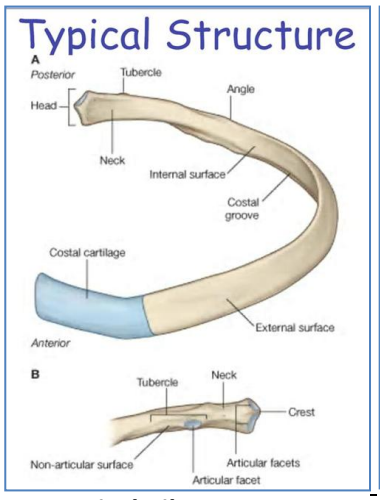
- **Neck:**
  - Trachea
  - Oesophagus
  - Major Nerves & Vessels

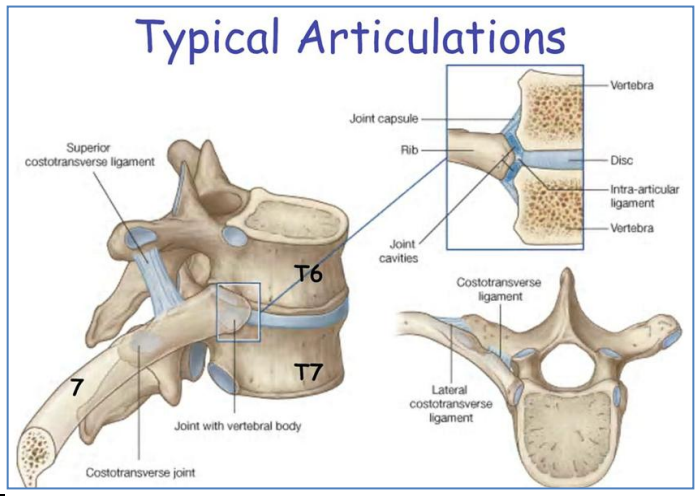


- **Abdomen:**
  - Inferior Vena Cava
  - Oesophagus
  - Aorta



- **12 Pairs of Ribs:**
  - 1-7 = 'True' Ribs (attach directly to sternum)
  - 8-12 = 'False' Ribs (don't attach directly to the sternum)
    - Ribs 11 & 12 are 'Floating' Ribs (insert into abdominal muscles & conn. tissue.
  - **Typical Articulations:**
    - Between **Head & Vertebrae** of the *same number*
    - Between **Head & Vertebrae *above***
    - Between the **Tubercle** & the **Transverse Process** of the **Vertebrae** of the *same number*

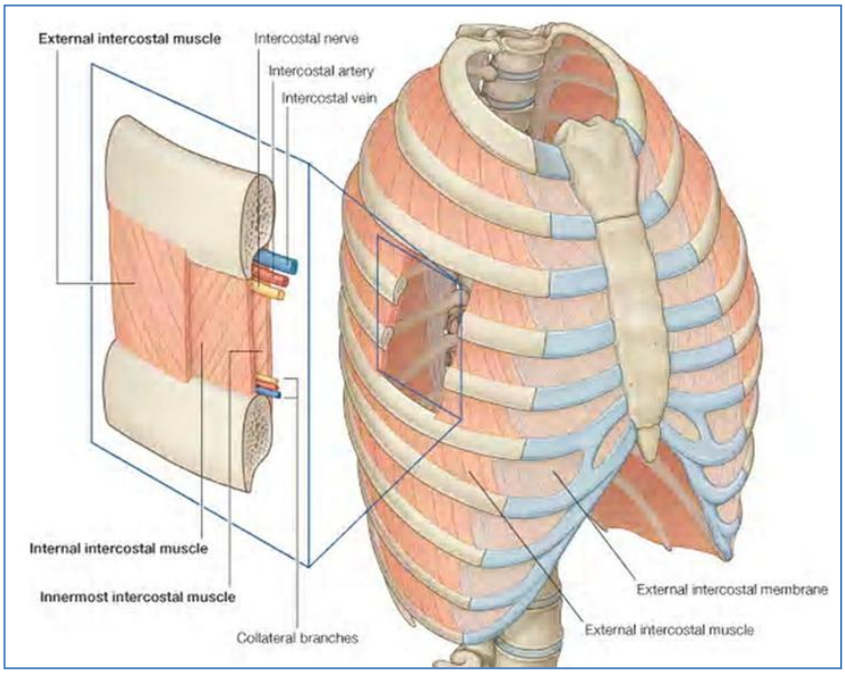




  - **Atypical Ribs:**
    - Ribs 1, 2, 10, 11 & 12.
    - Why?:
      - **Rib 1:**
        - Oriented horizontally (rather than vertically)
      - **Rib 2:**
        - Oriented horizontally (rather than vertically)
      - **Rib 10:**
        - Articulates *only with its own Vertebra* – only has 1 Facet on its head.
      - **Rib 11 & 12:**
        - Articulate *only with their own Vertebra*

Thoracic Wall (Muscular Component):

- **3 Layers:**
  - **External Intercostal Muscle:**
    - Oriented Diagonally Inferio-Anteriorly
  - **Internal Intercostal Muscle:**
    - → Transitions into the Posterior Intercostal *Membrane*
  - **Innermost Intercostal Muscle:**
    - Oriented Diagonally Inferio-Posteriorly



Accessory Muscles Of:

- **Inspiration:**
  - **Scalene Muscles**
  - **Sternocleidomastoid**
  - **External Intercostals**
  - **How:**
    - Pull the Ribs & Sternum *Superiorly* (i.e. Pump & Bucket-handle Movements)
- **Expiration:**
  - ***Abdominal* Wall Muscles**
    - By increasing intra-abdominal pressure (forces diaphragm up)
  - **Internal Intercostals**
    - Pull the Ribs & Sternum *Inferiorly* (i.e. Reverse of Pump & Bucket-Handle Movements)

Primary Muscle: The Diaphragm:

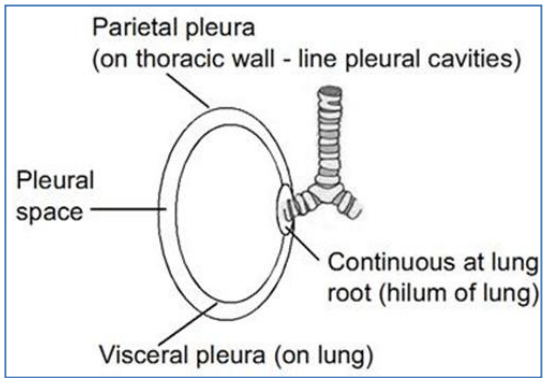
- Divides thorax from abdomen
- Primary muscle of respiration
- Contraction = Flattening (i.e. Downward movement) → Inspiration
- Relaxation = Doming into thoracic cavity (upward movement) → Expiration
- **Nerve Supply:**
  - Phrenic Nerve (C3, 4 & 5)
    - Receives sympathetic fibres from Cervical Ganglia → Voluntary & Autonomic Nerve Supply

Thoracic Movements of Breathing:

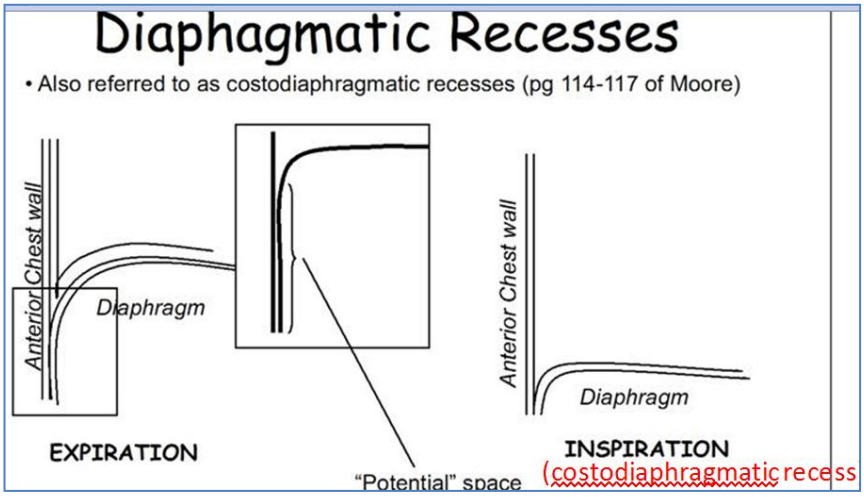
- Due to articulations, 2 groups of ribs create different movements:
  - **Upper 6 Ribs:**
    - *Pump Handle* Action
    - Increases **Anterio-Posterioir Diameter** of Thoracic Cavity
  - **Lower 6 Ribs:**
    - *Bucket Handle* Action
    - Increases the **Transverse Diameter** of Thoracic Cavity

Pleura:

- Each are continuous Serous Sacs
  - Each has a Visceral 'pleura' & A Parietal 'pleura'
  - Between these layers is a 'potential' space aka. The "Pleural Space"
  - This Pleural Space is contains lubricating Serous Fluid
    - Fluid creates surface tension
      - Keeps the lung inflated even during expiration.
      - Keeps the pleurae together.
- Pleurae line the lung & Pulmonary Cavities



- **Costodiaphragmatic Recess:** (or just Diaphragmatic Recess)
  - 'Extra' space allocated to the lungs for use during forced inspiration
  - Allow extra expansion of the lungs



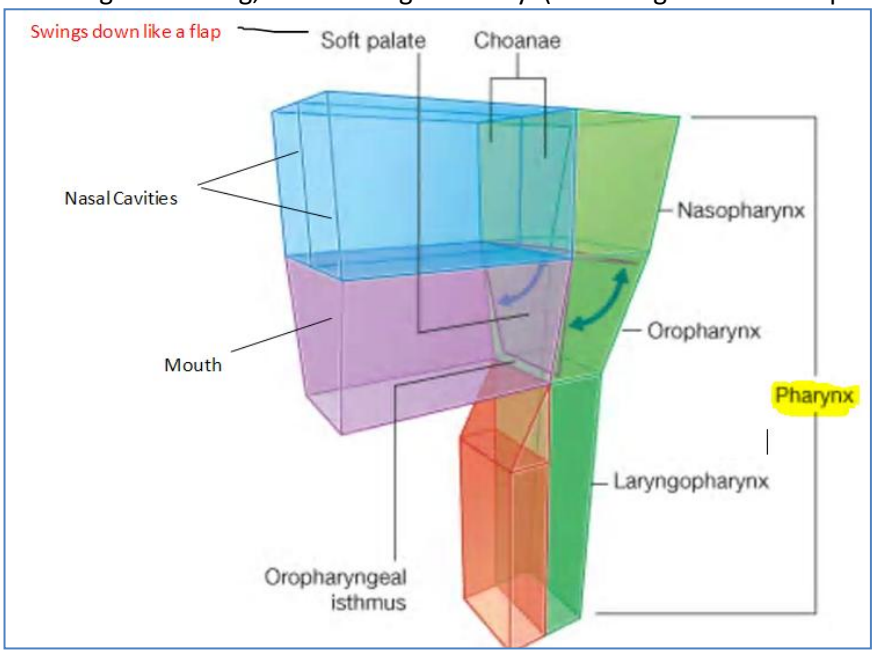
Airways Anatomy

Structural Divisions:

- **Upper Airways:**
  - Aka. 'Conducting' zones: Due to its conduit-like structure
  - Functions:
    - Filter particulate matter from air (debris & dust)
    - Mucosal Epithelium:
      - Warm incoming air
      - Moisten incoming air
  - Nose → Trachea
- **Lower Airways:**
  - Aka. 'Respiratory' zones: Due to site of gas exchange
  - Functions:
    - Facilitate Gas Exchange
    - O_2 in CO_2 out.
  - Bronchi → Lung

The Pharynx:

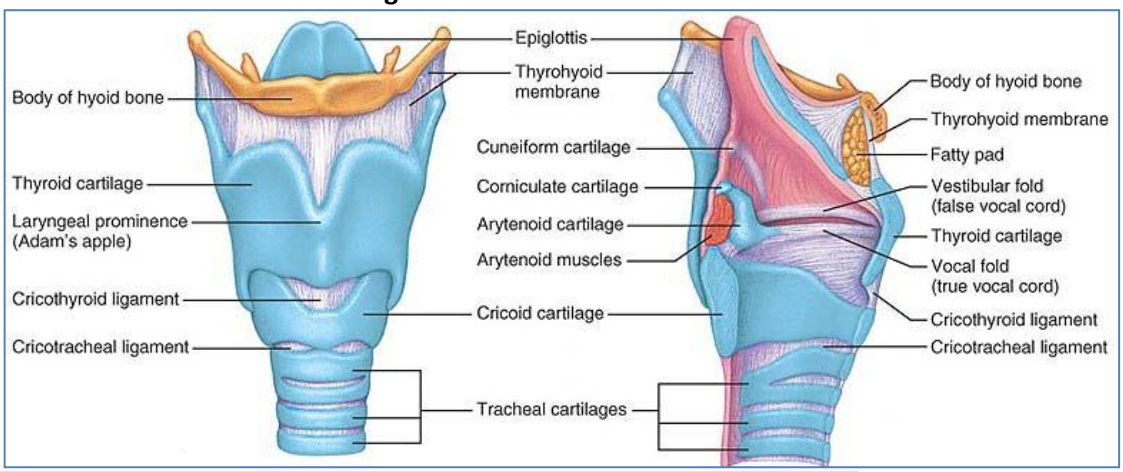
- Connects Nasal Cavities, Oral Cavity & Oesophagus
- **Epithelium of Each Region:**
  - **Nasopharynx:**
    - Air passageway ONLY.
    - *Pseudostratified Ciliated Epithelium*
  - **Oropharynx:**
    - Both Food & Air Pass Through it. → More protection is needed.
    - *Stratified Squamous Epithelium*
  - **Laryngopharynx:**
    - Both Food & Air Pass Through it. → More protection is needed.
    - *Stratified Squamous Epithelium*
    - During swallowing, food has 'right-of-way' (breathing is halted temporarily)



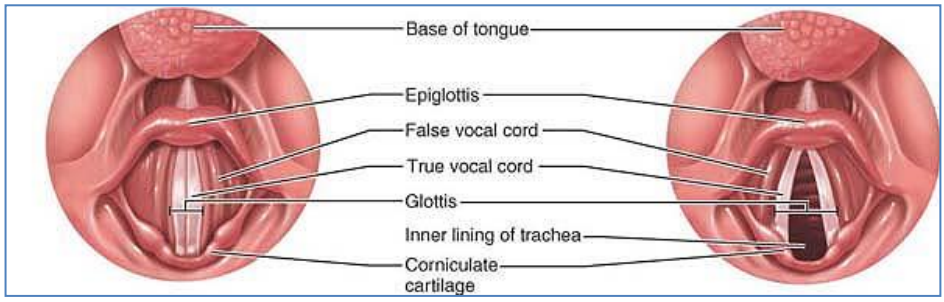
- **2 Muscle Groups: (DON'T NEED TO KNOW NAMES – JUST FUNCTION)**
  - **3x Constrictor Muscles:** (move food down to the *laryngopharynx*)
  - **3x Longitudinal Muscles:** (Elevate the Pharynx – prevent food in trachea)

The Larynx: ("Voicebox")

- Superiorly, it attaches to the Hyoid Bone
- Inferiorly, it merges with the Trachea
- **3 Functions:**
  - Provide an open airway (breathing)
  - Voice production. (Phonation)
- **Made of 9 Cartilages:**
  - **3 Unpaired Cartilages:**
    - Form the Tube-Like Skeletal Framework of Larynx
    - **Thyroid Cartilage**
    - **Cricoid Cartilage**
    - **Epiglottis**
  - **3 Paired Cartilages (6 total):**
    - Involved in moving the Vocal Ligaments (Adduction & Abduction)
    - **Arytenoid Cartilage**
    - **Cuneiform Cartilage**
    - **Corniculate Cartilage**



- **Vocal Ligaments:** '*True* Vocal Cords' ("Cricothyroid Ligament/Membrane")
  - Covered in mucosa
  - Made of Elastic Fibres
  - Fibres vibrate as air rushes up from lungs. (tighter = higher pitch)
  - Appear white – no blood vessels
- **Vestibular Folds:** *'False Vocal Cords'* ("Quadrangular Ligament/Membrane")
  - Play no part in sound production
  - Help to close the 'glottis' when swallowing.

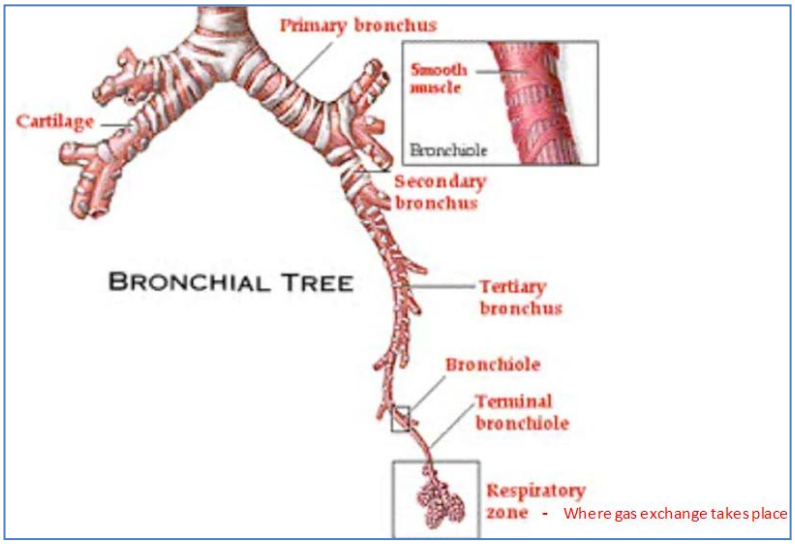


Trachea:

- The continuation of the pharynx
- A membranous tube of Conn. Tissue
  - + smooth muscle
  - Reinforced by 15-20 C-Shaped Cartilage Rings (incomplete posteriorly)
- Begins at C6
- Terminates at Bifurcation → Bronchi @ T4
  - NB. Right Bonchus is more vertical than the Left – hence inhaled objects tend to go down here.

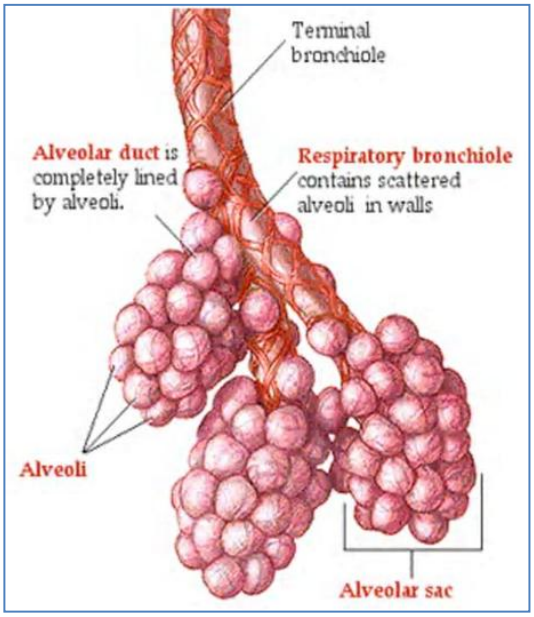
The Bronchial Tree:

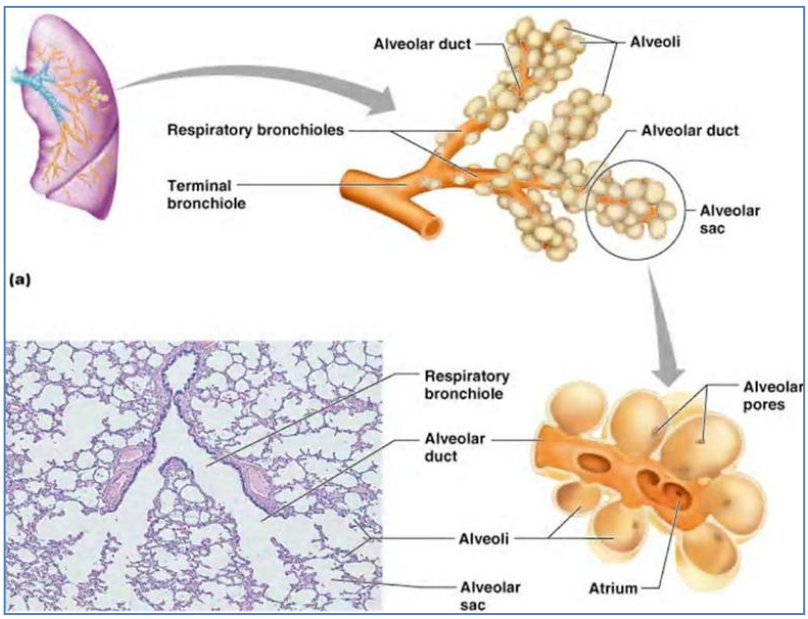
- Where *conducting structures* merge with *respiratory structures*.
- Once inside the lungs, the bronchi branch profusely until the *bronchioles* ("little bronchi") are <0.5mm thick.
- **Gradual Structural Changes:**
    - Cartilage rings replaced by irregular *plates* of cartilage.
    - No cartilage at all in *bronchioles*
    - Mucosal Epithelium thins from Pseudostratified → Columnar → Cuboidal in the bronchioles.
    - Cilia are sparse



The Respiratory Zone:

- Formed by alveoli
- Gas Exchange happens in 2 Places:
    - Tube-Like Ducts
    - Ballon-Like Sacs



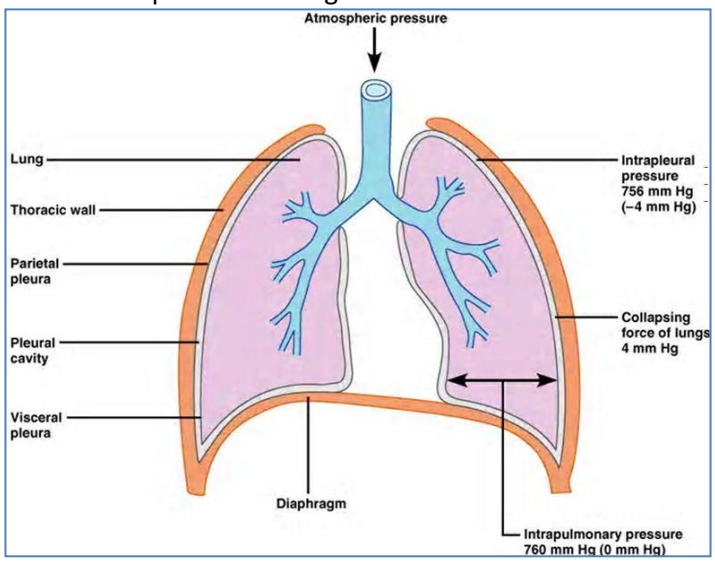


- **2 Types of Alveolar Cells:**
    - **Type I Alveolar Cells:**
        - Aka. Squamous Alveolar Cells
        - Gas Exchange Alveolar
        - Make up the Alveoli Walls
    - **Type II Alveolar Cells:**
        - Aka. Great Alveolar Cells
        - Secrete Pulmonary Surfactant (lower the surface tension of water → easier breathing.

The Physics Of Breathing:

- **Boyle's Law:**
  - At a constant temperature, the pressure of a gas is *inversely proportional* to its volume.
  - Ie. Gases move from High Pressure → Low Pressure
- **Dalton's Law (of partial pressures):**
  - The total pressure of a mixture of gasses is equal to the sum of each gas's partial pressure.
    - Eg. Atmospheric Pressure (sea) = 760mmHg = sum of $P_{Nitrogen}$, P_{Oxygen}, P_{Water} & $P_{CarbonDioxide}$
  - Also, the proportion (%age) of a gas in a mixture =
    - The %age of the total pressure that it contributes =
      - Its partial pressure.
  - Simply: *Each gas in a solution exerts a pressure exactly proportional to its abundance*.
- **Henry's Law (of dissolved gases):**
  - 'The amount of gas in solution is proportional to the partial pressure of that gas'
    - More gas dissolves in a solution when pressure (and hence partial pressure) is increased.
    - The only other factor is how *soluble* the gas is in that solvent.
- **Fick's Law (of gas diffusion)**
  - Diffusion increases with:
    - Increased Surface Area
    - Decreased Membrane Thickness
    - Increased Partial Pressure *Gradient* (Difference between $P_{Outside}$ & P_{Inside})
    - Increased Diffusion Constant (D) (D = Gas Solubility / √Molecular Weight)
      - I.e. The more soluble, the better the diffusion.
      - I.e. The smaller the molecule, the better the diffusion.

- **Pressure Changes:**
  - **Intrapleural Pressure:**
    - Negative Pressure between Visceral & Parietal Pleural Membranes....*Due To 2 Forces:*
      - Elastic Recoil of The Lungs
      - Surface Tension of *Alveolar Fluid* – acts to shrink alveoli to smallest possible.
    - **Always Subatmospheric (Negative):**
      - Becomes *more* subatmospheric during inhalation
      - Becomes *less* subatmospheric during exhalation
      - **NB: PneumoThorax:** Accumulation of air in the pleural cavity → Intrapleural pressure dissipates → lung collapses.
        - Traumatic (Penetrating/Non-penetrating)
        - Spontaneous (Disease complication)
  - **Intrapulmonary Pressure:**
    - Pressure in the Alveoli
    - **Alternates between Positive & Subatmospheric (Negative) Pressures.**
      - *Negative* pressure during Inhalation
      - *Positive* pressure during Exhalation



- **Inhalation:**
  - **Diaphragm:**
    - Contracts
    - Moves inferiorly
  - **External Intercostals:**
    - Contract
    - Move ribs out & up (bucket & pump handle mov'ts.)
  - **Accessory Muscles (If Forced):**
    - Scalenes
    - Sternocleidomastoids
    - Pectoralis MInors
  - **Lung Volume:**
    - Increases
  - **IntraPleural Pressure:**
    - Becomes *more* subatmospheric (more negative)
  - **IntraPulmonary Pressure:**
    - Becomes *negative.* (relative to P_{atm})
  - **Air:**
    - Flows In

- **Expiration:**
  - **Diaphragm:**
    - Relaxes
    - Moves superiorly
  - **External Intercostals:**
    - Relax
    - Rib cage descends due to recoil of costal cartilages
  - **Accessory Muscles (If Forced):**
    - Abdominal Wall Muscles (Transverse & Oblique)
    - Internal Intercostals
  - **Lung Volume:**
    - Decreases
  - **IntraPleural Pressure:**
    - Becomes *less* subatmospheric (more positive)
  - **IntraPulmonary Pressure:**
    - Becomes *positive.* (relative to P_{atm})
  - **Air:**
    - Flows Out

Respiratory Rates:

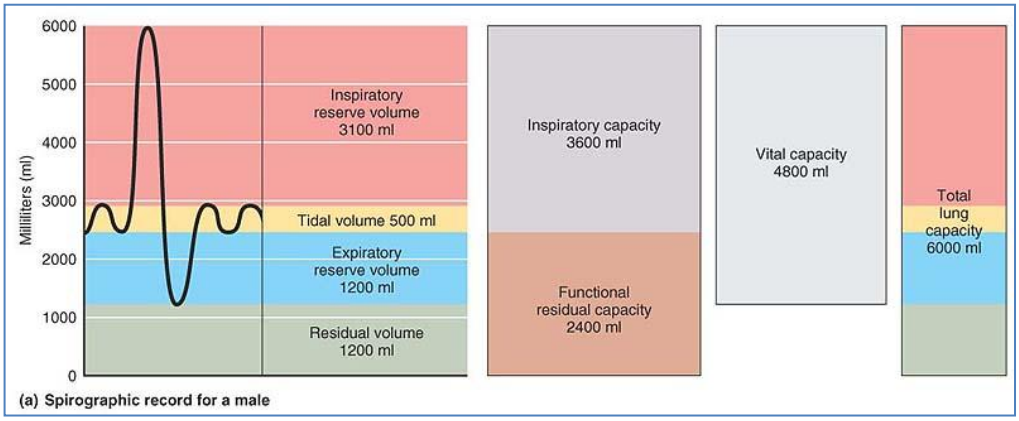
- **Respiratory Rate:** (f)
  - Breathing Frequency
- **Respiratory Minute Volume (Minute Ventilation Rate):** ($\dot{V}_E$)
  - Amount of air moved *via Tidal Ventilation* Each Minute.
  - **$\dot{V}_E = V_T \times f$**
    - Minute Ventilation Rate = Tidal Volume x Respiratory Rate
- **Alveolar Ventilation:** ($\dot{V}_A$)
  - Amount of air *reaching the Alveoli each minute*
  - **$\dot{V}_A = (V_T - V_D) \times f$**
    - Alveolar Ventilation = (Tidal Volume – Dead Space) x Frequency

Respiratory Volumes:

- **Tidal Volume:** (T_V)
  - Volume of air *inhaled* OR *exhaled during 1x Normal Breath.*
- **Dead Space:** (V_D)
  - Amount of air in *Conducting Zone* that doesn't take part in Gas Transfer.
  - There is always a small volume of air from the previous breath that will re-enter the alveoli.
- **Expiratory Reserve Volume:** (ERV)
  - Volume of Additional air that can be EXPIRED *After A Normal Quiet Expiration*
  - Ie. Beyond Tidal Volume.
- **Inspiratory Reserve Volume:** (IRV)
  - Volume of Additional air that can be INSPIRED *After A Normal Quiet Inhalation*
  - Ie. Beyond Tidal Volume.
- **Residual Volume:** (RV)
  - Air left in lungs after *Maximum Forced Expiration*.
  - Ie. Air that *can't* be breathed out (Therefore Cannot be seen/measured on a Spirometer)

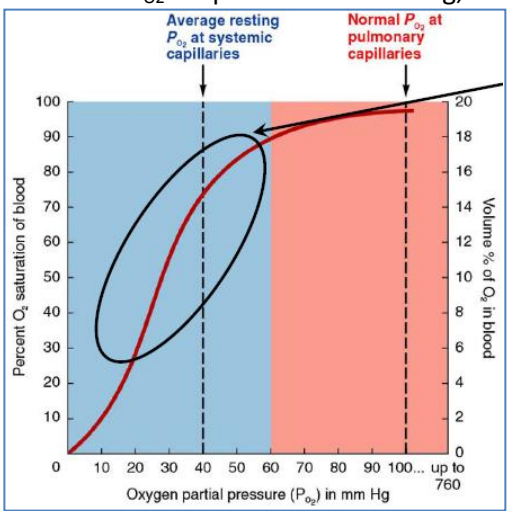
Respiratory Capacities:

- **Inspiratory Capacity:** (IC)
  - Volume of air that can be INSPIRED *After A Normal Quiet Expiration*
  - Ie. Tidal Volume + Inspiratory Reserve Volume
  - **$IC = V_T + IRV$**
- **Functional Residual Capacity:** (FRC)
  - Total Air Remaining *After A Normal Quiet Expiration*
- **Vital Capacity:** (VC)
  - Max Air you can Move Into OR Out of your lungs.
  - Ie. Expiratory Reserve + Tidal Volume + Inspiratory Reserve
  - **$VC = ERV + V_T + IRV$**
- **Total Lung Capacity:** (TLC)
  - Total Air in Lungs *After A Forced Inspiration*
  - Ie. Residual Volume + Expiratory Reserve Volume + Tidal Volume + Inspiratory Reserve Volume.
  - **$TLC = RV + ERV + V_T + IRV$**



Haemoglobin (Hb):

- **What is it?:**
  - A 4-Protein-Subunit Molecule
  - Each Protein-Subunit has a *Heme Unit* with *a Central Iron Molecule.*
- **Role in O_2 Transport:**
  - Each *Heme Unit* can carry *1xOxygen Molecule* (O_2)
  - Therefore 1xHaemoglobin can carry 4xOxygen Molecules.
- **Factors Altering Hb Affinity for O_2:**
  - **Things Changing its Shape/Functional Properties:**
    - Hb Saturation: % of Heme units containing bound O_2
      - Therefore also P_{O2}
    - P_{CO2}
    - Blood pH
    - Temperature
    - 2,3-BisPhosphoGlycerate (or DPG – disphosphoglycerate) (By-product of Glycolysis.)
- **The Physics Behind Hb's Function:**
  - **1. Greatly Increases O_2-Carrying Capacity of Blood:**
    - By binding O_2, Hb effectively removes the dissolved O_2 from solution.
      - Acts as an O_2 buffer.
      - → More of the Alveolar O_2 can diffuse into the blood (→ & Haemoglobin) before the *Partial Pressure Gradient* is equalized.
    - Hence, *Blood-O_2 Content = Dissolved O_2 + Hb-Bound O_2*
  - **2. Binds O_2 Co-Operatively:**
    - The more O_2 Molecules bound to Hb, the *easier* it becomes to bind another. (up to 4)
      - Due to Hb's conformational change between **2 States (isoforms):**
        - **T-State (Tense):**
          - Low O_2-Hb Saturation
          - Low affinity for O_2
        - **R-State (Relaxed):**
          - High O_2-Hb Saturation
          - High affinity for O_2
  - **3. O_2-Hb-Dissociation Curve:**
    - **Plateau Region (O_2 Loading Zone):**
      - In the lungs (P_{O2} = high)
      - NB: Normal P_{O2} in pulmonary capillaries ≈ 100mmHg, however the plateau region extends way below that (to ≈ 60mmHg).
        - This allows blood from lungs → Systemic circulation → Tissues, before releasing its oxygen.
    - **Steep Region (O_2 Un-Loading Zone):**
      - In Systemic Capillary Beds (P_{O2} = low)
      - The P_{O2} Range where Capillary beds *Unload* their O_2 → Tissue cells.
      - NB: As soon as P_{O2} drops below ≈ 60mmHg, Hb begins to 'Dump' its O_2.



- ***Shifting The Curve:***
  - **Right Shift:**
    - Favours *Unloading* of O_2 to Tissues
    - Reduces Hb's Affinity for O_2 → Stabilises 'T-Conformation'.
    - **Causes:**
      - ↑Temperature (eg. exercising muscles)
      - ↑ DPG (from Glycolysis)
      - ↑ P_{CO2} (causes ↑Carbonic Acid →↓*affinity* for O_2) →*Bohr Effect*
      - ↑ Acid (H^+) (↓*ability*$_{(not\ affinity)}$ to bind O_2) →*Root Effect*
  - **Left Shift:**
    - Favours *Loading* of O_2 to Tissues
    - Increases Hb's Affinity for O_2 → Stabilises 'R-Conformation'.
    - Hb-Saturation Increases.
    - **Causes:**
      - Opposites of Above

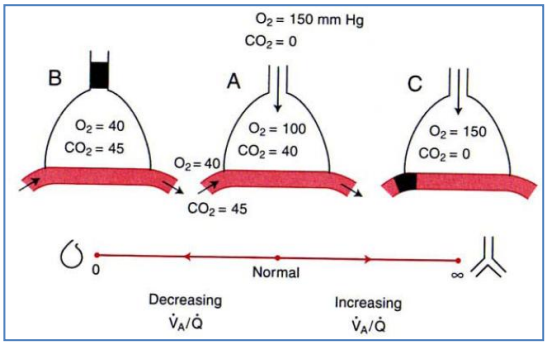
Mechanisms of CO_2 Transport

- **3 Routes To The Lungs:**
  - **1. Dissolved In Plasma:**
    - Tissue CO_2 → Dissolved Plasma CO_2 → Pulmonary Capillaries → Diffusion to Alveoli
  - **2. Bound to Hb:**
    - Tissue CO_2 → Dissolved RBC CO_2 → CO_2 + Hb → $HbCO_2$ → Pulmonary Capillaries (P_{CO2} ↓as dissolved CO_2 diffuses to Alveoli) → Dissolved RBC CO_2 → Diffusion to Alveoli
  - **3. In Bicarbonate-Ion Form:**
    - Tissue CO_2 → Dissolved RBC CO_2 → H_2CO_3 → HCO_3 → Exits RBC to Plasma →Pulmonary Capillaries → Re-Enters RBC from Plasma → Dissolved RBC CO_2 → Diffusion to Alveoli
    - Converted to Bicarb by ***Carbonic Anhydrase:***
      - $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3$

Ventilation vs. Perfusion

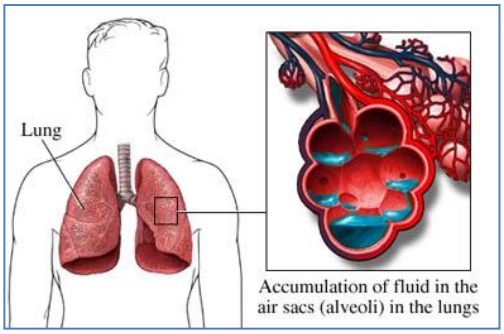
Regional Pulmonary Blood Flow:

- **Ventilation-Perfusion Matching:**
  - Not All Alveoli are Perfused or Ventilated equally.
  - **Ventilation-Perfusion Ratios:**
    - $\dot{V}_A/\dot{Q}$ (Alveolar Ventilation *Rate* / Blood Flow *Rate*)
  - **Zone 1:**
    - Capillary Pressure never exceeds Alveolar Air Pressure.
    - No Blood Flow at all.
    - V/Q Ratio →Infinity
  - **Zone 2:**
    - Capillary Pressure only exceeds Alveolar Air Pressure during Systole.
    - Intermittent Blood Flow (Flow during systolic pressure)
    - V/Q Ratio = Normal
  - **Zone 3:**
    - Capillary Pressure always exceeds Alveolar Air Pressure.
    - Constant Blood Flow.
    - V/Q Ratio → Still Normal, but lower.



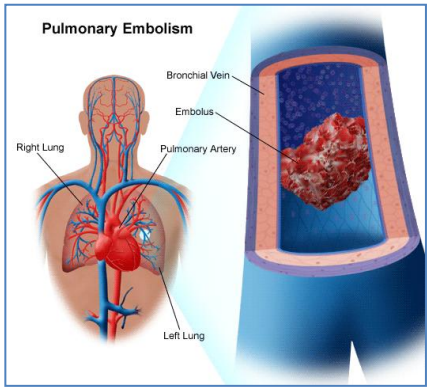
Preventing Pulmonary Oedema:

- **Negative Interstitial Pressure:**
  - Slightly Negative Interstitial Hydrostatic Pressure
  - Keeps alveoli 'dry'
  - Fluid in Alveoli is sucked into Interstitium → Lymphatics
- **Lymphatic Vessels:**
  - Actively pump Interstitial Fluid → Blood Vessels
- **Oedema Safety Factor:**
  - For oedema to occur, Pul.Cap-Pressure must rise above Colloid Osmotic Pressure.
    - Pul.Cap-Pressure ≈ 7mmHg
    - C.Osmotic Pressure ≈ -28mmHg
  - Therefore a +21mmHg rise in Pul.Cap-Pressure is needed.



Pulmonary Embolism:

- Foreign fragments blocking a blood pulmonary vessel.
- Often due to Blood Clot (Thrombus)
- Blockage of vessel in lung will impact/prevent effective oxygenation of blood.



Body Acid-Base Balance

Acid Production:

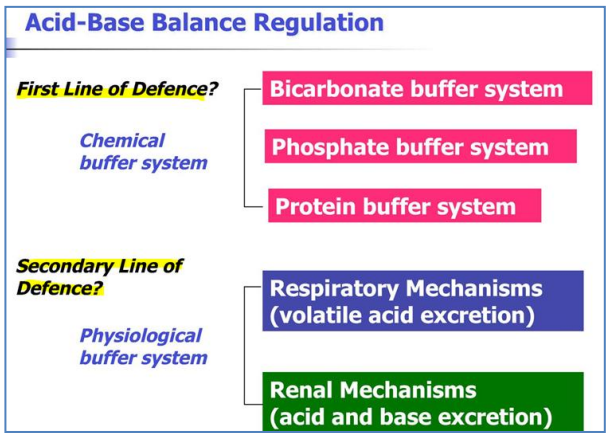
- **The Body *turns over* up to 150*Moles* of H^+ per day – THAT'S A LOT!!**
- **Where does it come from?**
  - **Metabolic Processes:**
    - **Most H^+ comes from *Hydrolysing ATP* (ie. *Aerobic Metabolism*)**
      - ATP + H_2O → ADP + P_i + H^+
      - NB: The Body turns over ≈40kg of ATP *per day!*
    - **Much H^+ also comes from:**
      - Anaerobic Glucose Metabolism
      - Amino Acid Metabolism
      - Fatty Acid B-Oxidation.
      - Nucleic Acid Metabolism.
- **Despite LOADS OF H^+ produced, *Body pH* is *Finely Regulated.***
  - Ie. Very small pH changes observed in body.

Physiological pH Values:

- **Arterial pH = 7.40**
  - NB: pH of <6.9 can be lethal
- **Venous pH = 7.35** - more acidic due to *higher HCO_3* (ie. Higher P_{CO2})
- **Urine pH =** 4.5 to 8.0
- **Stomach pH =** 0.8 - requirement of chemical digestion & activation of digestive enzymes.
- **Bile pH =** 7.8 to 8.6 - needs to be alkaline to break down fats.

Acid-Base Homeostasis Regulated By:

- **Buffers:**
  - **What are they?:**
    - Solutions of A Weak Conjugate Acid & A Weak Conjugate Base that Resist changes in pH
  - **pK of A Buffer:**
    - Mathematically → The –log of the Equilibrium Constant (**K_{eq} = [Products] ÷ [Reactants]**)
    - The pH of the Buffer Solution where both the Conjugate Acid & Base are at **50% dissociation**.
    - It is the pH that the Buffer Solution wants to be at.
    - Hence – yields Max. Buffering Power.
      - Ie. If an experiment required a pH of 7.4, you would conduct it in a buffer of pK=7.4
- **Acid-Base Balance Lines of Defence:**
  - **1. Chemical Buffer Systems:**
    - #1.Bicarbonate Buffer System
    - Phosphate Buffer System
    - Protein Buffer System
  - **2. Physiological Buffer Systems:**
    - Respiratory Mechanisms
    - Renal Mechanisms



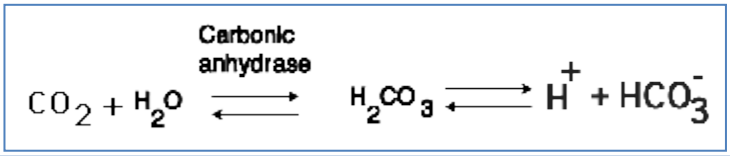
-1st Line Of Defence: Chemical Buffer Systems:

- **#1. Carbonic-Acid-Bicarbonate Buffer System:**
  - The most important Body Buffer System
  - Occurs **within the Red Blood Cell**
    - ***Carbonic Anhydrase*** (in RBC) catalyses: **($CO_2 + H_2O \rightarrow H_2CO_3$)**
  - Operates **in conjunction with the respiratory system**.
    - Ie. Blowing off CO_2 shifts eq. To the left → Less $[H^+]$ → pH increases.

  - **Clinical Assessment of Acid/Base:**
    - **3 Factors Required:**
      - 1. Blood pH
      - 2. Blood P_{CO2}
      - 3. Plasma Bicarbonate

  - **When the ratio of $[HCO_3^-]/[H_2CO_3]$ = 20:1, The blood pH will be *normal* = pH 7.4**
    - Ie. The [Bicarbonate] : [Carbonic Acid] = 20:1
    - Ie. The [Bicarbonate] : [Carbon Dioxide]= 20:1

    - **Changing this ratio – Changes Blood pH:**
      - **pH ↑ When:**
        - [Bicarbonate]↑ (Pushes Equation to the Left)
        - [Carbon Dioxide]↓ (Pushes Equation to the Left)
      - **pH ↓When:**
        - [Bicarbonate]↓ (Pushes Equation to the Right)
        - [Carbon Dioxide]↑ (Pushes Equation to the Right)



$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^- \text{ (pK 6.11)}$$

Carbon Dioxide — Carbonic Acid — Bicarbonate Ion

Simplified Equation

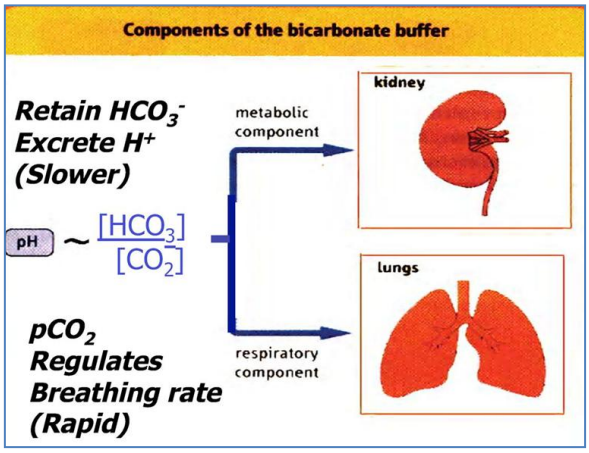
$$\text{Net } CO_2 \text{ (dissolved)} + H_2O \leftrightarrow H^+ + HCO_3^- \text{ (pK 6.11)}$$

- **#2. Phosphate Buffer System:**
  - Second most important Body Buffer System
  - Operates in the internal fluid of all cells.

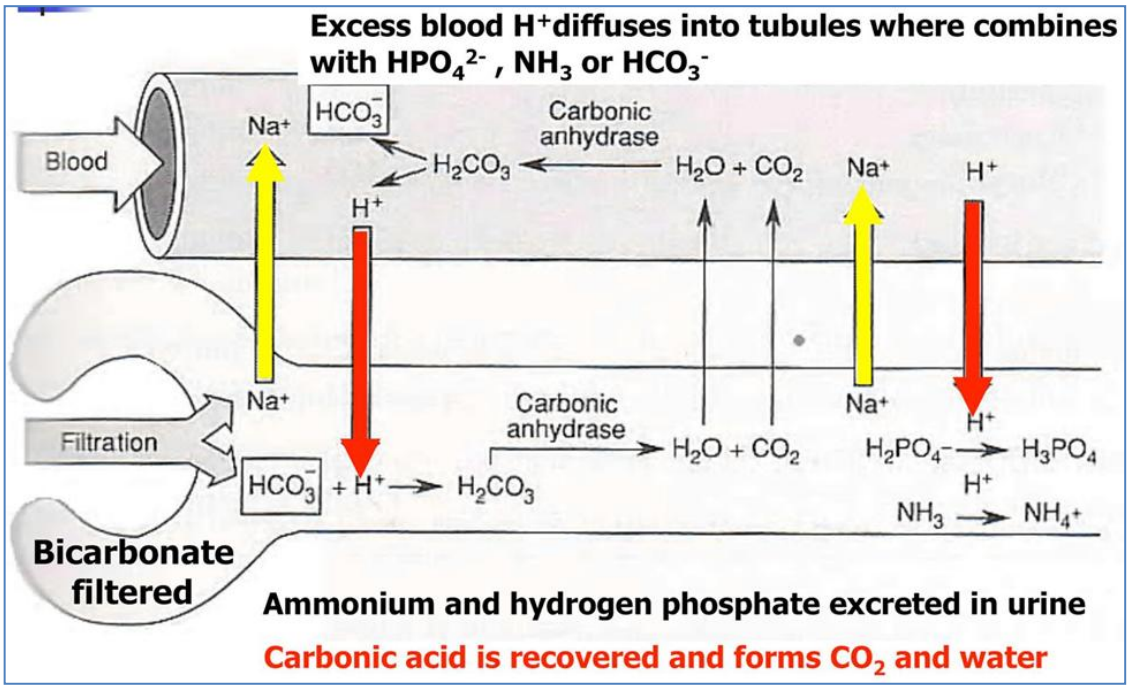
$$H_2PO_4^-(aq) \rightleftharpoons H^+(aq) + HPO_4^{2-}(aq)$$

- **#3. Protein Buffers (in RBCs & Intracellular Buffers)**
  - Both intracellular and extracellular **proteins have negative charges and can serve as H^+ buffers**.
  - However, because most proteins are inside cells, this primarily is an **intracellular** buffer system.
    - Eg. Haemoglobin (Hb) is an excellent intracellular buffer because of its ability to bind H^+.
    - Forms a *weak acid + carbon dioxide (CO2).*
    - After O_2 is released (in the peripheral tissues), Hb binds CO2 and H^+ ions.
    - As blood reaches the lungs these actions reverse themselves →Hb binds O_2, releasing the CO_2 and H^+ ions.
    - The H^+ combines with bicarbonate (HCO_3) → carbonic acid (H_2CO_3). The H_2CO_3 breaks down to form water (H2O) and carbon dioxide (CO2) which are excreted via expiration through the lungs. Therefore respirations help maintain pH.

- 2nd Line Of Defence: Physiological Buffer Systems:

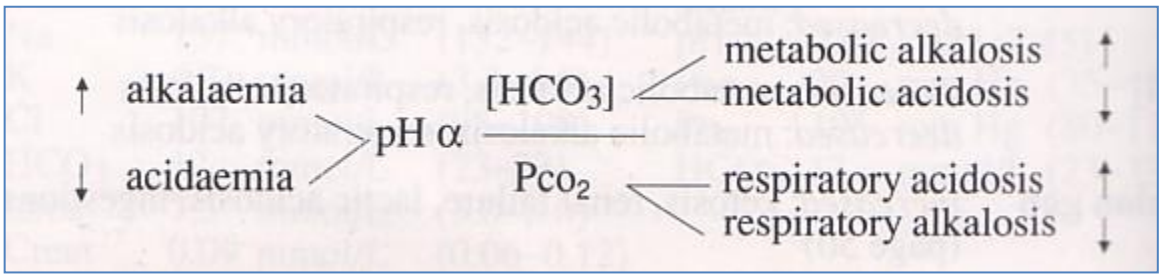


- **Respiratory System – Short Term:**
  - (CO_2 Excretion)
  - CO_2 constantly produced during Metabolic Processes
  - Eliminated by lungs.
  - If not eliminated from body, pH would quickly become *Acidic* (Bicarb-Buffer Eqn. Shifts to Right)
  - **CO_2: The Controller Of Ventilation:**
    - CO_2 is the main controller because H^+ can't cross the *Blood-Brain-Barrier.*
    - **ΔP_{CO2} → ΔpH of Cerebro-Spinal Fluid → Sensed by Medulla (respiratory centres)→ ΔResp's**
      - ↑P_{CO2} Increases Ventilation Rate + Depth (eg. Exercise)
      - ↓P_{CO2} Decreases Ventilation Rate + Depth (eg. After Hyperventilating)
- **Kidneys – Long Term:**
  - **Kidneys Control Acid/Base by excreting either:**
    - Acidic Urine
    - Basic Urine
  - **Mechanism:**
    - **HCO_3^-** Filtered → Renal Tubules →Combined with H^+ → Carbonic Acid → $H_2O + CO_2$ → Blood
    - **H^+** Filtered → Renal Tubules → Combines with HCO_3 →Carbonic Acid →$H_2O + CO_2$ → Blood
      → Combines with HPO_4^{2-} or NH_3 → Excreted in Urine.
    - In Short:
      - Carbonic Acid is recovered → CO_2 & H_2O → Blood
      - Ammonium & Hydrogen Phosphate → Excreted in Urine.



Metabolic Vs. Respiratory pH Disturbances:

- **Metabolic –**
  - **– Acidosis:**
    - Due to ↓[HCO_3]
    - (Due to inability of the body to form bicarbonate (HCO_3^-) in the kidney)
    - (Or, Due to Lactic/Keto Acid build-up)
  - **– Alkalosis:**
    - Due to ↑[HCO_3]
    - (Due to Loss of H^+ in Urine or Vomiting)
    - (Or, Due to Retention of Bicarbonate (HCO_3))
- **Respiratory –**
  - **– Acidosis:**
    - Due to ↑P_{CO2}
    - (Due to decreased ventilation of the pulmonary alveoli, →elevated P_{CO2}).
  - **– Alkalosis:**
    - Due to ↓P_{CO2}
    - (Due to increased alveolar respiration (hyperventilation) →decreased plasma [CO_2])



- **Compensatory Mechinisms:**
  - In either Metabolic or Respiratory Acidosis/Alkalosis, the compensatory mechanism will always be the other system.
    - Ie. If Metabolic Acidosis, the Compensatory Mech. Will be the Respiratory System (viseversa)
  - NB: Regulation of breathing – normally via P_{CO2} (because H^+ can't cross Blood-Brain Barrier). However, in *Metabolic Acidosis*, the P_{CO2} is already lower than normal (due to right-shift in equil.) and therefore can't stimulate breathing. *Instead,* the Primary Factor would be *Blood pH* on *Peripheral Chemoreceptors*.

Ventilatory Response To Exercise:

- NB: Gas levels remain stable during exercise – (Ventilation is well matched to O_2 Consumption)
- **During Light-Moderate Exercise:** – Linear Relationship between O_2 Demand & Ventilation.
- **During Severe Exercise:** - O_2 Consumption Exceeds Body's ability to supply it → Anaerobic Metabolism:
  - Lactic Acid Buildup → Lactic-Acidosis → Hyperventilation.

Control Of Breathing:

- **Upper Respiratory Tract Reflexes:**
  - Eg. Cough/Sneeze Reflexes. – Don't Know Details
  - Receptors in Nose/Pharynx/Larynx
    - Respond to Toxins/Irritants/Temperature

- **Lung Reflexes:**
  - **Pulmonary Stretch Receptors:**
    - **Slowly Adapting Stretch-Receptors (SARs):**
      - Sensitive to Inflation/Deflation.
      - Ie. Lung-Volume Sensors
    - **Rapidly Adapting Stretch-Receptors: (RARs):**
      - Sensitive to Tidal Volume, Frequency, Or Lung Compliance.
      - Also Nociceptive & Chemosensitive.
  - ***Inflation Reflex: ("Hering Breuer Reflex"):**
    - Prevents *Over*-Inflation
    - - Activated in response to ↑Pulmonary 'Stretch'
  - **Deflation Reflex:**
    - Prevents Lung *Collapse* (*Over*-Deflation)
    - - Stimulates Inspiration when Lung-Volume is too Low.

- **Chemical Control of Respiration:**
  - ***↑Arterial PCO_2:**
    - **Central Chemoreceptors – (Chemosensitive Area of Medulla):**
      - ****↑Arterial PCO_2 → ↑*CSF*-$[H^+]$** (Cerebro-Spinal Fluid)
      - ↑CSF-$[H^+]$ Acts Directly on *Chemosensitive Area on Medulla.*
      - ↑CSF-$[H^+]$ Stimulates Respiratory Centre
    - **Peripheral Chemoreceptors – (Aortic & Carotid Bodies):**
      - **↑Arterial PCO_2 → ↑*Arterial*-$[H^+]$**
      - ↑Arterial-CO_2→HCO_3 + Arterial-H^+ … Via the Bicarbonate-Buffer System.
        - ↑H^+ Stimulates Ventilation
        - ↓H^+ Depresses Ventilation
  - **Arterial Non-CO_2 $[H^+]$:**
    - **Peripheral Chemoreceptors – (Aortic & Carotid Bodies):**
      - **↑Non-CO_2-Generated $[H^+]$ → ↑Arterial-$[H^+]$**
        - **NB:** Non-CO_2-Generated $[H^+]$ = Lactic-Acid/Keto-Acids/Etc.
        - ↑H^+ Stimulates Ventilation
        - ↓H^+ Depresses Ventilation
  - **↓Arterial O_2:**
    - **Peripheral Chemoreceptors – (Aortic & Carotid Bodies):**
      - ↓Arterial-O_2 (to below ≈100mmHg) → Strong Respiratory Stimulation
        - Increased Breathing Rate
        - Increased Breathing Depth
      - **NB: Acclimatization:**
        - In Low O_2 environments (mountain climbing), the Central Respiratory Centres lose sensitivity for CO_2. Therefore, Low-O_2 takes over as the #1. Respiratory Driver.

Obstructive Vs. Restrictive Pulmonary Diseases:

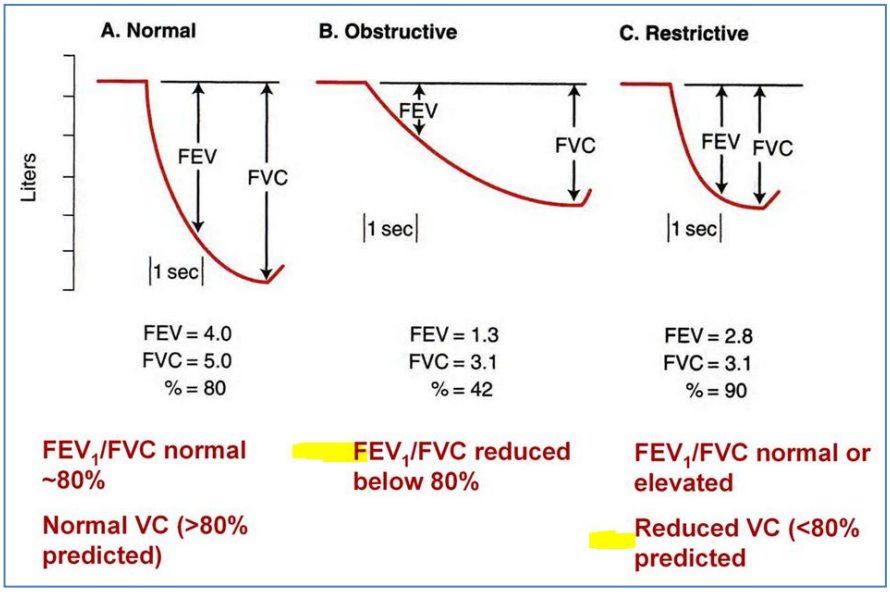
- **Obstructive:**
  - Involves *Airway* Obstruction → ↑*Airway* Resistance
  - **Effects on Lung Capacities/Volumes:**
    - ↑TLC (Total Lung Capacity)
    - ↑RV (Residual Volume)
    - ↑FRC(Functional Residual Capacity)

    } Due To Gas-Trapping & Hyperinflation of The Lungs

    - ↓VC (Vital Capacity) - Because They Can't Expel All the Gas in their Lungs
    - ↓FEV_1 (Forced Expiratory Volume in 1 Sec) – Because of Dynamic Airway Compression
  - **Key Diagnostic Feature:**
    - If their **FEV_1 is *Less Than* 80% of FVC**
      - (FEV_1 = Forced Expiratory Volume in 1 Second)
      - (FVC = Forced Vital Capacity = Max Air Expired After Full Inspiration)

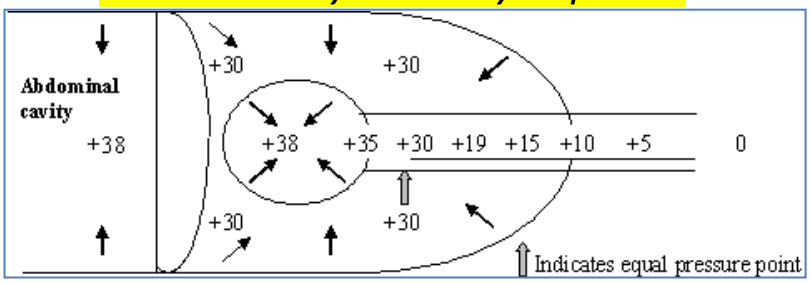
- **Restrictive:**
  - Involves *Lung* Restriction → ↑Resistance to *Lung Expansion*
  - (ie. ↓Chest or Lung Compliance / Obesity → Weight on Chest / Pregnancy → ↑Abdominal Pressure)
  - NB: *Normal* Airway Resistance.
  - **Effects on Lung Capacities/Volumes:**
    - ↓TLC (Total Lung Capacity)
    - ↓VC (Vital Capacity)
    - ↓IC (Inspiratory Capacity)

    } Due to ↑Resistance to *Lung Expansion*
  - **Key Diagnostic Feature:**
    - If their ***Measured VC*** is ***Less Than* 80%** of their ***Predicted VC*.**
      - (Measured Vital Capacity = Patient's VC Measured by Spirometry)
      - (Predicted Vital Capacity = Average Healthy VC based on Age/Sex/Size)

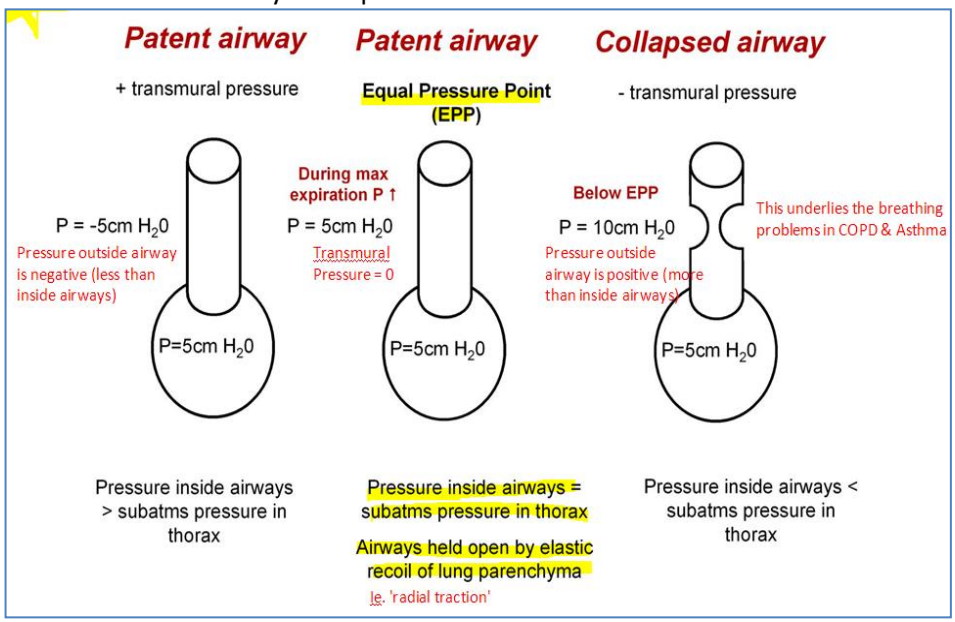


Dynamic Airway Compression:

- **Equal Pressure Point:**
  - ***EPP:*** Is The Location in an Airway where Intrapleural (Thoracic) Pressure = The Intra-Airway Pressure.
    - If EPP occurs in Larger, Cartilaginous Airways, the Airways Remain Open.
    - However, If EPP Occurs in Smaller, Unsupported Airways, the Airways will Collapse.
      - This is Known as "***Dynamic Airway Compression"***



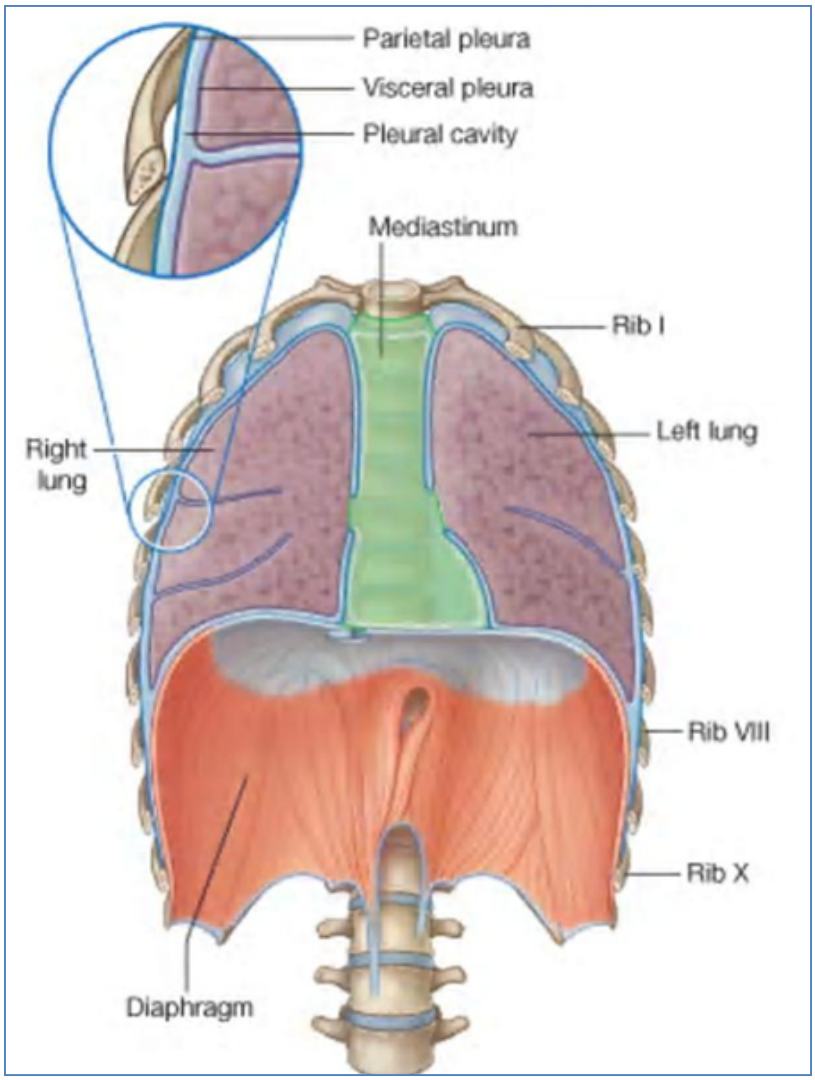
  - **During *Passive Expiration***:
    - The Alveolar Pressure is Mostly due to The Elastic Recoil of The Lungs (& Partly due to the Recoil of the Thoracic Cage.)
    - Since the Highest Proportion of the Alveolar Pressure is due to the Lung's Elastic Recoil, The Thoracic Pressure is Relatively Low.
    - Therefore, the EPP will occur *High Up* in the Larger, Cartilaginous Airways.
      - →Airways Remain Patent
  - **During *Forced Expiration***:
    - (IE. IN OBSTRUCTIVE CONDITIONS)
    - The Alveolar Pressure is Mostly due to The Expiratory Muscles →↑Thoracic Pressure. (& Partly due to Elastic Recoil of Lungs.)
    - Since the Highest Proportion of the Alveolar Pressure is due to the ↑*Thoracic Pressure*, The Pressure of the Lung's Elastic Recoil is Relatively Low.
    - Therefore, The EPP will occur *Lower Down* in the Smaller, less-supported Airways.
      - →Airways Collapse.



Respiratory Medicine Notes

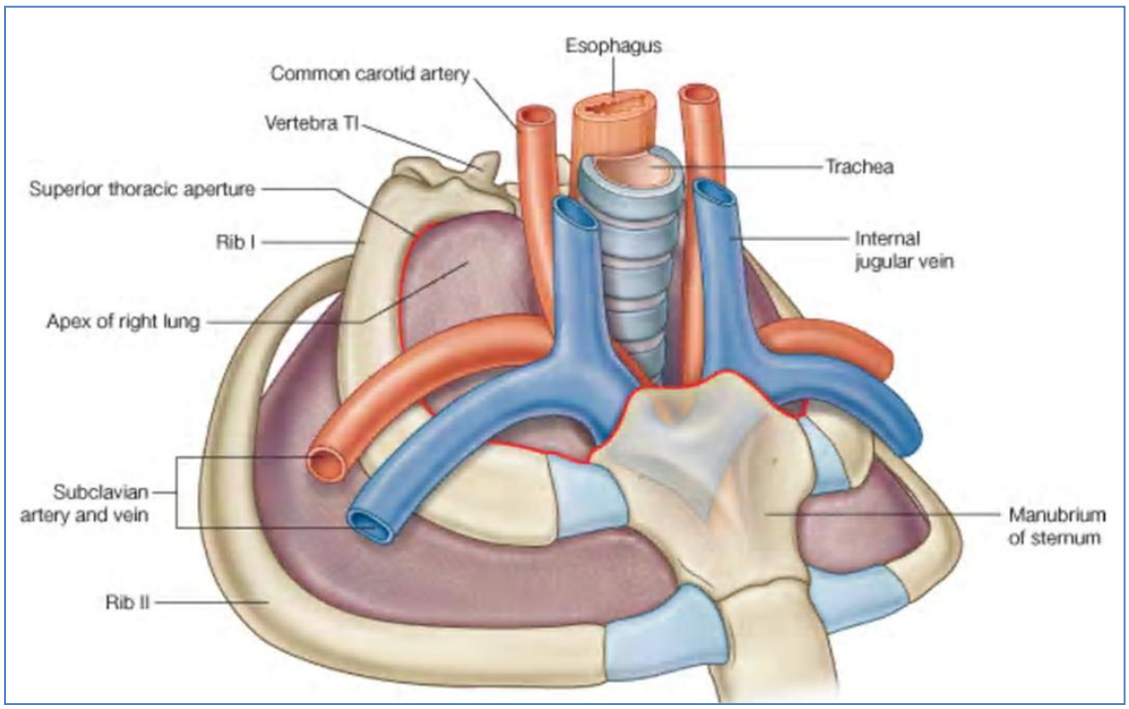
Thoracic Overview:

- Thorax = Chest region
- **3 Parts:**
  - Thoracic Cage (skeletal components)
  - Thoracic Wall (muscular components)
  - Thoracic Cavity (internal area)
- **3 Functions:**
  - Protection of Vital Organs (by the thoracic cage)
  - Muscular Movements of Breathing (by thoracic wall & diaphragm)
  - Passageway for structures to pass between the neck & abdomen (oesophagus/vessels/nerves)
- **3 Internal Compartments:**
  - **Central Mediastinum**
    - Containing the Heart/oesophagus/trachea/nerves/vessels
  - **Left Pleural Cavity**
    - Containing the L-Lung
  - **Right Pleural Cavity**
    - Containing the R-Lung

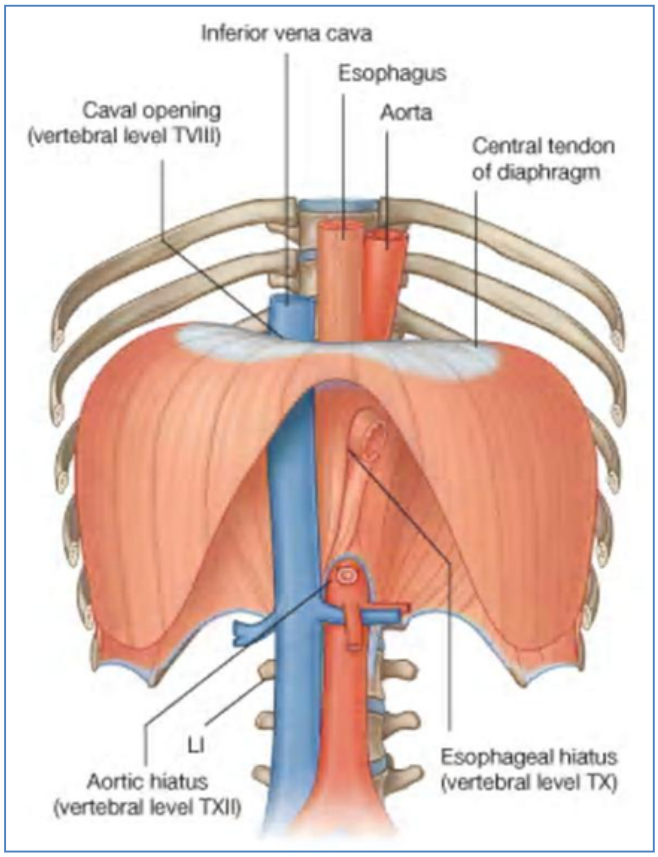


Relationship to Other Regions:

- **Neck:**
  - Trachea
  - Oesophagus
  - Major Nerves & Vessels

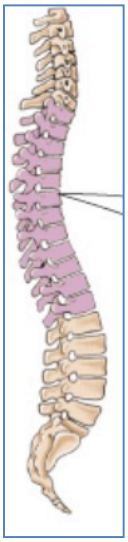


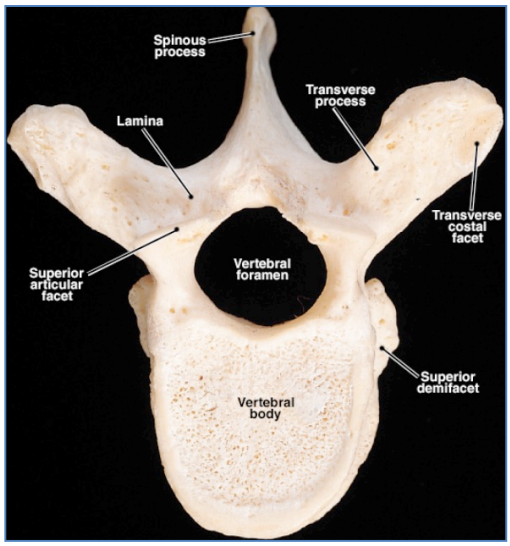
- **Abdomen:**
  - Inferior Vena Cava
  - Oesophagus
  - Aorta

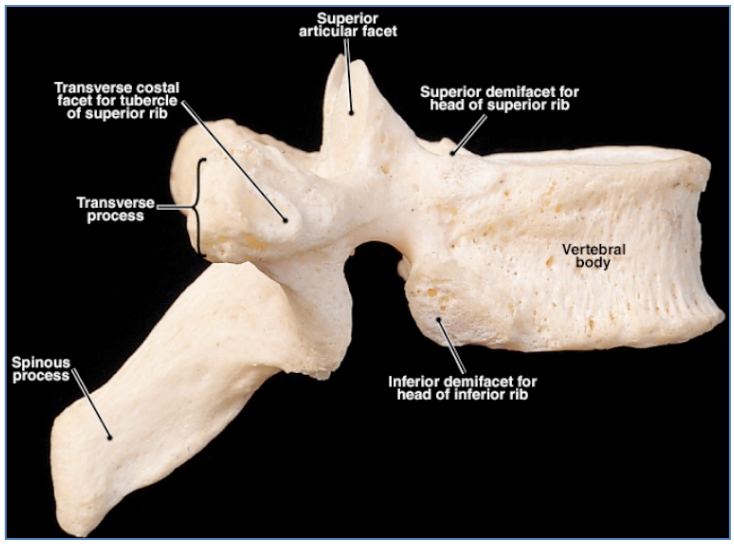


Thoracic Skeleton (Cage):

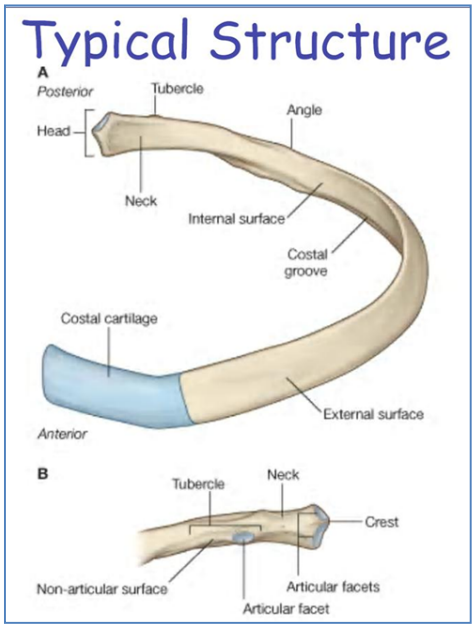
- **12 Thoracic Vertebrae:**
  - T1 - T12
  - **Distinguishing Features:**
    - **Heart-Shaped Body** (for extra weight-bearing)
    - **Inferiorly Projecting Spine** (Allows a degree of mobility that would otherwise not be possible due to ribs)
    - **Large Transverse Processes** (To support articulations with ribs)
    - **Costal Demifacets** (small articulation points) for articulation with the ribs.

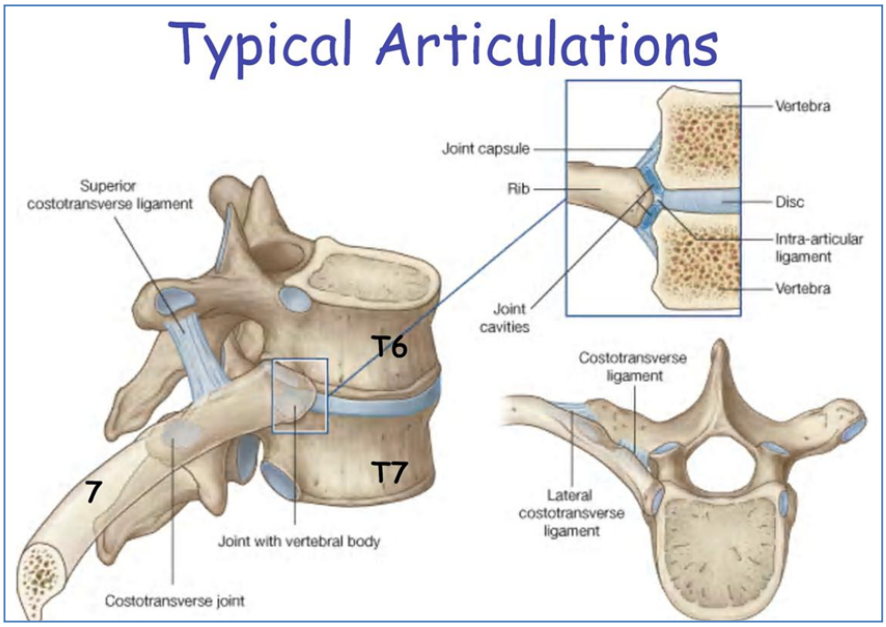




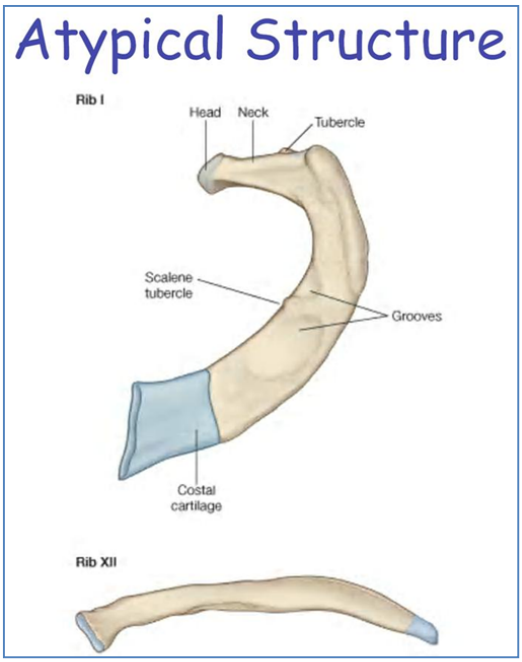


- **12 Pairs of Ribs:**
  - 1-7 = 'True' Ribs (attach directly to sternum)
  - 8-12 = 'False' Ribs (don't attach directly to the sternum)
    - Ribs 11 & 12 are 'Floating' Ribs (insert into abdominal muscles & conn. tissue.
  - **Distinguishing Features:**
    - **Posterior End:**
      - has a **head, neck & tubercle** (for attachment of ligaments & to vertebrae)
    - **Curved shaft:**
      - Generally thin & flat
      - Oriented Vertically
      - Has a subcostal groove running on the inside of its inferior aspect.
    - **SubCostal Groove:**
      - Houses the I**ntercostals Nerve, Artery & Vein**
    - **Anterior End:**
      - Sits more inferior than the posterior end.
      - Attach to sternum via **Costal Cartilage** – forms a *cartilaginous joint*
  - **Typical Articulations:**
    - Between **Head & Vertebrae** of the *same number*
    - Between **Head & Vertebrae *above***
    - Between the **Tubercle** & the **Transverse Process** of the **Vertebrae** of the *same number*

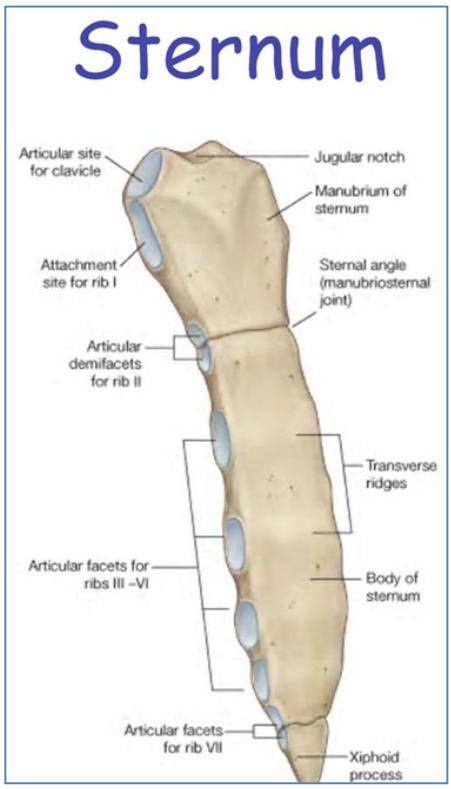


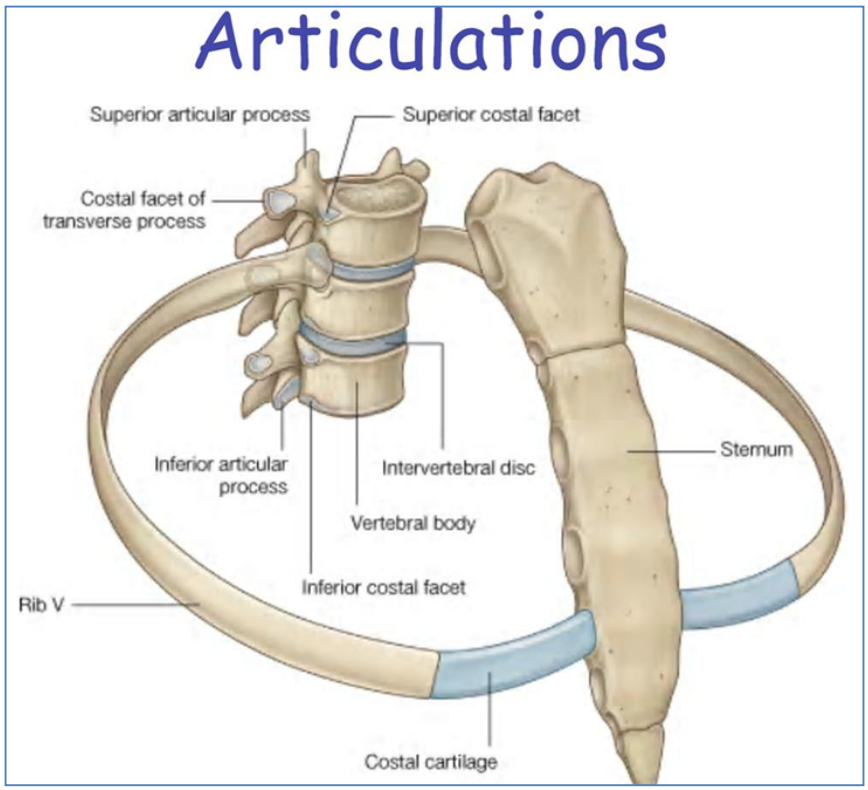


- **Atypical Ribs:**
  - Ribs 1, 2, 10, 11 & 12.
  - Why?:
    - **Rib 1:**
      - Oriented horizontally (rather than vertically)
      - Much shorter
      - Articulates *only* with the *body* of *T1*.
      - Scalene Tubercle – attachment point of Anterior Scalene Muscle
      - Grooves for Subclavian Veins & Arteries
    - **Rib 2:**
      - Oriented horizontally (rather than vertically)
      - Otherwise typical
    - **Rib 10:**
      - Articulates *only with its own Vertebra* – only has 1 Facet on its head.
    - **Rib 11 & 12:**
      - Articulate *only with their own Vertebra*
      - No Tubercles / Necks
      - No Anterior Articulation



- **Sternum:**
  - **3 Parts:**
    - Manubrium
    - Body of Sternum
    - Xiphoid Process
  - **Sternal Angle:**
    - Between the Manubrium & the Body
    - Important Landmark for:
      - Bifurcation of Trachea
      - Aortic Crest
      - T-4 Vertebrae
      - 2nd Rib
  - **Articulations:**
    - **Ribs 1-7:** Via ***Sternocostal Joints*** (Synovial Joints)
    - **Ribs 8-10:** Have ***Interchondral Joints*** between the costal cartilages (i.e. Indirect articulation with sternum.

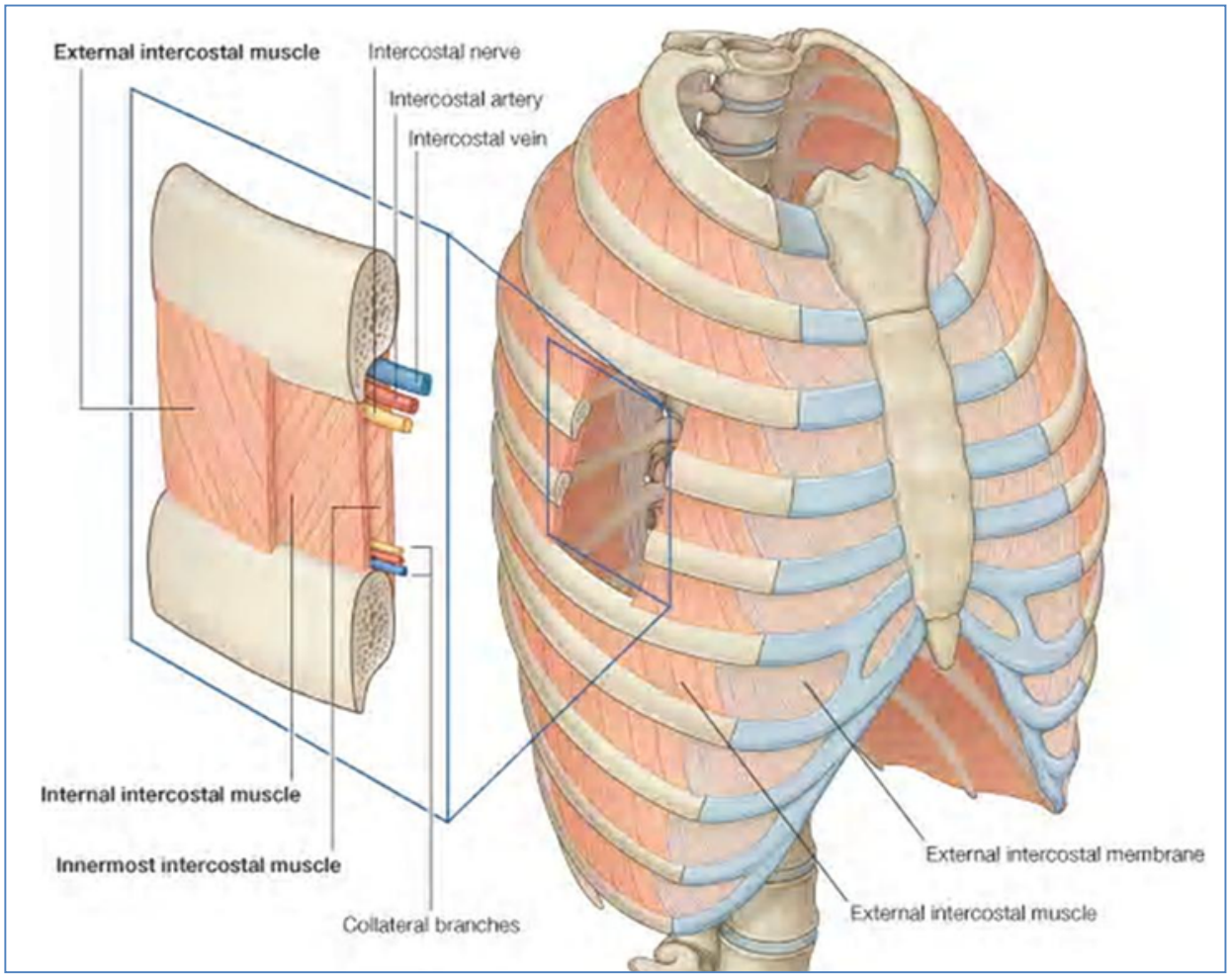




- NB: all bones of the Thoracic Cage are interconnected by articulations (cartilaginous & synovial), each offering a small amount of movement. However, despite limited movement of individual joints, their combined movements make the Thoracic Cage remarkably mobile.

Thoracic Wall (Muscular Component):

- **3 Layers:**
  - **External Intercostal Muscle:**
    - Oriented Diagonally Inferio-Anteriorly
    - Incomplete Anteriorly → Transitions into the Anterior Intercostal *Membrane*
  - **Internal Intercostal Muscle:**
    - → Transitions into the Posterior Intercostal *Membrane*
  - **Innermost Intercostal Muscle:**
    - Oriented Diagonally Inferio-Posteriorly
    - Incomplete Posteriorly
- **Blood Supply:** (segmental)
  - **Posterior Intercostal Arteries** (Branches of Descending Aorta)
  - **Anterior Intercostal Arteries** (Branches of Internal Thoracic Arteries- From Subclavian Arteries)
- **Nerve Supply:**
  - Anterior Rami of Thoracic Spinal Nerves directly supply intercostals muscles.

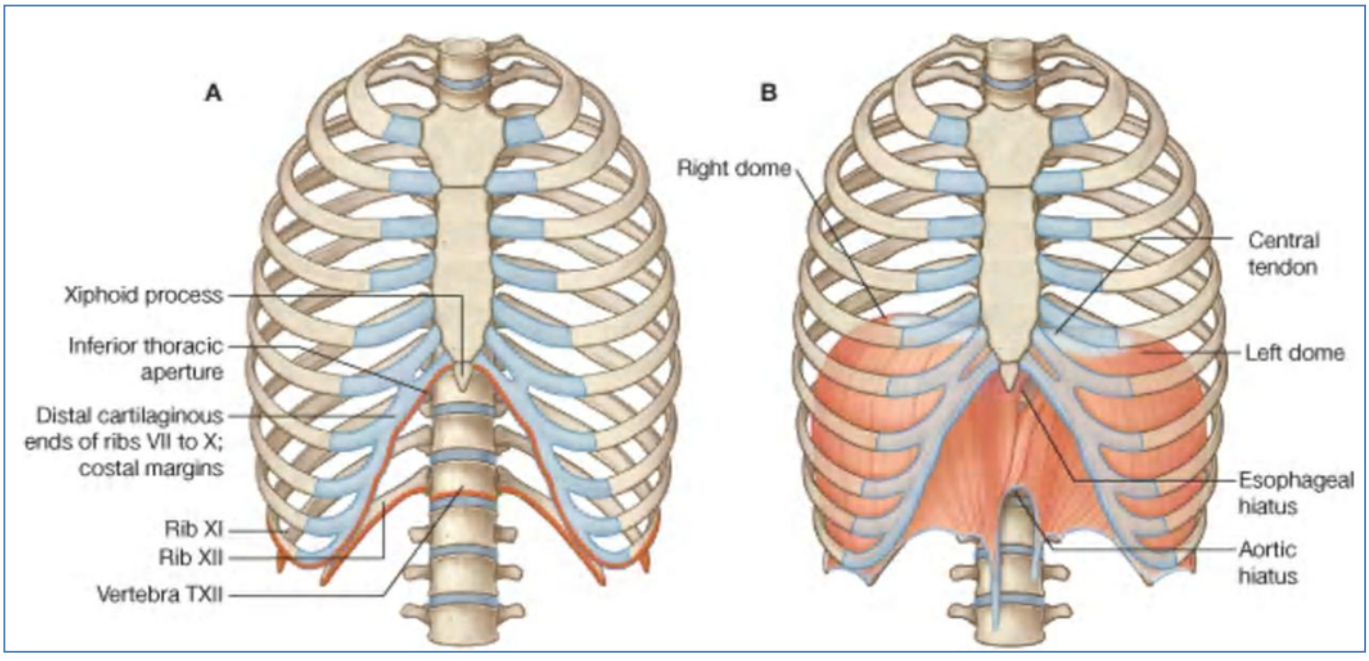


Accessory Muscles Of:

- **Inspiration:**
  - **Scalene Muscles**
  - **Sternocleidomastoid**
  - **External Intercostals**
  - **How:**
    - Pull the Ribs & Sternum *Superiorly* (i.e. Pump & Bucket-handle Movements)
- **Expiration:**
  - ***Abdominal* Wall Muscles**
    - By increasing intra-abdominal pressure (forces diaphragm up)
  - **Internal Intercostals**
    - Pull the Ribs & Sternum *Inferiorly* (i.e. Reverse of Pump & Bucket-Handle Movements)

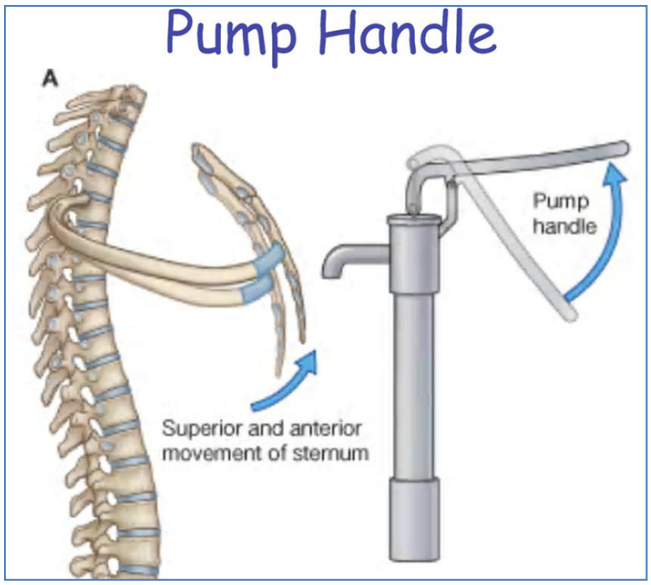
Primary Muscle: The Diaphragm:

- A MusculoTendinous Structure
- Divides thorax from abdomen
- Primary muscle of respiration
- Contraction = Flattening (i.e. Downward movement) → Inspiration
- Relaxation = Doming into thoracic cavity (upward movement) → Expiration
- **Origins:**
  - Xiphoid Process
  - **Costal Margin** (approx 7th rib)
  - Lateral Lower Ribs (11 & 12)
  - Body of T12 Vertebra.
- **Inserts Onto:**
  - A central tendon
- **Blood Supply:**
  - Phrenic Arteries (superior & Inferior)
- **Venous Drainage:**
  - Brachiocephalic Veins
  - Azygous Veins
  - Inferior Vena Cava
- **Nerve Supply:**
  - Phrenic Nerve (C3, 4 & 5)
    - Receives sympathetic fibres from Cervical Ganglia → Voluntary & Autonomic Nerve Supply

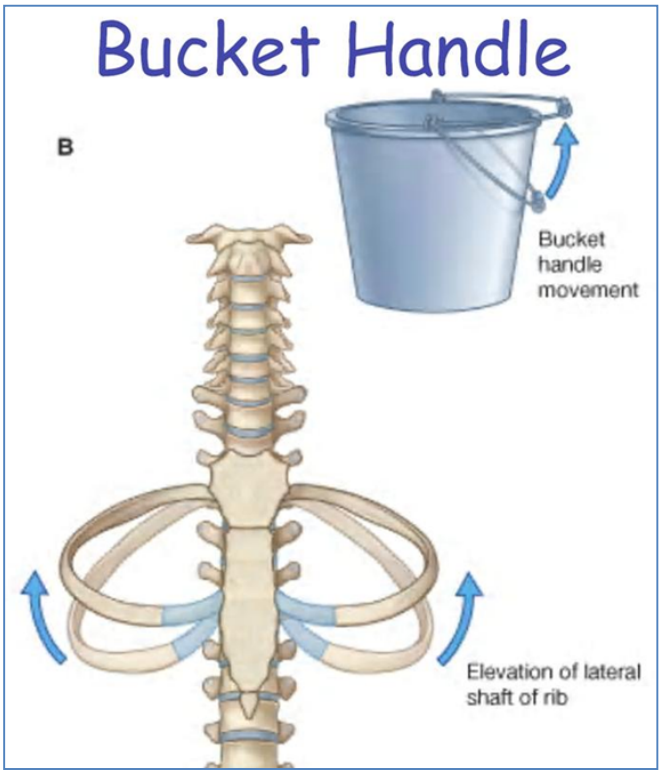


Thoracic Movements of Breathing:

- Brought about by muscles of the Thoracic Wall & Accessory Muscles
- Breathing is **not** just movement of the diaphragm
- Due to articulations, 2 groups of ribs create different movements:
    - **Upper 6 Ribs:**
        - *Pump Handle* Action
        - Increases **Anterio-Posterioir Diameter** of Thoracic Cavity

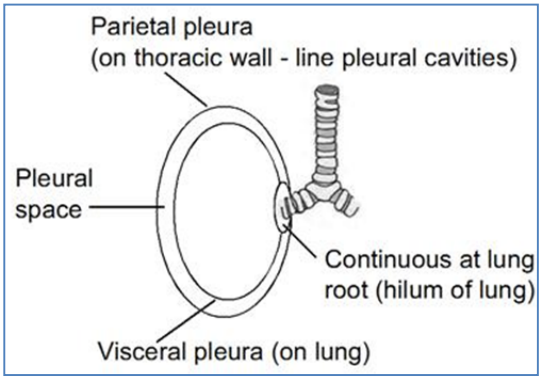


    - **Lower 6 Ribs:**
        - *Bucket Handle* Action
        - Increases the **Transverse Diameter** of Thoracic Cavity

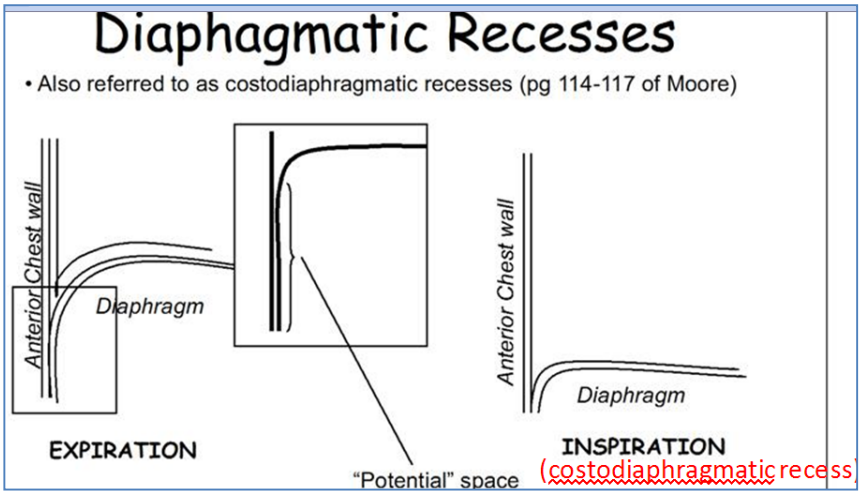


Pleura:

- One on Left & Right Side
- Each are continuous Serous Sacs
    - Each has a Visceral 'pleura' & A Parietal 'pleura'
    - Between these layers is a 'potential' space aka. The "Pleural Space"
    - This Pleural Space is contains lubricating Serous Fluid
        - Fluid creates surface tension
            - Keeps the lung inflated even during expiration.
            - Keeps the pleurae together.
- Pleurae line the lung & Pulmonary Cavities



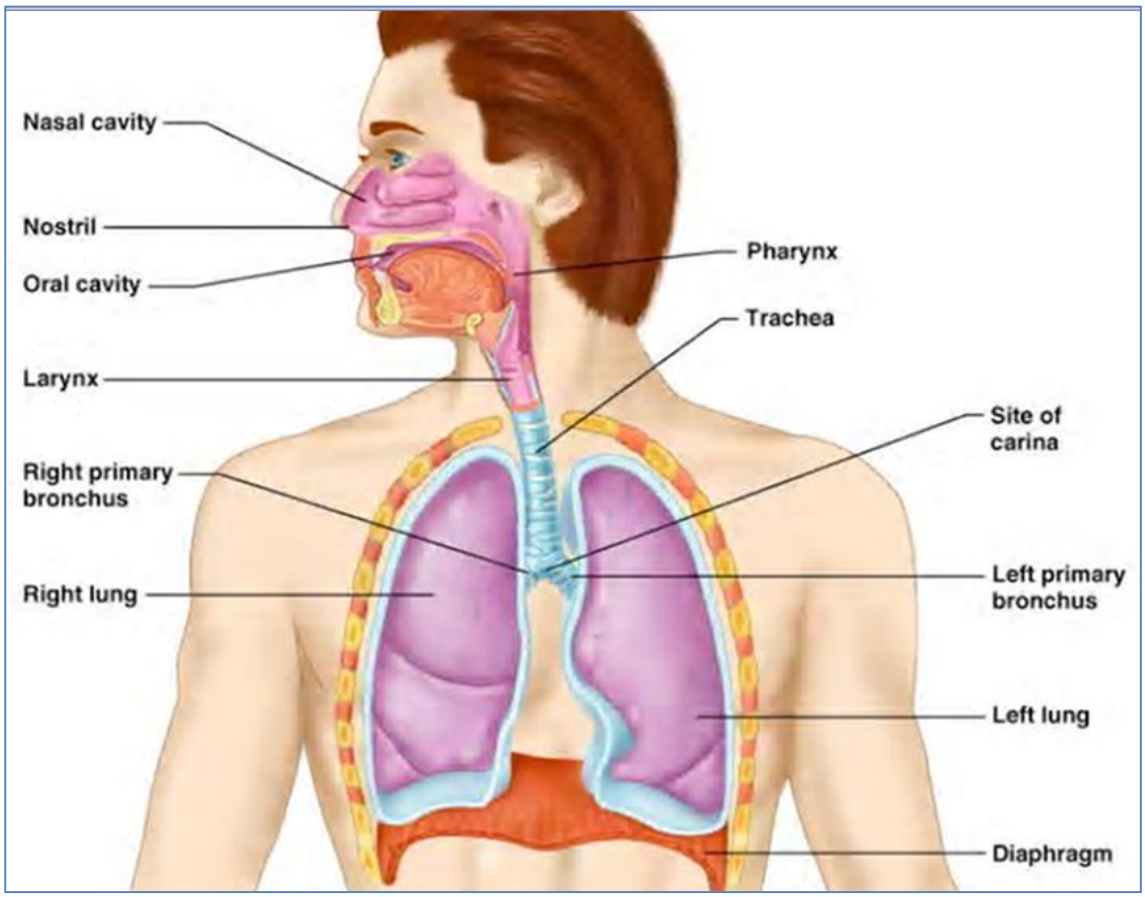
- **Costodiaphragmatic Recess:** (or just Diaphragmatic Recess)
    - 'Extra' space allocated to the lungs for use during forced inspiration
    - Allow extra expansion of the lungs



Respiratory Medicine Notes
Airways Anatomy

Structural Divisions:

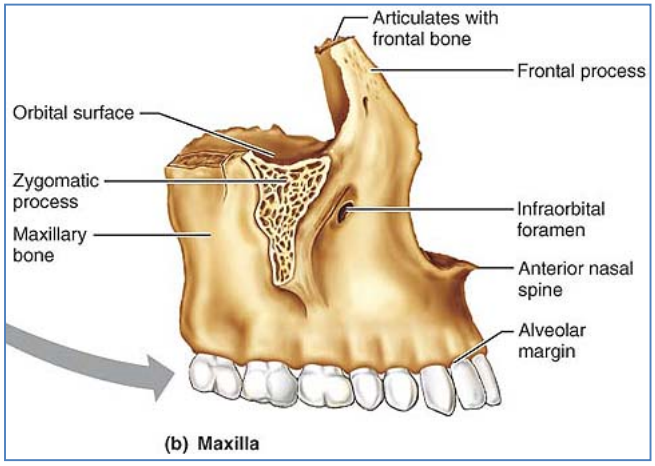
- **Upper Airways:**
  - Aka. 'Conducting' zones: Due to its conduit-like structure
  - Functions:
    - Filter particulate matter from air (debris & dust)
    - Mucosal Epithelium:
      - Warm incoming air
      - Moisten incoming air
  - Nose → Trachea
    - Nose
    - Nasal Cavities
    - Pharynx
      - Nasopharynx
      - Oropharynx
    - Larynx
    - Trachea
- **Lower Airways:**
  - Aka. 'Respiratory' zones: Due to site of gas exchange
  - Functions:
    - Facilitate Gas Exchange
    - O_2 in CO_2 out.
  - Bronchi → Lung
    - Respiratory bronchioles
    - Alveolar Ducts
    - Alveoli



The Facial Skeleton:

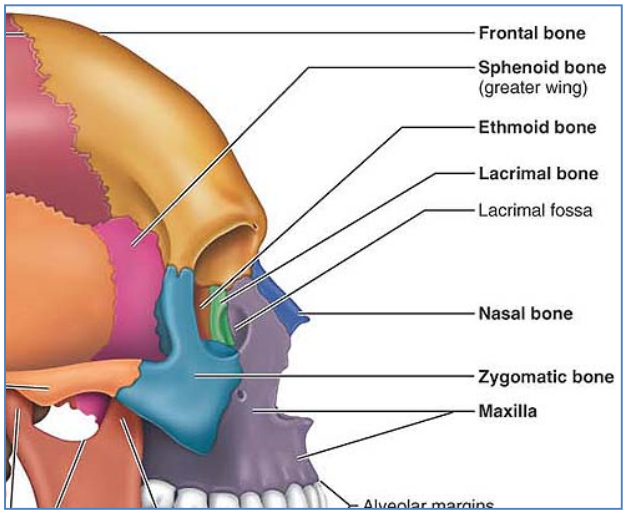
- **Important Communication Routes Exist Between:**
  - Eye Orbits & Nasal Cavities (**NasoLacrimal Duct (Tear Duct))**
  - Nasal Cavities & Paranasal Sinuses
  - Nasal Cavities & Oral Cavities
  - Ears & Pharynx (**Eustachian Tube** – equalises pressure within mid ear)
  - Pharynx & Larynx

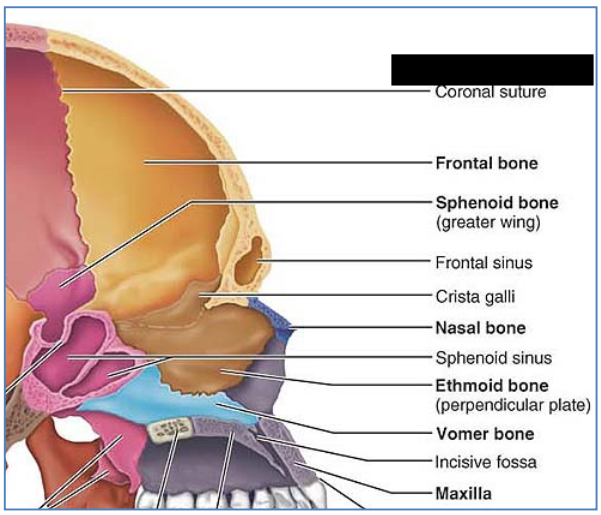
- **2 Maxillae:**
  - Fused Medially
  - Carry the upper teeth
  - Forms front 2/3 of hard palate.
  - 'Keystone' of the facial skeleton (Articulates with all facial bones except mandible)



- **Frontal Bone:**
  - Anterior Cranium
  - Contains the (frontal) sinuses
  - Connects to Ethmoid bone

- **Nasal Bones:**
  - Form the 'bridge' of the nose
  - Provide support for external cartilage -->nose structure

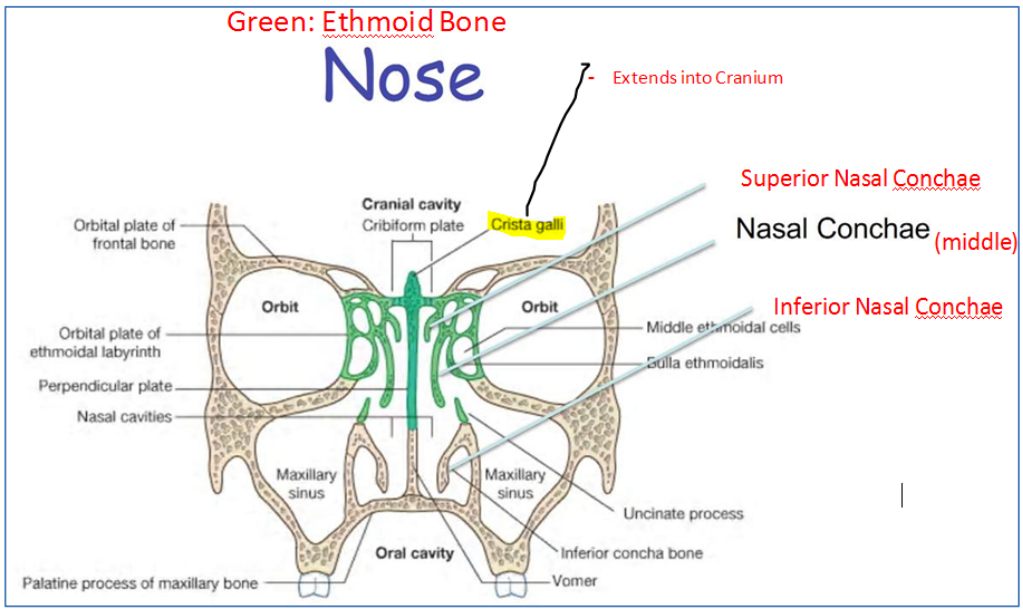


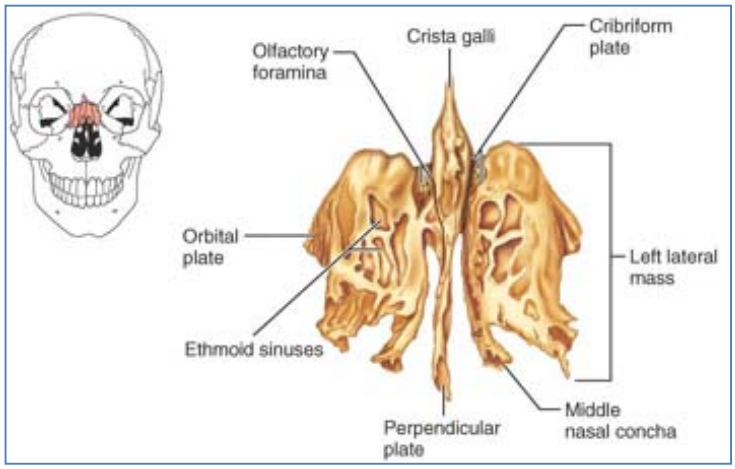


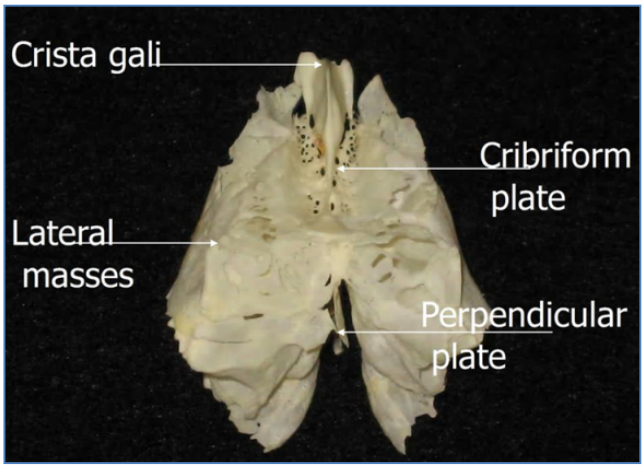
- **Ethmoid:**
  - Forms majority of nasal cavity
  - Anchors the cartilage of the nose
  - Turbulates the air - moisten + warm + filters
  - **Important Components:**
    - **2 Cribriform Plates** - Punctured by *olfactory foramina* – for olfactory nerves
    - **Crista Gali** (inside cranium) - Triangular process between the Crbriform Plates – Anchors the brain.
    - **Perpendicular Plate** (superior part of nasal septum) - Separates R&L Nasal Cavities
    - **L & R lateral Masses** – riddled with *ethmoid sinuses*
  - **Superior Nasal Conchae**
    - Turbulates the air - moisten + warm + filters
  - **Middle Nasal Cohchae**
    - Turbulates the air - moisten + warm + filters

- **Inferior Nasal Conchae:**
  - Small scroll of bone
  - Sit in inferior portion of nasal cavity
  - Paired
  - Attach to part of maxilla
  - Turbulates the air - moisten + warm + filters

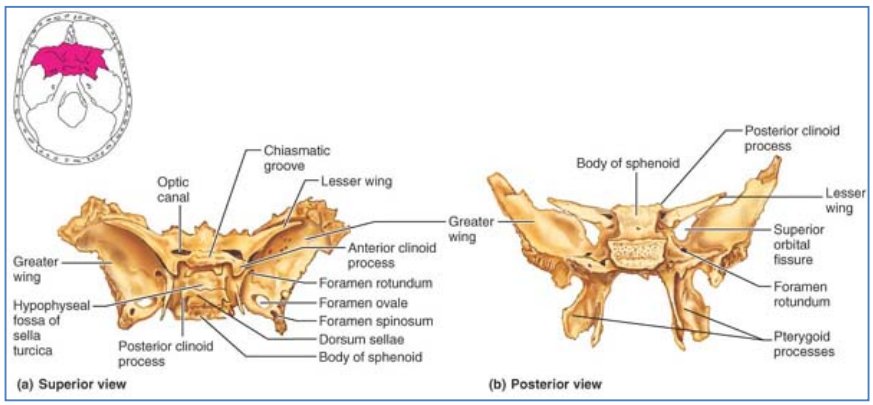
- **Vomer:**
  - Separates L & R nasal cavities (in association with the *Perpendicular Plate* of the *Ethmoid Bone*)
  - Base of nasal cavity





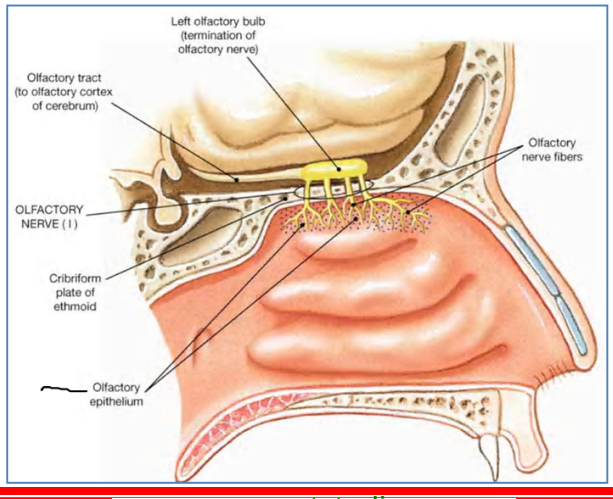


- **Sphenoid:**
  - 'keystone' of the cranium (articulates with all bones of cranium)
  - Butterfly-shaped
  - Contain paired Sphenoid sinuses

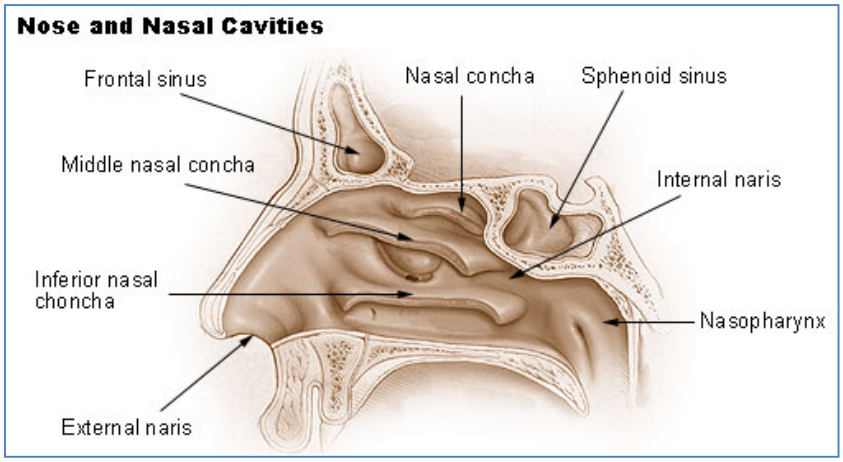


The Nose:

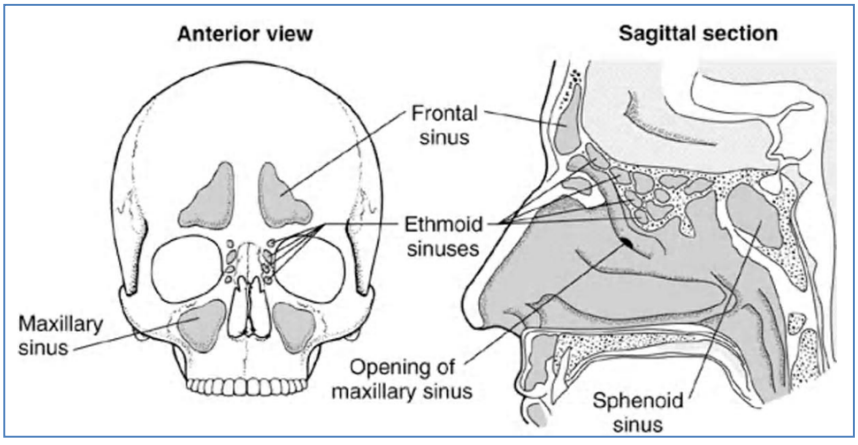
- Provides an airway for respiration
- Moistens & warms entering air
- Filters inspired air
- Doubles as a resonance chamber during speech
- Houses Olfactory (Smell) Receptors
- **External Nose:**
  - Skeletal framework consists of:
    - Nasal & Frontal bones Superiorly
    - Maxillary bones Laterally
    - Flexible Plates of Cartilage Inferiorly
- **Nasal Cavity:**
  - **Air Enters Through Nostrils:**
    - Lined with skin
    - Sebaceous & sweat glands
    - Numerous ***Vibrissae*** (Hair Follicles) – filter coarse particles from air.
  - **Epithelial Linings:**
    - **Olfactory Mucosa:**
      - Specialized epithelium involved with smell
      - Surface littered with olfactory neurons (receptors)
      - Olfactory neurons synapse with #1 CN (the Olfactory Nerve)
    - **Respiratory Mucosa:**
      - Pseudostratified Columnar Epithelium
      - Ciliated
      - Scattered Goblet Cells
      - Base of Lamina Propria rich in mucous & serous glands.



- **Divided in the middle by the nasal septum:**
  - Perpendicular Plate of Ethmoid (upper 2/3)
  - Vomer of the Sphenoid (lower 1/3)
- **Roof Formed by:**
  - Ethmoid Bone
  - Sphenoid Bone
- **Floor Formed by the *Palate*:**
  - Hard Palate – Palatine Bone
  - Soft Palate (Uvula) – Musculo-Tendinous Structure
- **Lateral Walls: *Conchae***
  - 3 on each wall
  - Superior/Middle/Inferior
  - Increase Mucosal Surface Area
    - Heat & Moisten the air during Inspiration.
    - Reclaims Heat & Precipitates Moisture during Expiration.
  - Enhance Turbulence – heavier, nongaseous particles are flung onto & stick to the mucosa



- **<u>Paranasal Sinuses:</u>**
  - **<u>Exist In 4 Bones:</u>**
    - **Maxillae**
    - **Frontal**
    - **Sphenoid**
    - **Ethmoid**
  - All continuous with nasal cavity
  - Increase surface area
  - Create turbulance
  - Help to humidify & warm inflowing air.
  - Lighten the skull
  - Provides resonance for 'quality' of voice. (eg. Voice changes with blocked sinuses)



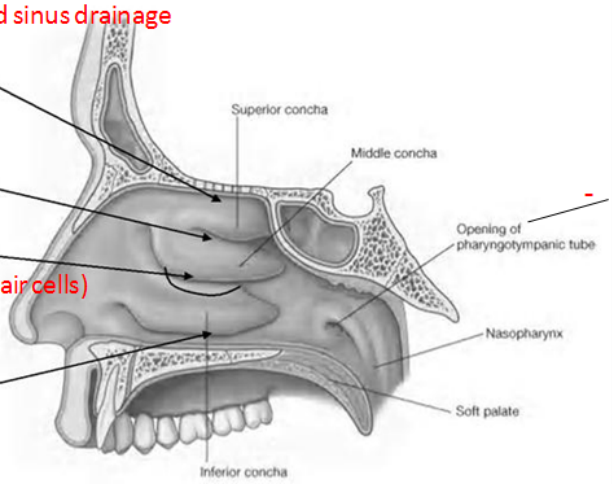
Meatal Regions - where the sinuses drain into the nasal cavity

Where each of the sinuses drains to:

Paranasal Sinuses

- Sphenoethmoidal recess:
  - Sphenoid sinus
- Superior Meatus
  - Posterior ethmoidal cells (air cells)
- Middle Meatus
  - Middle/anterior ethmoidal cells (air cells)
  - Frontal sinus
  - Maxillary sinus
- Inferior Meatus
  - nasolacrimal duct
    - Drainage point from the eye to the nasal cavities
    - Runs through the lacrimal bone
    - Explains why when you cry, you get a runny nose

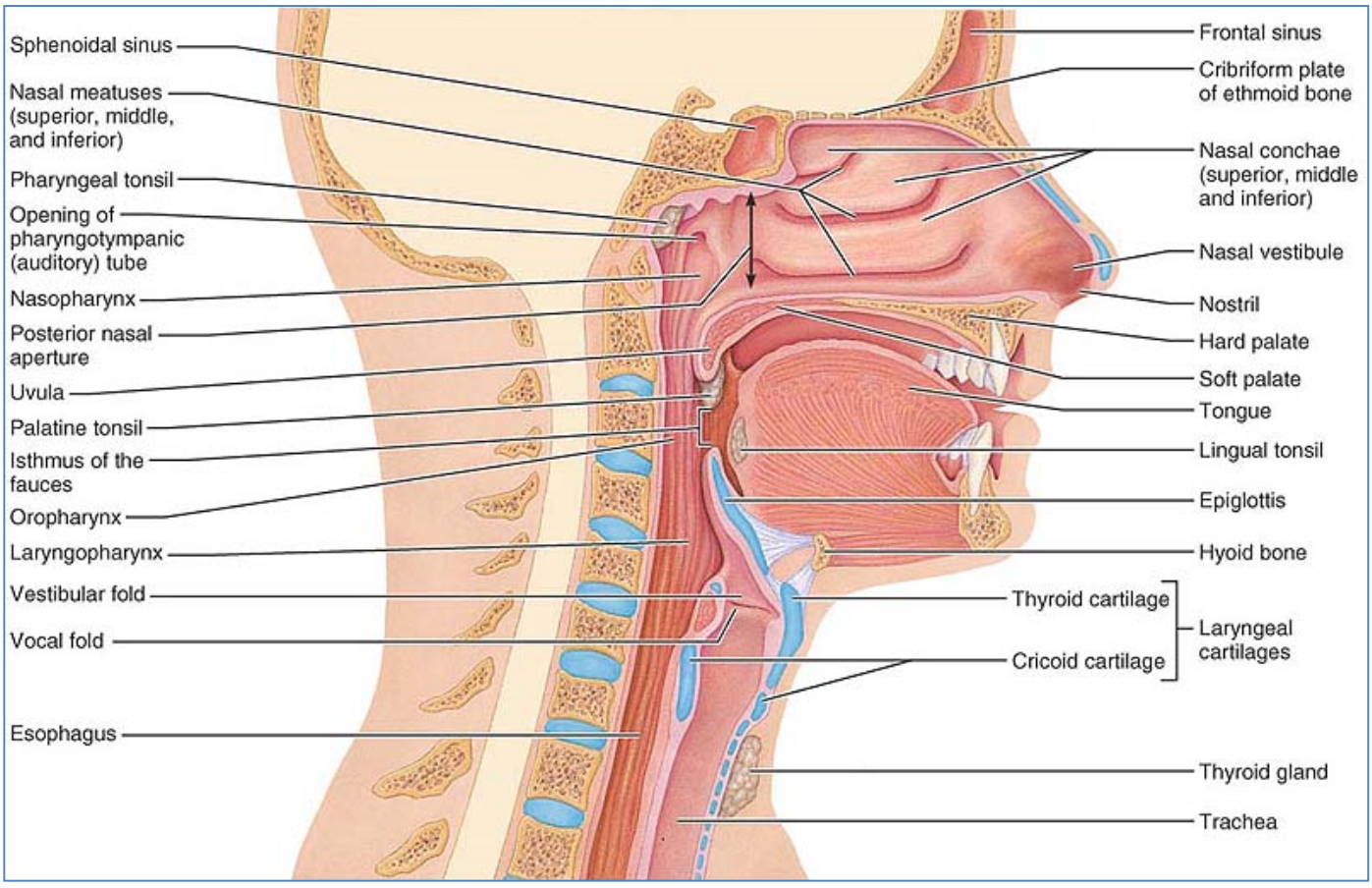
Sphenoid sinus drainage



- For equalising the pressure in the middle ear with the external atmospheric pressure.

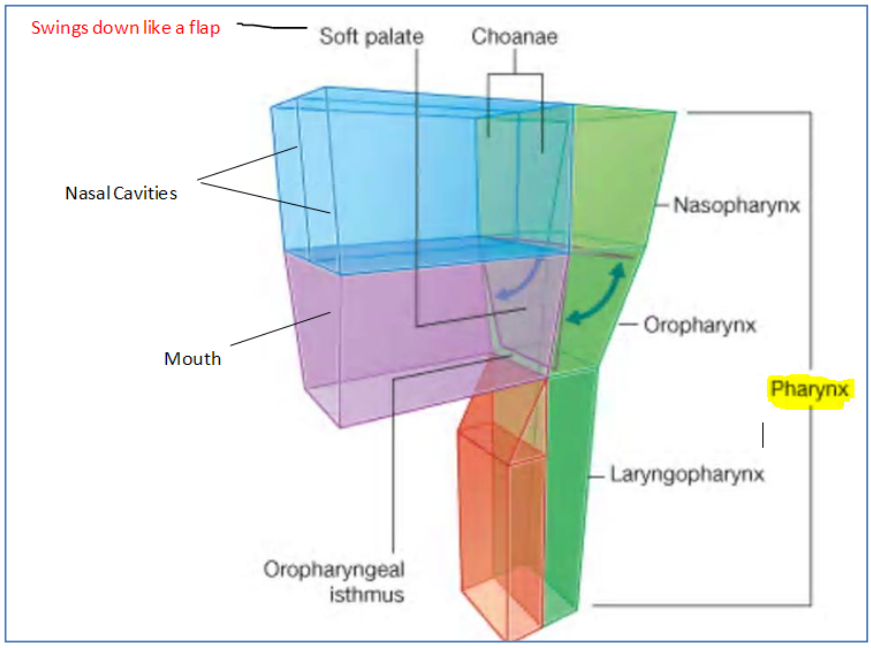
NB: During infection, the openings of the sinuses may become blocked by excessive mucus production.

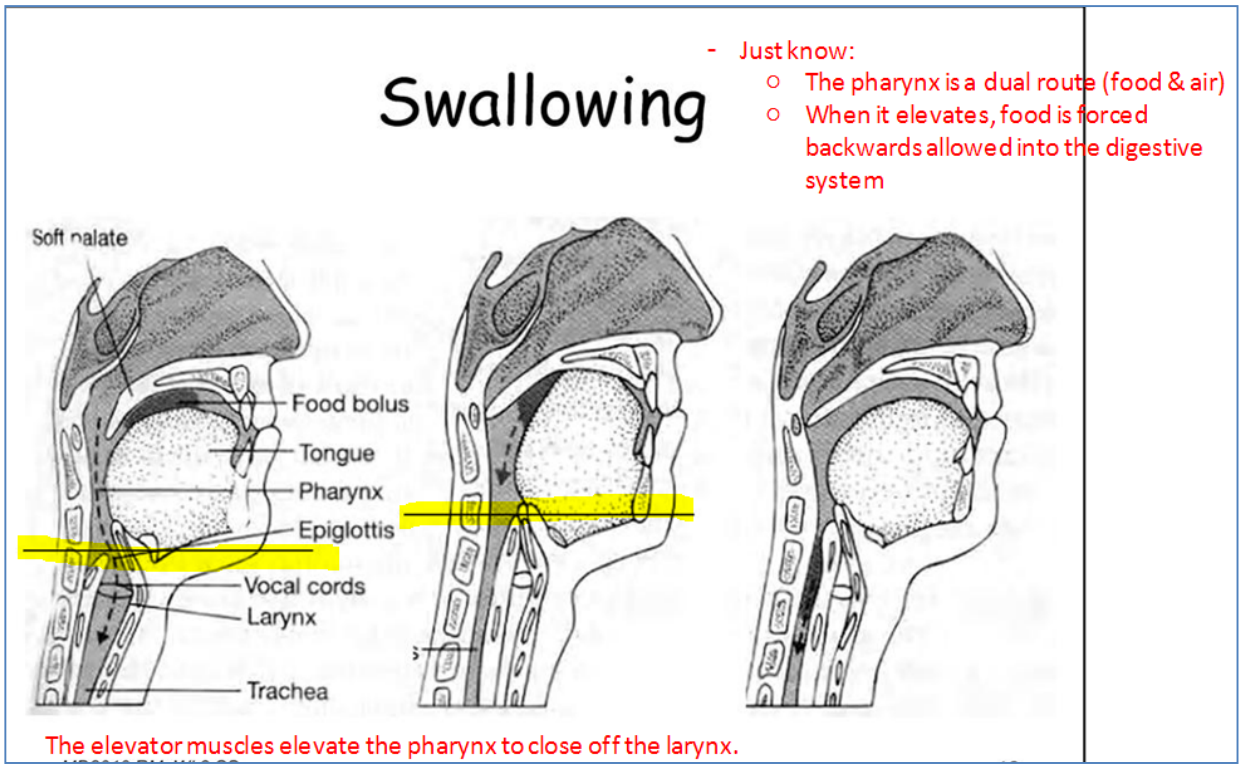
- This can lead to excessive pressure inside the sinuses → pain



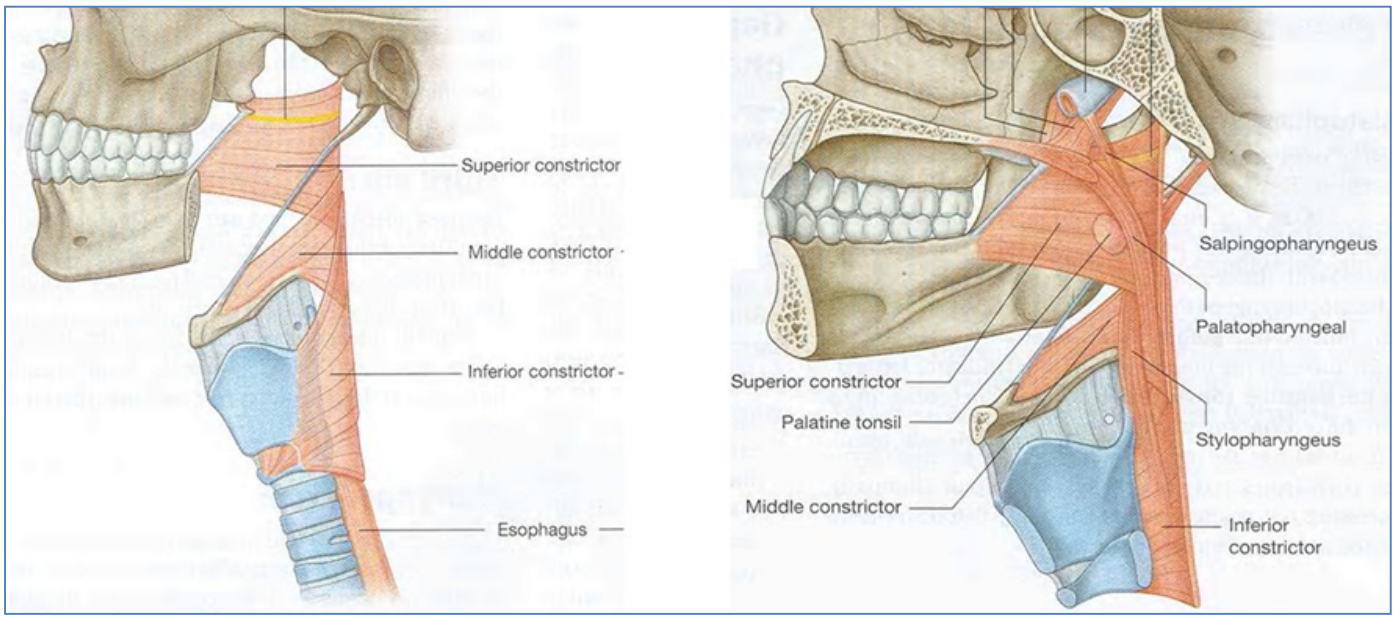
The Pharynx:

- Upper part of GIT
- Connects Nasal Cavities, Oral Cavity & Oesophagus
- Completely Muscular Tube – Origins: Base of skull (Temporal/Sphenoid/& Occipital Bone)
- **Epithelium of Each Region:**
    - **Nasopharynx:**
        - Air passageway ONLY.
        - *Pseudostratified Ciliated Epithelium*
    - **Oropharynx:**
        - Both Food & Air Pass Through it. → More protection is needed.
        - *Stratified Squamous Epithelium*
    - **Laryngopharynx:**
        - Both Food & Air Pass Through it. → More protection is needed.
        - *Stratified Squamous Epithelium*
        - During swallowing, food has 'right-of-way' (breathing is halted temporarily)

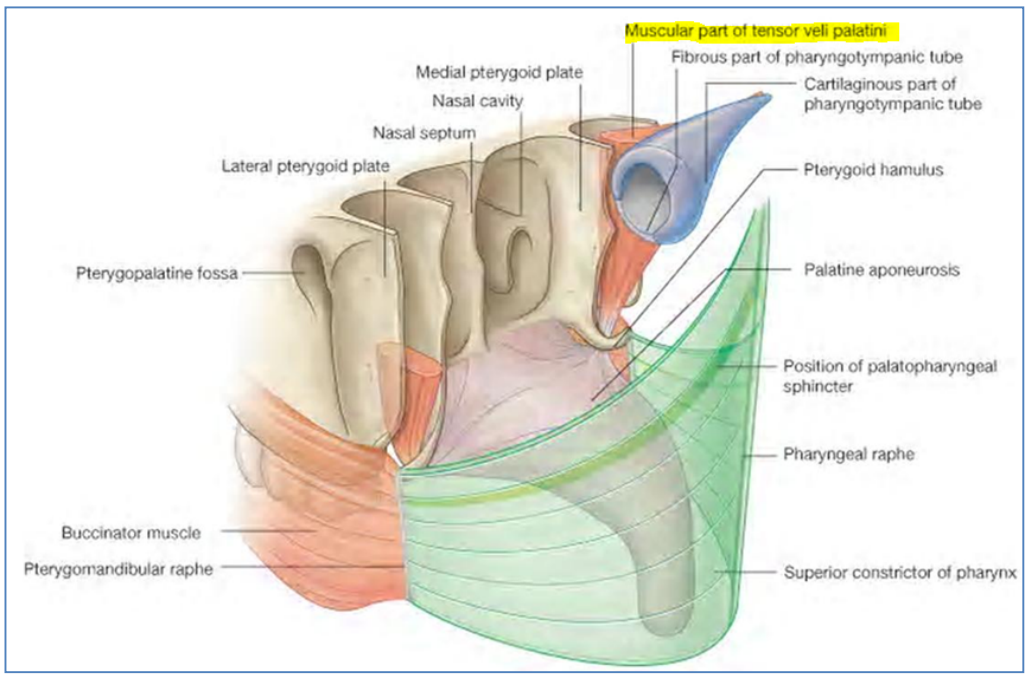




- **2 Muscle Groups: (DON'T NEED TO KNOW NAMES – JUST FUNCTION)**
  - **3x Constrictor Muscles:** (move food down to the *laryngopharynx*)
    - Superior/Middle/Inferior
  - **3x Longitudinal Muscles:** (Elevate the Pharynx – prevent food in trachea)
    - Palatopharyngeus/Saspingopharyngeus/Stylopharyngeus



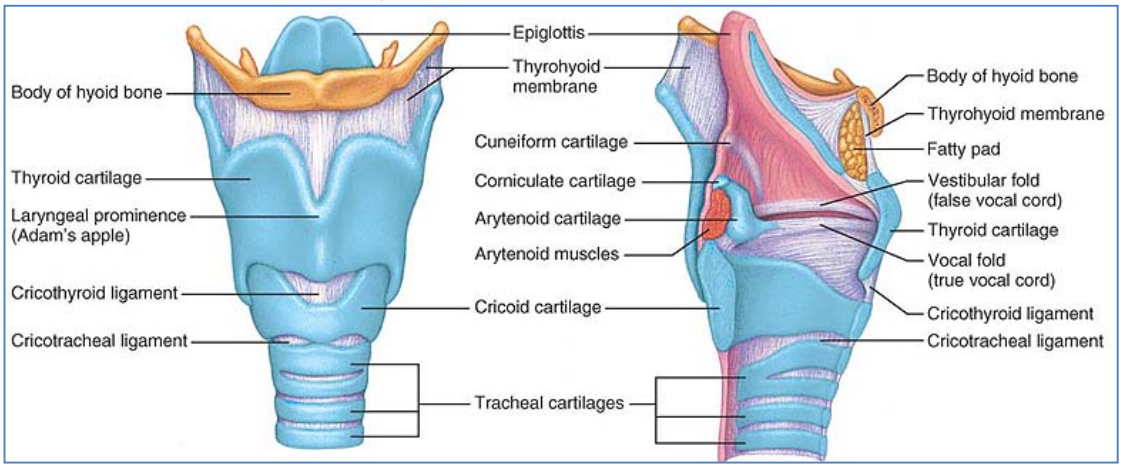
- **Soft Palate:**
  - Posterior aspect of oral cavity
  - Separates Oral Cavity & Nasopharynx
  - Involved during *Deglutition*
  - Made of & Operated By 5 Muscles:
    - Levator Veli Palatini
    - Tensor Veli Palatini
    - Palotoglossus
    - Palatopharyngeus
    - Musculus Uvulae
  - Supplied by *Vagus Nerve*



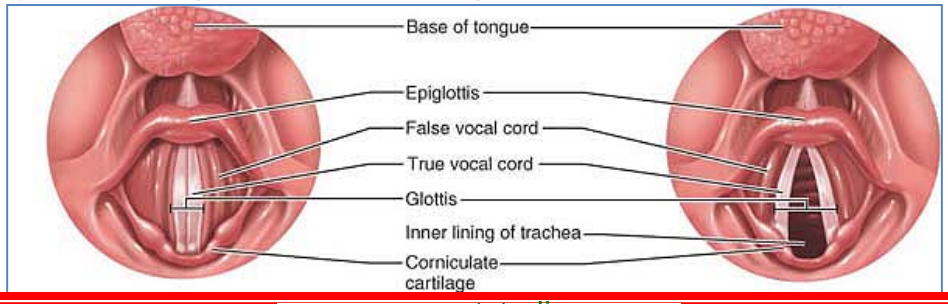
- **Eustachian Tube:**
  - Between Nasopharynx & Middle Ear
  - Important in equalising pressure in the 2 cavities.
- **Hard Palate:**
  - Formed by Maxillae & Palatine Bones.

The Larynx: ("Voicebox")

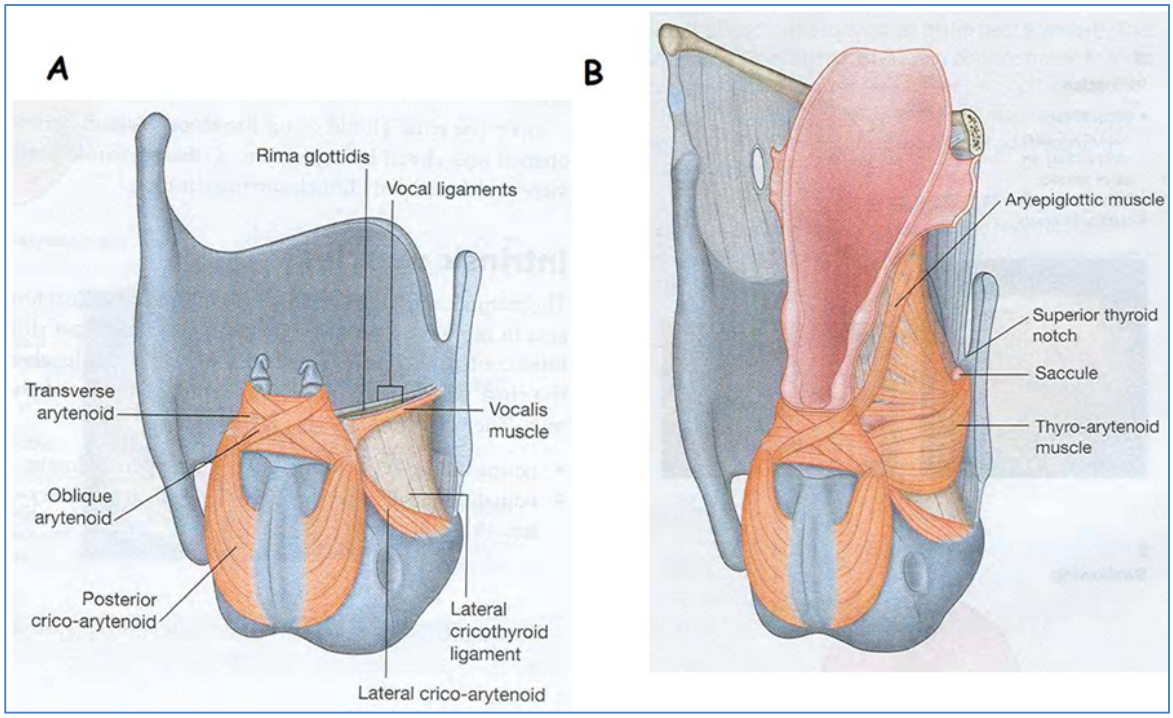
- Opens into the Laryngopharynx
- Superiorly, it attaches to the Hyoid Bone
- Inferiorly, it merges with the Trachea
- **3 Functions:**
  - Provide an open airway (breathing)
  - Direct Air & Food into proper channels
  - Voice production. (Phonation)
- **Made of 9 Cartilages:**
  - **3 Unpaired Cartilages:**
    - Form the Tube-Like Skeletal Framework of Larynx
    - **Thyroid Cartilage**
    - **Cricoid Cartilage**
    - **Epiglottis**
  - **3 Paired Cartilages (6 total):**
    - Involved in moving the Vocal Ligaments (Adduction & Abduction)
    - **Arytenoid Cartilage**
    - **Cuneiform Cartilage**
    - **Corniculate Cartilage**



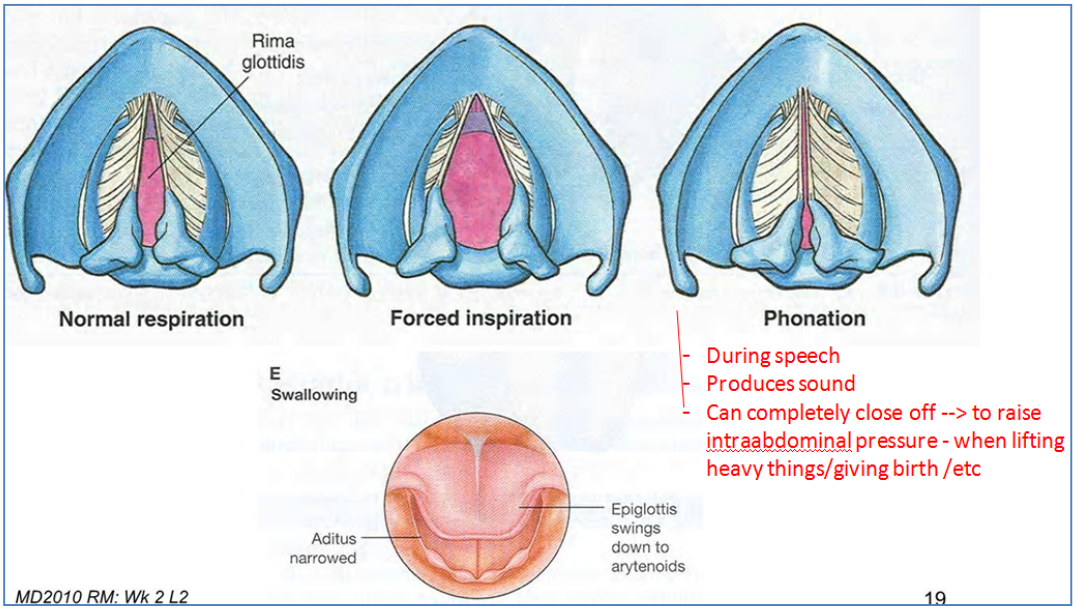
- **Vocal Ligaments:** '*True* Vocal Cords' ("Cricothyroid Ligament/Membrane")
  - Covered in mucosa
  - Made of Elastic Fibres
  - Fibres vibrate as air rushes up from lungs. (tighter = higher pitch)
  - Appear white – no blood vessels
  - Attach the *Arytenoid Cartilages* to the *Thyroid Cartilage*
  - Form the 'Vocal Folds' or '*True* Vocal Cords'.
- **Vestibular Folds:** *'False Vocal Cords'* ("Quadrangular Ligament/Membrane")
  - Play no part in sound production
  - Help to close the 'glottis' when swallowing.



- **Muscles:** (aka. Intrinsic laryngeal muscles)
  - Work to affect tension/length/position of vocal cords.
  - All Controlled By the Vagus Nerve
    - **2x Cricothyroid Muscle**
    - **2x Vocalis**
    - **2x Transverse Arytenoids**
    - **2x Oblique Arytenoids**
    - **2x Posterior Crico-Arytenoids**
    - **2x Lateral Crico-Arytenoids**
    - **2x Thyromuscularis**
  - **DON'T NEED TO REMEMBER NAMES!**

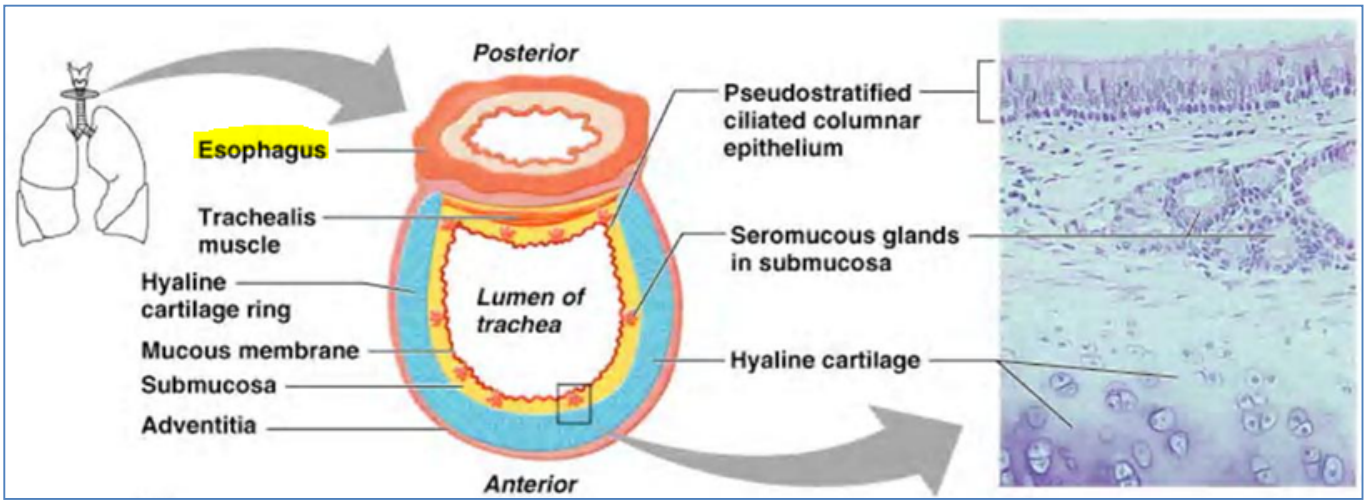


- **Vocal Ligament Positions:**



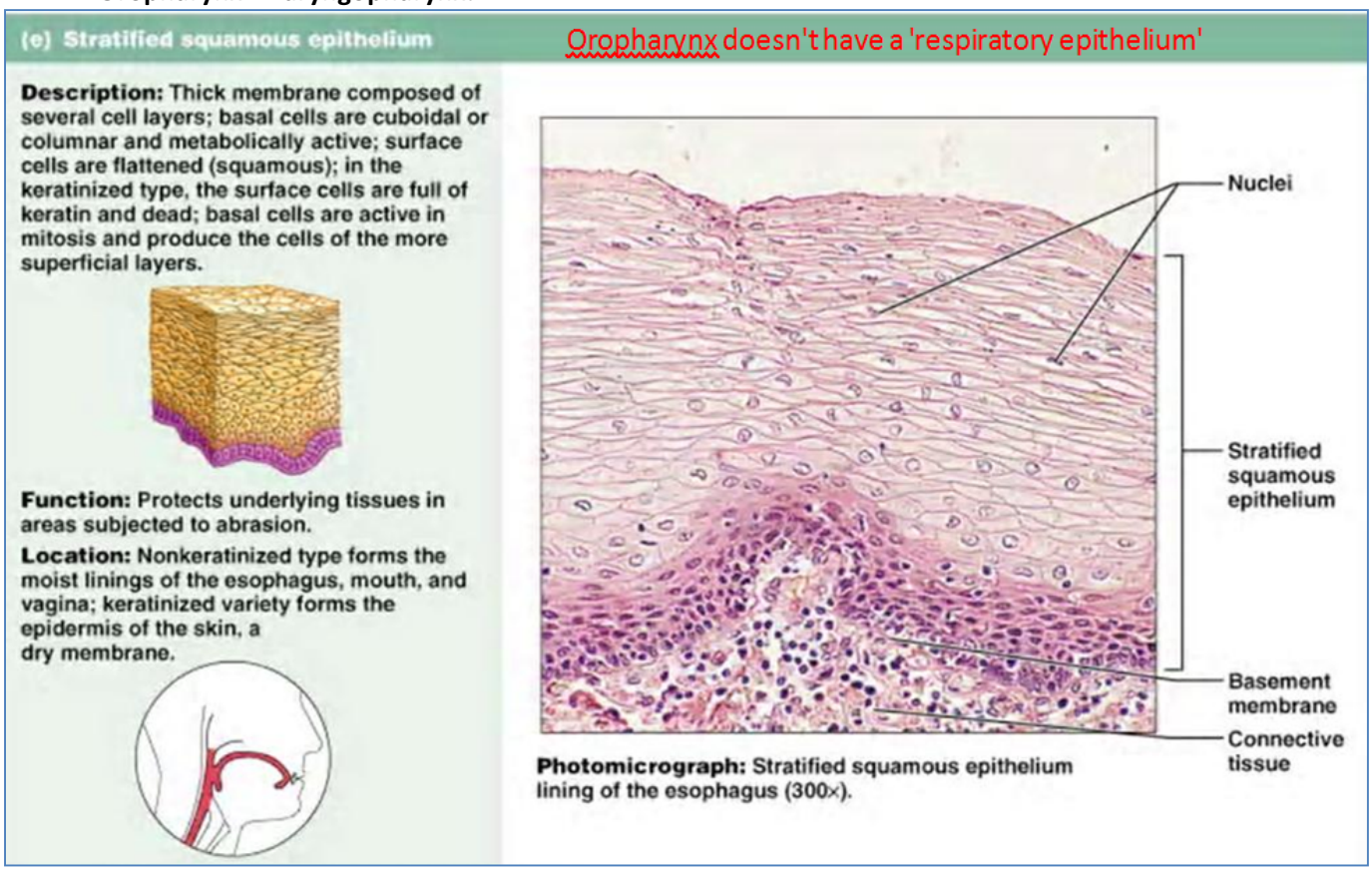
Trachea:

- The continuation of the pharynx
- A membranous tube of Conn. Tissue
    - + smooth muscle
    - Reinforced by 15-20 C-Shaped Cartilage Rings (incomplete posteriorly)
- Begins at C6
- Terminates at Bifurcation → Bronchi @ T4
    - NB. Right Bonchus is more vertical than the Left – hence inhaled objects tend to go down here.

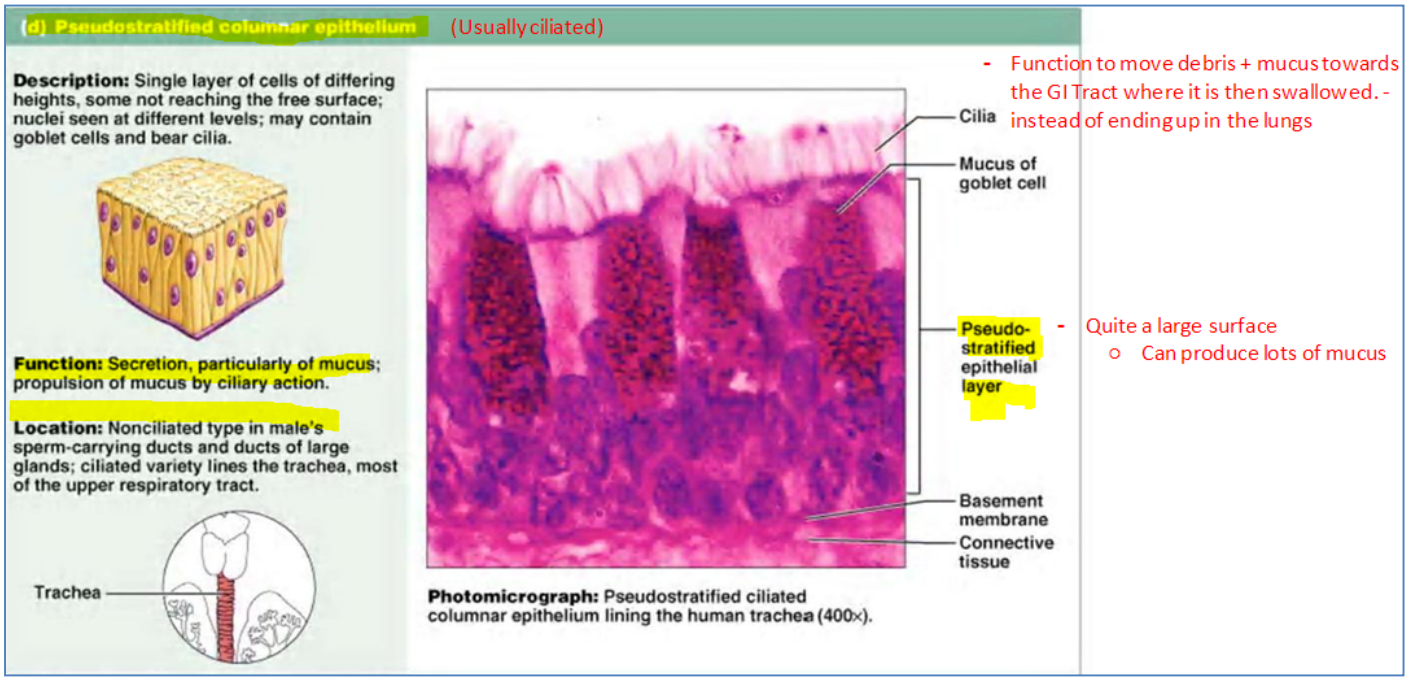


Mucosal Linings:

- **Oropharynx + Laryngopharynx:**

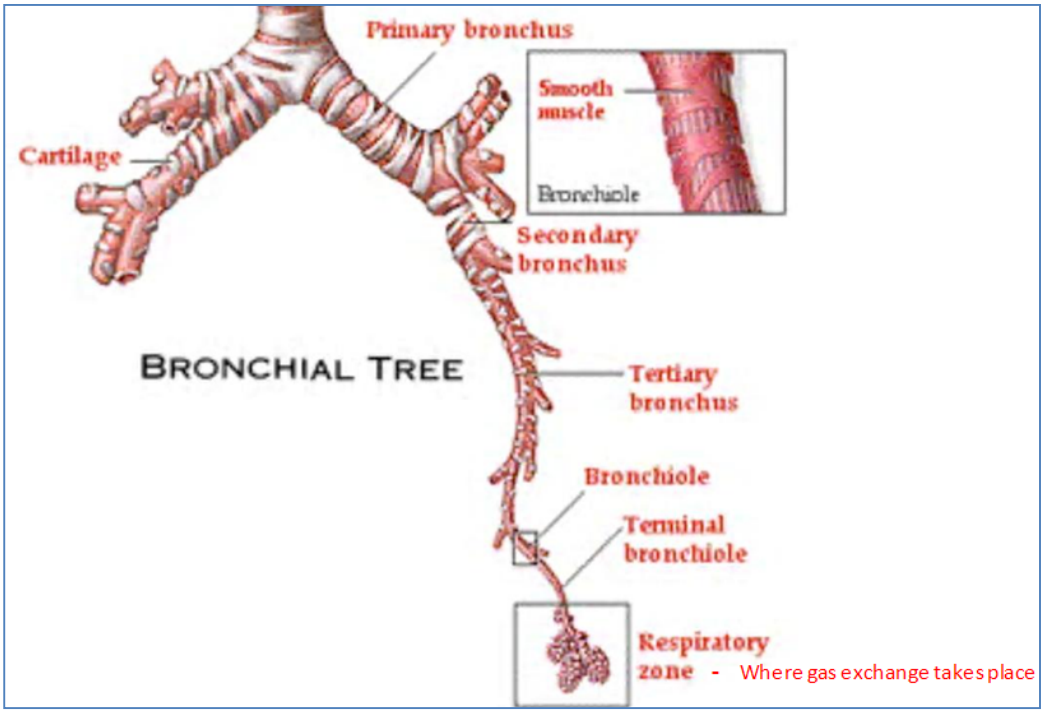


- **Trachea:**



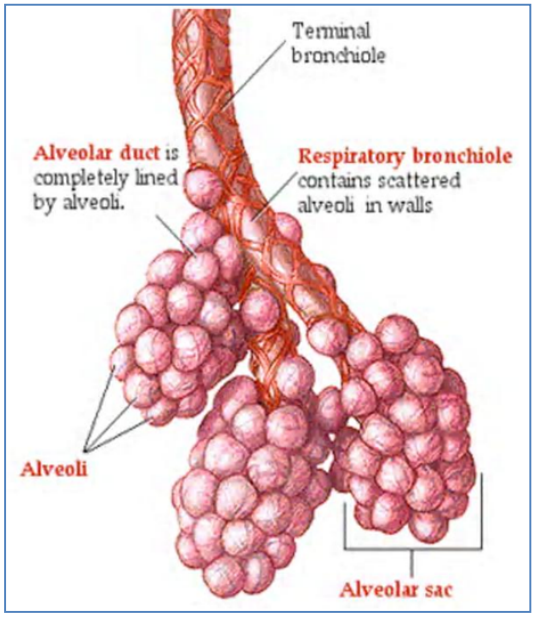
The Bronchial Tree:

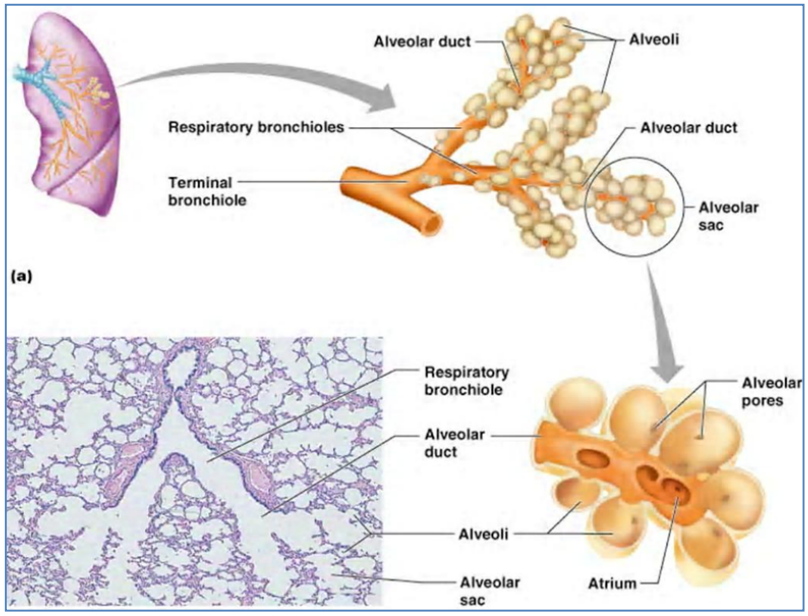
- Where *conducting structures* merge with *respiratory structures*.
- Once inside the lungs, the bronchi branch profusely until the *bronchioles* ("little bronchi") are <0.5mm thick.
- **Gradual Structural Changes:**
  - Cartilage rings replaced by irregular *plates* of cartilage.
  - No cartilage at all in *bronchioles*
  - Mucosal Epithelium thins from Pseudostratified → Columnar → Cuboidal in the bronchioles.
  - Cilia are sparse



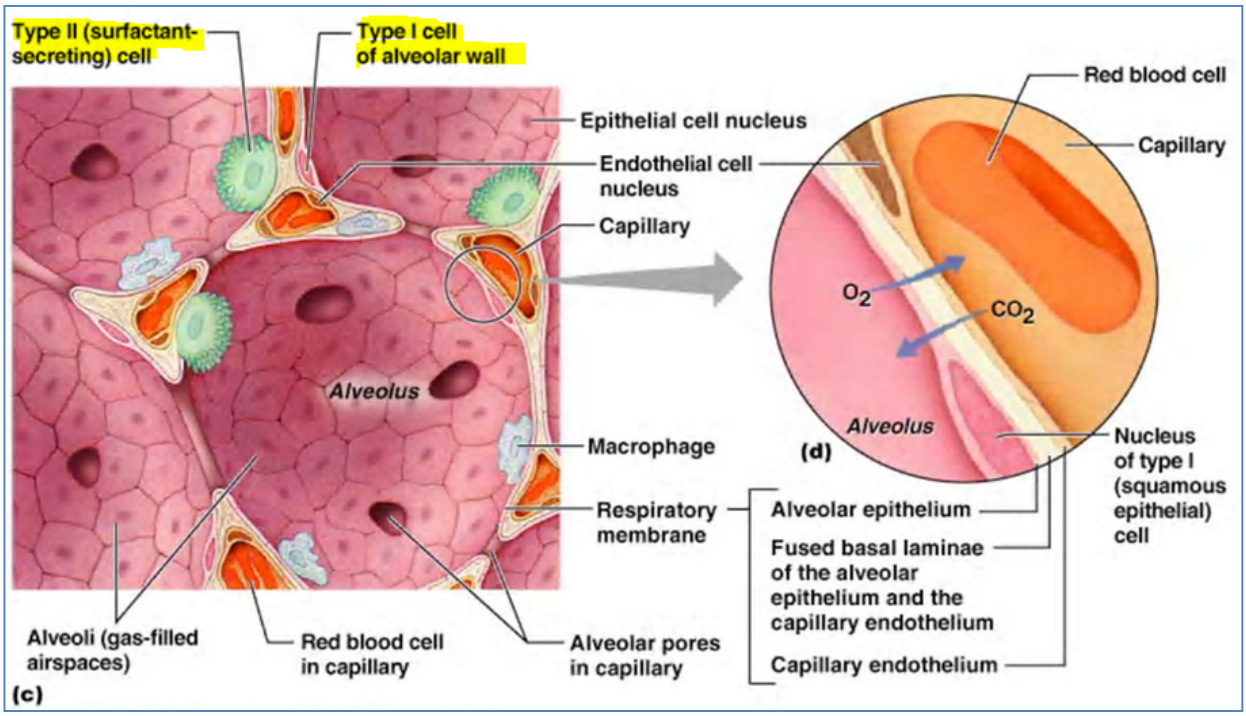
The Respiratory Zone:

- Formed by alveoli
- Gas Exchange happens in 2 Places:
  - Tube-Like Ducts
  - Ballon-Like Sacs
- Large SA – for Gas Exchange





- **2 Types of Alveolar Cells:**
  - **Type I Alveolar Cells:**
    - Aka. Squamous Alveolar Cells
    - Gas Exchange Alveolar
    - Make up the Alveoli Walls
  - **Type II Alveolar Cells:**
    - Aka. Great Alveolar Cells
    - Secrete Pulmonary Surfactant (lower the surface tension of water → easier breathing.



Lung Challenges in Premature Births:

- **Immature Lung: (Premature Birth – Under 34 Weeks of Gestation)**
    - Thick Blood-Gas Barrier
        - Impedes diffusion of gasses across the membranes
    - Immature epithelial cells:
        - Less surfactant production (ordinarily lowers the surface tension of the fluid in lung)
            - Means it will be harder for the lungs to inflate
    - Small area for gas exchange:
        - Effective diffusion of gasses requires huge surface areas.
    - Poorly Vascularised:
        - Lower capacity to oxygenate blood.
    - High Resistance to blood flow

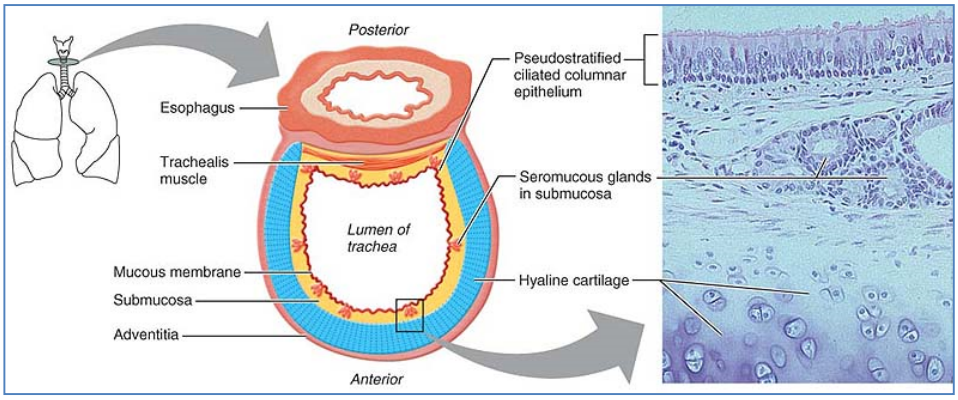
- **Mature Lung: (34+ Weeks of Gestation)**
    - Thin Blood Gas Barrier
        - Facilitates diffusion of gasses across the membranes
    - Mature epithelial cells
    - Adequate surfactant production
    - Large area for gas exchange
    - Highly vascularised
    - Low resistance to blood flow

- **NB:** 34 Weeks: an age marker for premature birth.
    - Babies born before this may suffer respiratory stress & possibly die.

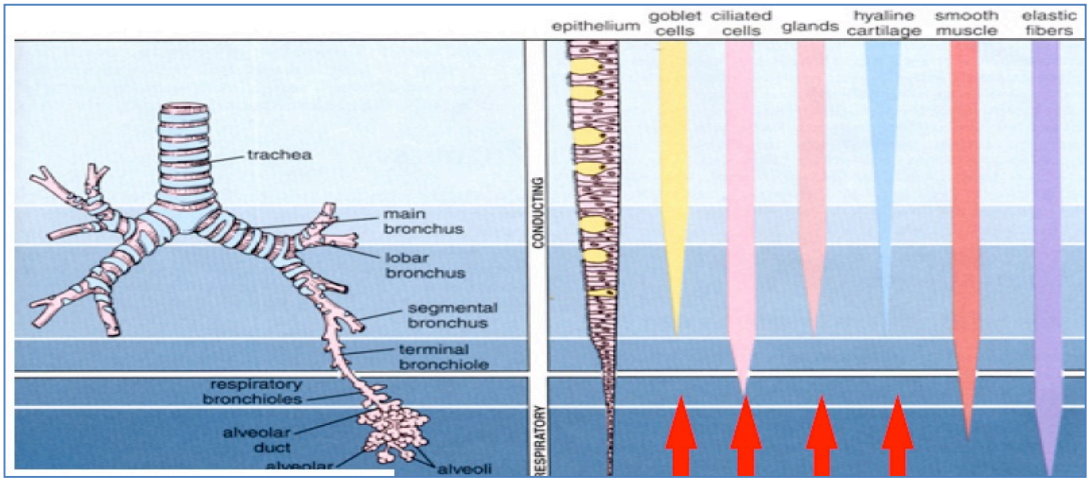
Airway Mucosal Function + Intro To Chronic Bronchitis & Cystic Fibrosis

Features of Airway Mucosa:

- **Trachea:**
  - **Mucosa:**
    - Ciliated PseudoStratified Epithelium
    - Goblet Cells → Mucous
    - Lamina Propria (of dense elastic fibres → high elasticity)
  - **Submucosa:**
    - Submucosal Mucous Glands (Seromucous Glands)
  - **Adventitia (Outer Covering):**
    - Conn. Tissue
    - Cartilage Rings
    - Trachealis Muscle (- Constricts trachea during coughing)
  - NB: Place at Highest Risk of Infection – Common Infection best @ 33-35°C (Lower Airways Hotter)

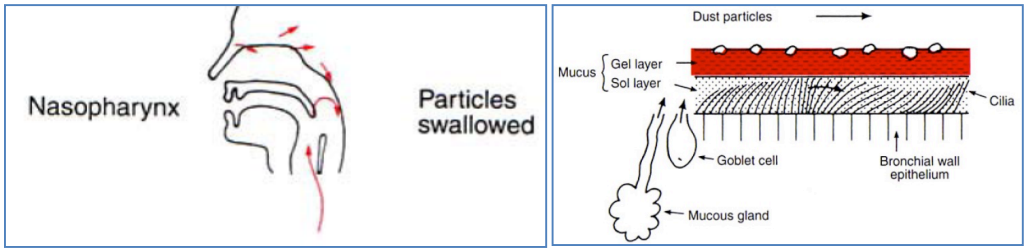


- **Bronchi:**
  - **Mucosa:**
    - Ciliated Pseudostratified → Ciliated Columnar Epithelium (lower bronchi)
    - Goblet Cells → Mucous
    - Cilia Decreases
  - **Submucosa:**
    - Submucosal Mucous Glands (Seromucous Glands)
  - **Adventitia:**
    - Irregular Cartilage Rings → Cartilage Plates (lower bronchi)
    - Proportion of Smooth Muscle Increases
- **Bronchioles:**
  - Sparsely-Ciliated Simple Cuboidal Epithelium
  - No Goblet Cells
  - No Submucosal Mucous Glands
  - No Cartilage Support (Elastic Fibres Instead → Radial Traction)
  - Increased Proportion of Smooth Muscle

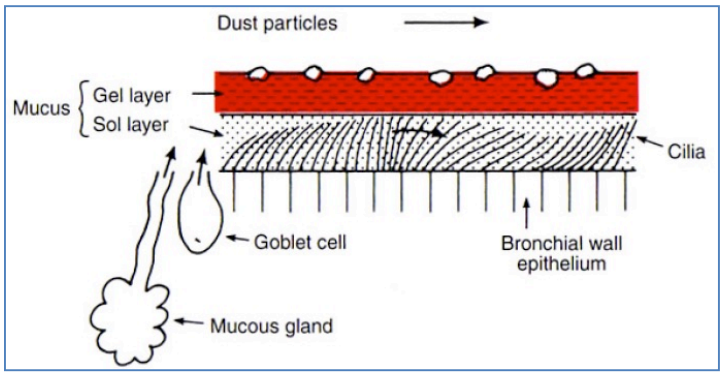


Clearance of Inhaled Particles:

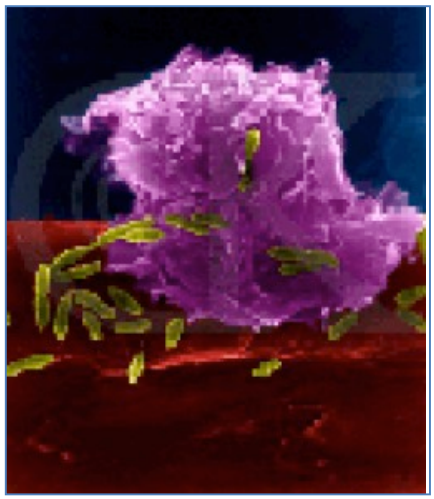
- **Cilia in Nasopharynx:**
  - Cilia Beat Backwards towards Pharynx → Swallowed

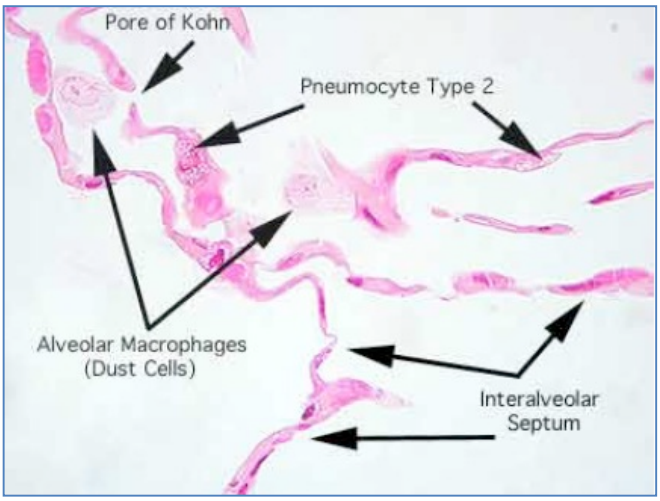


- **Mucociliary Escalator:**
  - Ciliated Epithelium in *Conducting Zone*
  - Mucous from Goblet Cells & Submucosal Glands → Traps Particles
  - Cilia Beat Upwards towards Pharynx → Swallowed/Coughed Up.
    - 2 Strokes = Power & Recovery
    - Mucous Movement ≈ 1-2mm/min
  - Airway Surface Liquid Layer (Sol) Critical for Cilia Function.



- **Alvoli Macrophages:**
  - Particles Phagocytosed by Alveolar Macrophages
  - Able to Migrate *Into* Alveoli
  - Use Destructive Enzymes to Destroy Foreign Particles + Bacteria.
    - NB: Dead Macrophages *Release* these enzymes → Lung Damage.
  - Debris Are Either:
    - Dumped into Lymphatics
    - Delivered to Mucociliary Escalator

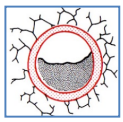




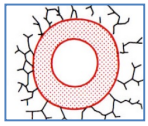
Chronic Obstructive Pulmonary/Airway Diseases (COPD/COAD):

- **What Are They?:**
  - Permanent *NARROWING/OBSTRUCTION of the AIRWAY.*
  - Ie**. Increased Resistance to AirFlow.**
    - NB: Airway has Greatest Resistance to Airflow in the entire Respiratory System – Due to Smallest Cross-Sectional Area
  - – Is an 'Umbrella Term' – Usually Refers to Chronic Bronchitis, Emphysema, or Mixture of BOTH.
  - NB: Non-permanent airway obstruction (eg. Asthma) = VOPD/VOAD (Variable Obstructive……..)

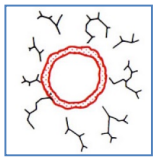
- **3 Causes:**
  - **1. Conditions With The Lumen:**
    - Excessive Mucous Production
    - Aspiration of Foreign Material



  - **2. Conditions Within The Wall of the Airway:**
    - Inflammation of Mucosa (Chronic Bronchitis or Asthma)
    - Oedema of Airway Wall (Chronic Bronchitis or Asthma)
    - Contraction of Bronchial Smooth Muscle (Asthma)
    - Hypertrophy of Mucous Glands (Chronic Bronchitis)



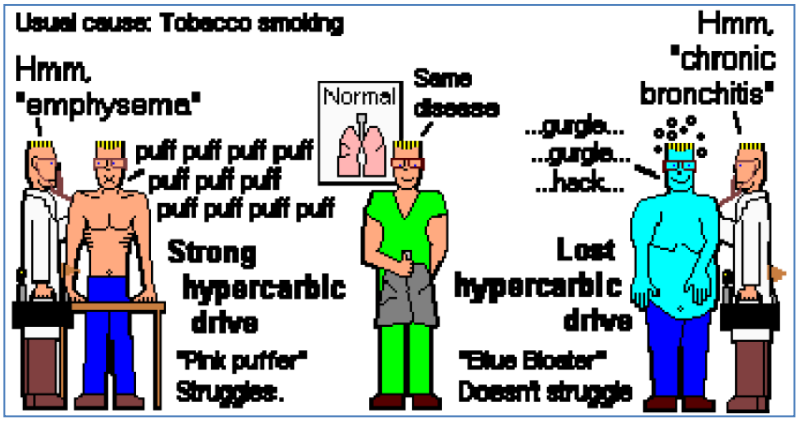
  - **3. Conditions Outside The Airway:**
    - Destruction of Lung Parenchyma (eg. Emphysema)
      - ↓Radial Traction
      - ↓Airway Diameter
    - Localised Compression of Airway
    - Peribronchial Oedema
      - ↑Transmural Pressure → ↓Airway Diameter



- **Clinical Features:**
  - **Type A – Pinker 'Puffer':**
    - **Indicative of: *Emphysema***
    - Blood Gasses Normal
    - Little/No Cough
    - Breathless
    - Quiet Breath Sounds
    - No Peripheral Oedema

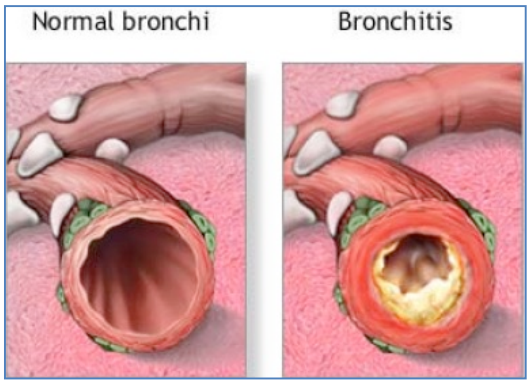
  - **Type B – Blue 'Bloater':**
    - **Indicative of: *Chronic Bronchitis***
    - Low O_2 + High CO_2 + Cyanosis → Blue (hence name)
    - Frequent Productive Cough
    - Breathless
    - Loud, Abnormal 'Crackling' Breath Sounds ("Crepitations"/"Rales")
    - May Have Peripheral Oedema

  - NB: patients may exhibit both.



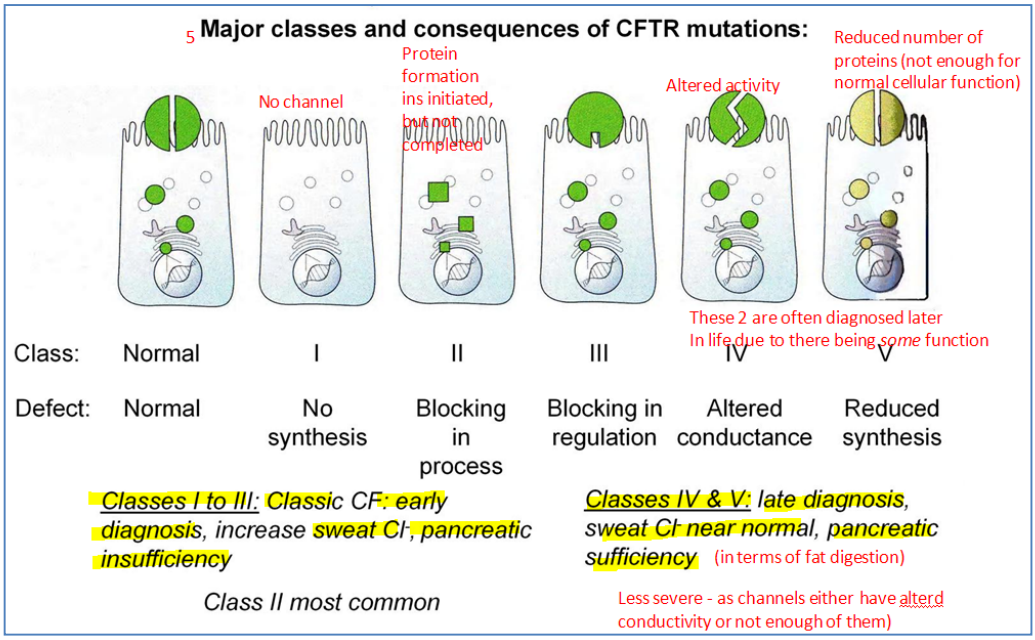
COPD Examples:

- **Chronic Bronchitis (CB):**
  - **What is It?**
    - *Excessive, Continuous Long-Term Mucous Production in Bronchial Tree* → Excessive Sputum
    - Very Common in Smokers & Polluted Cities.
  - **Pathogenesis:**
    - 2 Major Factors:
      - Chronic Irritation & Inflammation – By Inhaled Substances
      - Infection
  - **Pathology:**
    - ↑Number & Size of Mucosal & Submucosal Glands
      - →↑Mucosal Thickness
      - (Extent of Gland Hypertrophy – Measured by Reid Index):
        - Ratio of Gland Size: Submucosa Thickness
    - Mucous-Secreting Cells Spread to Lower Airways (*Bronchioles*) – (Where they shouldn't).
      - Cilia Can't handle Excess Mucous → Semisolid Mucous *Plugs* Occlude Small Airways.
    - Inflammation → Increased Airway Thickness
  - **End Result:**
    - Narrowed Airway...By:
      - ↑Mucous Production
      - ↑Mucosa Thickness
    - ↑Energetic Cost of Breathing (normally 3-5%...CB can reach 30% or RMR)

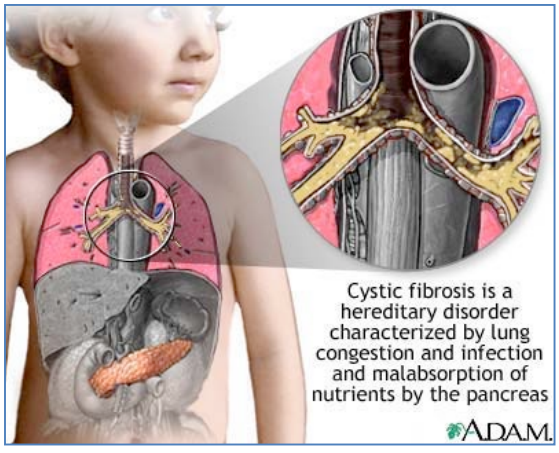


  - **Treatment:**
    - **Clearing of Sputum:**
      - Maintaining Hydration
      - Postural Physiotherapy
    - **Drugs:**
      - **β-Agonists (Via Nebuliser):**
        - Bronchodilators
        - Stimulate the β-Adrenergic Receptors (usually stimulated by the sympathetic NS) → dilation of the airways → reduced obstruction → Better airflow.
      - **Anticholinergic Drugs (Ipratropium Bromide):**
        - Inhaled
        - Blocks Muscarinic Receptors in Lung →
          - Inhibits Bronchoconstriction
          - Inhibits Mucus Production
      - **Corticosteroids + Antihistamines:**
        - Anti-Inflammatory Drugs →
          - Reducing swelling
          - Reduce mucus production in the airways

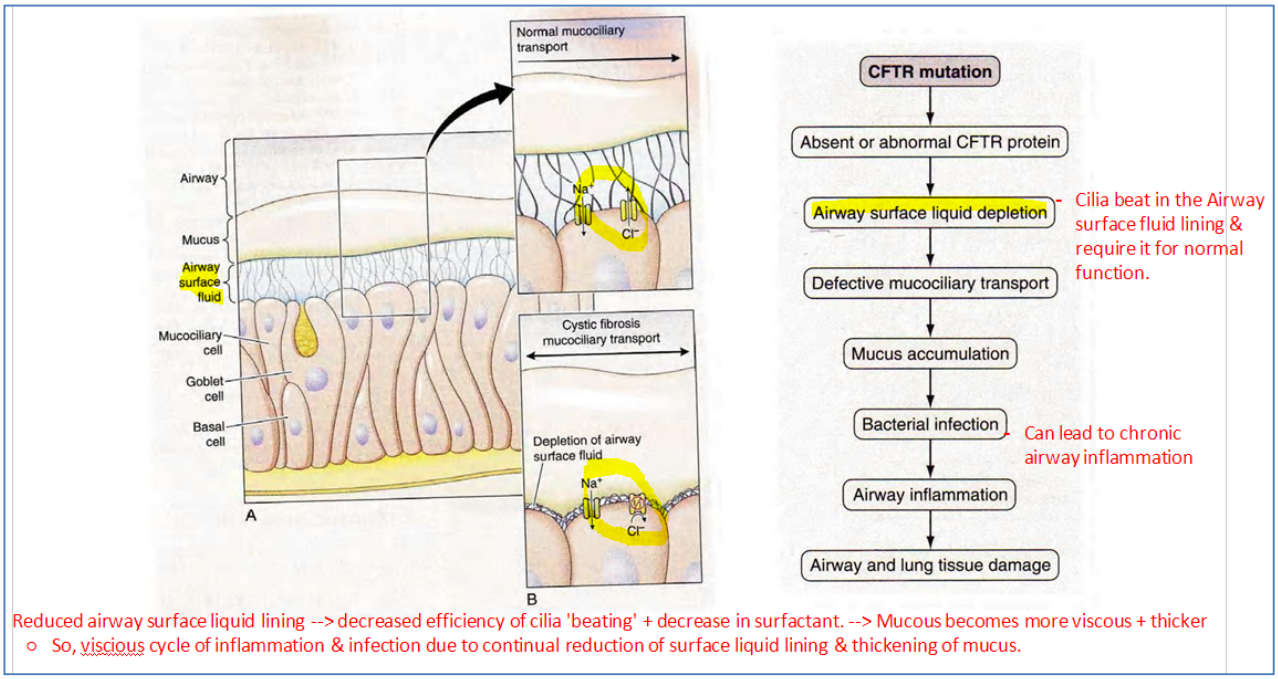
- **Cystic Fibrosis (CF):**
  - **What is It?**
    - **Genetics:**
      - **Simple Autosomal Recessive** Mendelian Inheritance
        - ≈1/25 people are carriers.
      - **Mutation/s in the CFTR Gene on Chromosome 7**
        - CFTR – Encodes for a specific Active-Cl^- -Ion-Channel
        - Normally Regulates Salt-Concentration in Epithelial Secretions
        - Cl^- Channels linked to Epithelial Na^+ Channels (ENaC) → Control Na^+ Resorbtion.
      - **Different mutations** → Different Effects/Symptoms/Onset
    - **5 Classes of CFTR Cl^- Channel Mutations:**
      - I - No Channel At All
      - II - Channel Formation Initiated – But Not Completed → No Channel
      - III – Channel Formed – Regulation ("On-Switch") is Disabled
      - IV – Channel Formed – But Activity Altered/Slowed.
      - V - Channels Formed – But Not Enough For Cellular Function



  - **Clinical Features:**
    - Mainly Pancreas Affected → Malabsorpiton of Nutrients → Malnutrition
    - Salty Sweat
    - Fatty, Liquid Stools
    - Chronic Lung Obstruction/Infection – Due to:
      - Bronchiectasis – Local, Irreversible Dilation of Bronchial Tree → Chronic Sputum
      - Bronchiolitis – Inflammation of Bronchioles
      - Mucociliary Insufficiency



- **Pulmonary Pathology:**
  - **Airway Surface Liquid Depletion:**
    - Due to Absent/Abnormal CFTR Protein.
    - Cilia Normally beat in this fluid lining (ie. Required for Ciliary Function)
    - Depletion → Defective Mucociliary Transport
    - ↓Surfactant → Thicker + More Viscous Mucous
  - **Neutrophil Death → Extracellular DNA:**
    - Rapid Turnover of Neutrophils – Due to chronic infections
    - Extracellular DNA → ↑Mucous Viscosity
  - **Mucus Thickening + Accumulation:**
    - Hypertrophied Mucus Glands → Excessive Secretion
    - Impaired Ciliary Activity → Mucus Plugs
    - →Chronic Infection
    - Crepitations (Crackling) & Rhonchi (Rattling/Whistling) – Heard through stethoscope



Reduced airway surface liquid lining --> decreased efficiency of cilia 'beating' + decrease in surfactant. --> Mucous becomes more viscous + thicker
- So, viscious cycle of inflammation & infection due to continual reduction of surface liquid lining & thickening of mucus.

- **Pulmonary Function:**
  - Abnormal Ventilation *Distribution* – (Dramatic Shifts in Local VQ-Ratios)
  - ↓FEV_1 (Forced Expiratory Volume in 1 Second) – Ie. Max Air Expelled in 1 Sec.
  - ↑Reserve Volume & Functional Reserve Capacity (Due to Air-Trapping in lungs)
  - ↓Elastic Recoil of lung (due to fibrosis)

- **Management:**
  - Antibiotics for Infections
  - Physio & Postural Drainage of Sputum
  - Mucolytic Agents (Eg. DNAse → Destroys Extracellular DNA → ↓Mucous Viscosity)
  - Future 'Cure' → Gene Therapy

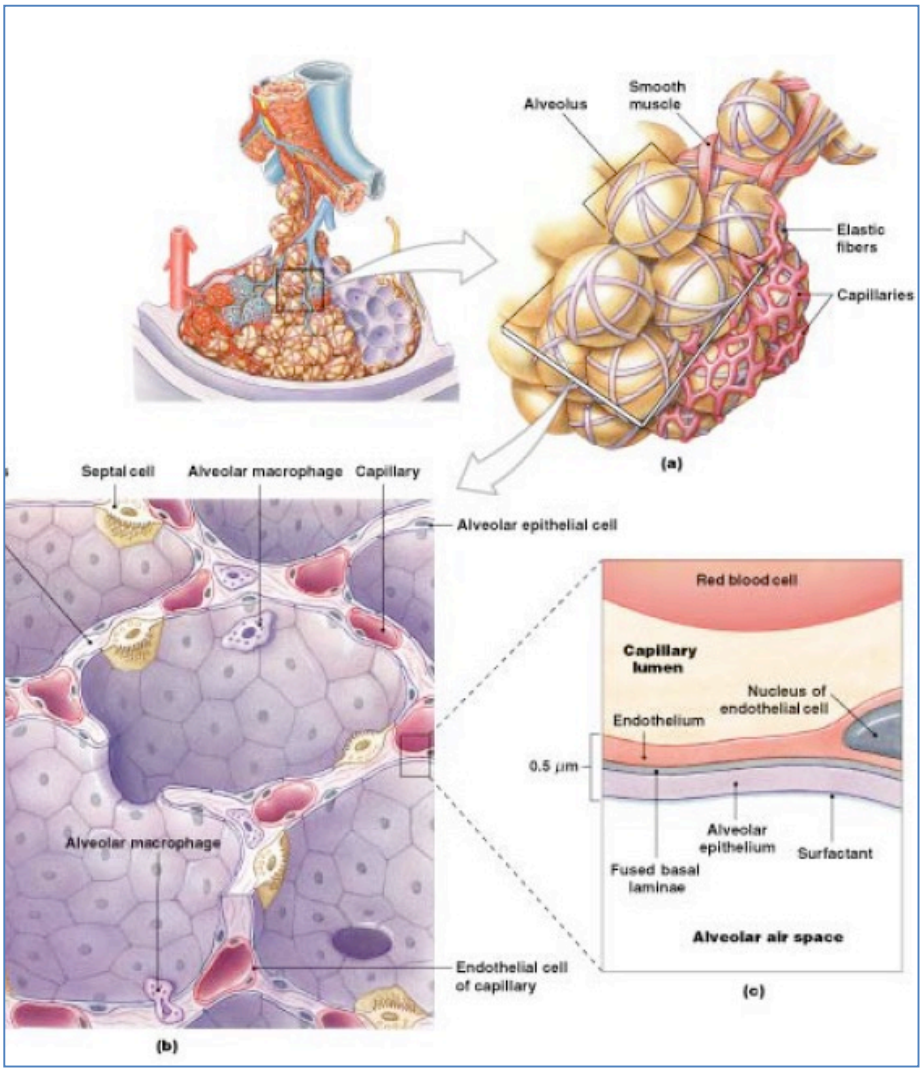
Respiratory Medicine Notes
Alveolar Gas Exchange & Gas Transport

Body's Aim:

- **Get O_2 from Lungs → Blood**
- **Get CO_2 from Blood → Lungs**

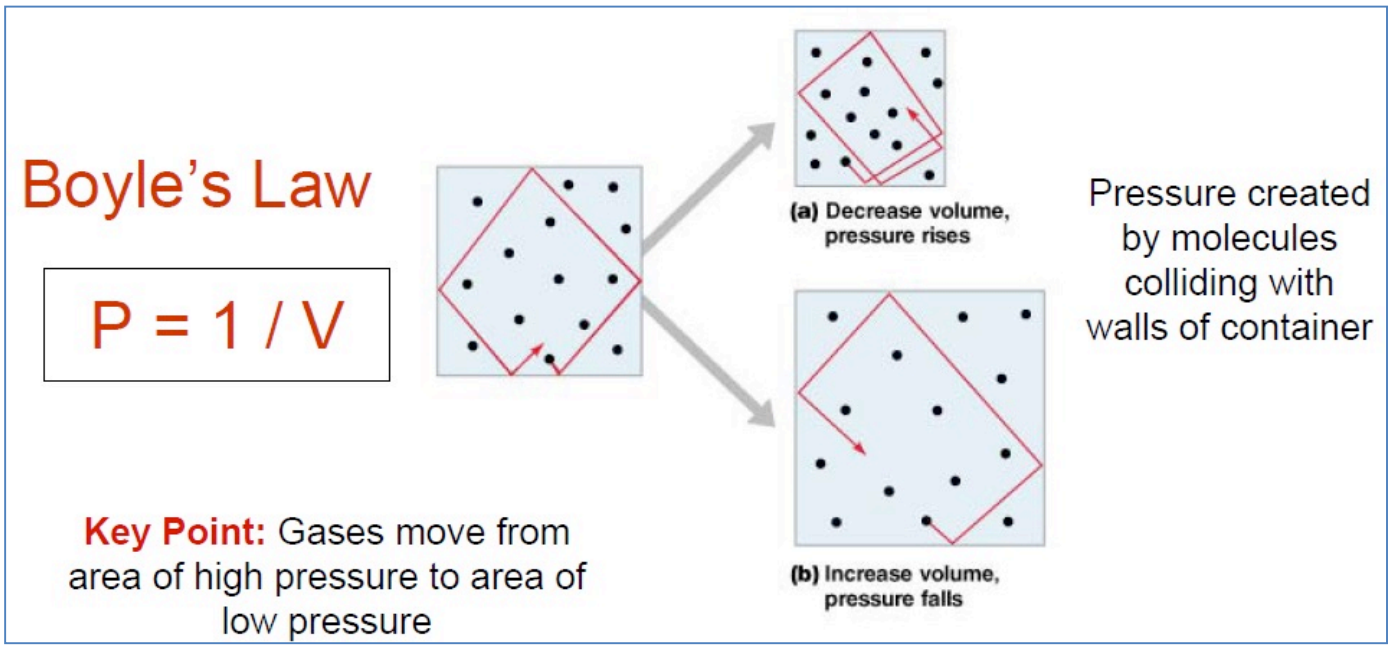
Path of Oxygen Molecules From Air → Blood:

- **Convection: Air into Lungs (Active)**
  1. Atmosphere
  2. Alveoli
- **Diffusion: Air Diffuses into Blood (Passive)**
  3. Alveolar Fluid Lining (surfactant)
  4. Tissue Barrier
     - Alveolar Epithelium
     - Basal Lamina
     - Interstitium
     - Endothelium (Vessel wall)
  5. Blood Plasma
  6. RBC Membrane
  7. Uptake by Haemoglobin
- **Convection: Blood Pumped Around Body (Active)**
- **Diffusion: Air Diffuses From Blood → Peripheral Cells (Passive)**



Laws Governing Movement of Respiratory Gasses:

- **Boyle's Law (of gas volumes):**
  - Facilitates movement of Air *Into/Out-of* the Lungs.
  - (*inverse relationship* between *gas volume & pressure*)
    - $P_1/V_1 = P_2/V_2$
  - Gases move from areas of High → Low Pressure.



- **Dalton's Law (of partial pressures):**
  - The total pressure of a mixture of gasses is equal to the sum of each gas's partial pressure.
    - Eg. Atmospheric Pressure (sea) = 760mmHg = sum of $P_{Nitrogen}$, P_{Oxygen}, P_{Water} & $P_{CarbonDioxide}$
  - Also, the proportion (%age) of a gas in a mixture =
    - The %age of the total pressure that it contributes =
      - Its partial pressure.
  - Simply: *Each gas in a solution exerts a pressure exactly proportional to its abundance*.

Remember: Atmospheric pressure is 760 mmHg (at sea level)

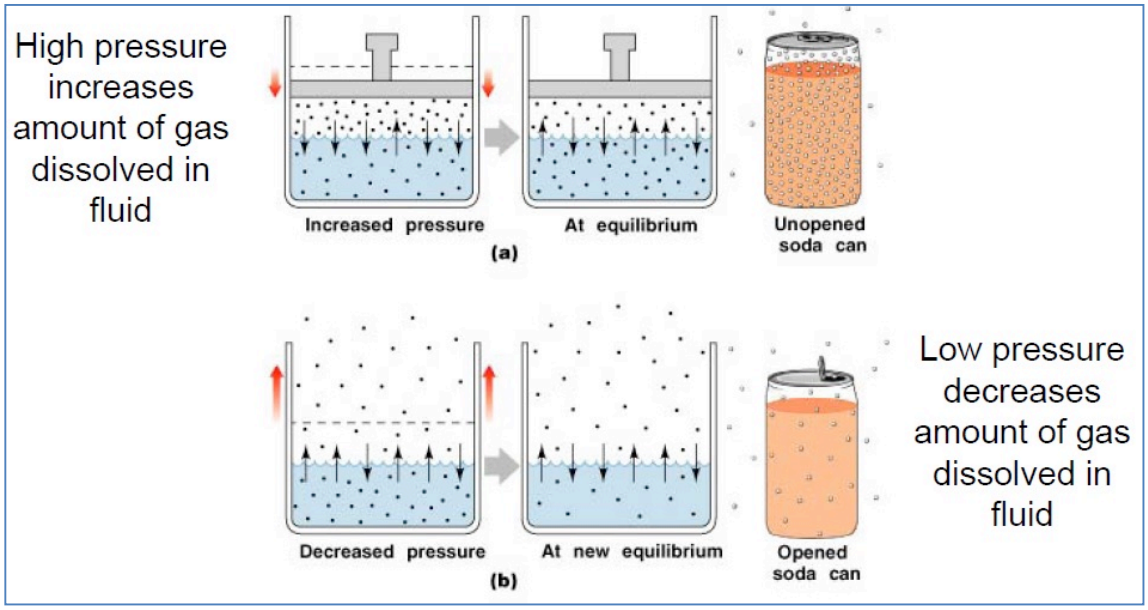
Abundance in air:	Collisions:	Partial Pressure:
78.6% N_2 (Nitrogen)	78.6% N_2	N_2 78.6% x 760 = 597 mmHg
20.9% O_2 (Oxygen)	20.9% O_2	O_2 20.9% x 760 = 159 mmHg
0.5% H_2O (Water)	0.5% H_2O	H_2O 0.5% x 760 = 3.8 mmHg
0.04% CO_2 (Carbon dioxide)	0.04% CO_2	CO_2 0.04% x 760 = 0.3 mmHg

$$P_{N_2} + P_{O_2} + P_{H_2O} + P_{CO_2} = 760 \text{ mmHg}$$

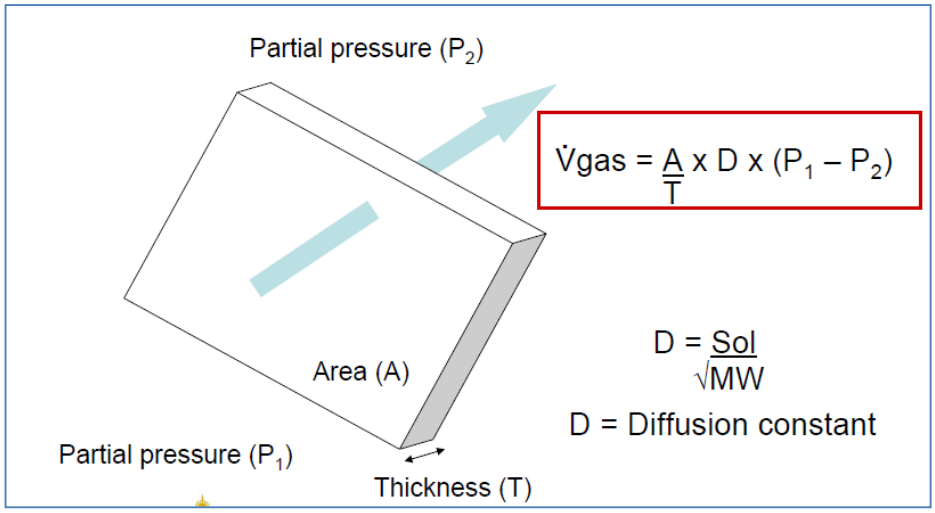
Gases exert a pressure proportional to their abundance

More gas = higher pressure

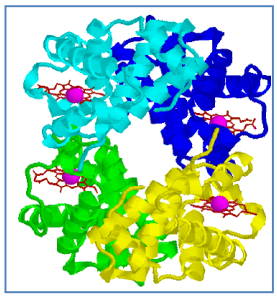
- **Henry's Law (of dissolved gases):**
  - 'The amount of gas in solution is proportional to the partial pressure of that gas'
    - More gas dissolves in a solution when pressure (and hence partial pressure) is increased.
    - The only other factor is how *soluble* the gas is in that solvent.



- **Fick's Law (of gas diffusion)**
  - Diffusion increases with:
    - Increased Surface Area
    - Decreased Membrane Thickness
    - Increased Partial Pressure *Gradient* (Difference between $P_{Outside}$ & P_{Inside})
    - Increased Diffusion Constant (D) (D = Gas Solubility / √Molecular Weight)
      - I.e. The more soluble, the better the diffusion.
      - I.e. The smaller the molecule, the better the diffusion.
  - **Implications for Lung Design:**
    - Alveolar Surface Area must be large as possible
    - Basal laminae of alveoli & capillaries are fused → minimises thickness of membrane.
  - **NB: In a healthy resting lung**, the only factor that significantly changes with each breath is the *Partial Pressure Gradients*.
    - Therefore - the main determinant of the rate of gas diffusion across the alveolar membrane.
  - **NB: In a pathological lung**, other factors (Surface area/membrane thickness/Gas Solubility (due to surfactant composition)) may determine the rate of gas diffusion across the alveolar membrane.
    - Eg. Pneumonia – Increases Thickness
    - Eg. Emphysema – Decreases Surface Area



Haemoglobin (Hb):



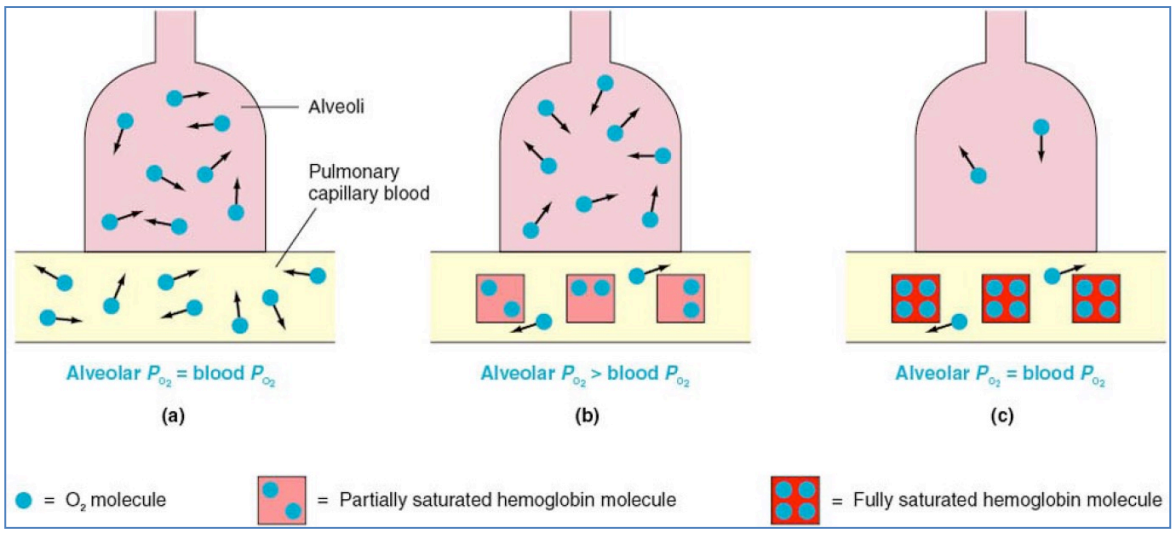
- **What is it?:**
  - A 4-Protein-Subunit Molecule
  - Each Protein-Subunit has a *Heme Unit* with *a Central Iron Molecule.*

- **Role in O_2 Transport:**
  - Each *Heme Unit* can carry *1xOxygen Molecule* (O_2)
  - Therefore 1xHaemoglobin can carry 4xOxygen Molecules.
  - Transports O_2 from Lungs → Tissues (NB: Also Transports CO_2 from Tissues → Lungs)

$$HbH_4 + 4O_2 \rightleftharpoons Hb(O_2)_4 + 4H^+$$

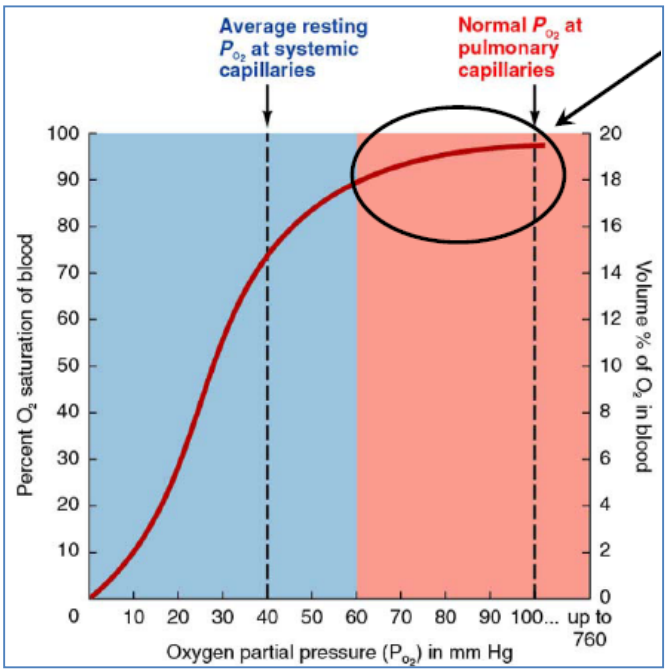
- **Factors Altering Hb Affinity for O_2:**
  - **Things Changing its Shape/Functional Properties:**
    - Hb Saturation: % of Heme units containing bound O_2
      - Therefore also P_{O2}
    - P_{CO2}
    - Blood pH
    - Temperature
    - 2,3-BisPhosphoGlycerate (or DPG – disphosphoglycerate) (By-product of Glycolysis.)

- **The Physics Behind Hb's Function:**
  - **1. Greatly Increases O_2-Carrying Capacity of Blood:**
    - By binding O_2, Hb effectively removes the dissolved O_2 from solution.
      - Acts as an O_2 buffer.
      - → More of the Alveolar O_2 can diffuse into the blood (→ & Haemoglobin) before the *Partial Pressure Gradient* is equalized.
    - Hence, *Blood-O_2 Content = Dissolved O_2 + Hb-Bound O_2*
    - As P_{O2} ↑, %Hb-saturation ↑

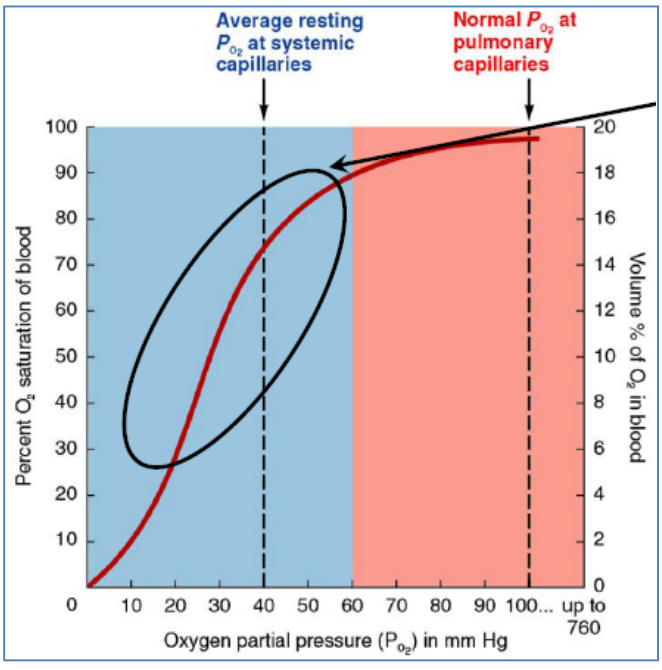


  - **2. Binds O_2 Co-Operatively:**
    - The more O_2 Molecules bound to Hb, the *easier* it becomes to bind another. (up to 4)
      - Due to Hb's conformational change between **2 States (isoforms):**
        - **T-State (Tense):**
          - Low O_2-Hb Saturation
          - Low affinity for O_2
        - **R-State (Relaxed):**
          - High O_2-Hb Saturation
          - High affinity for O_2

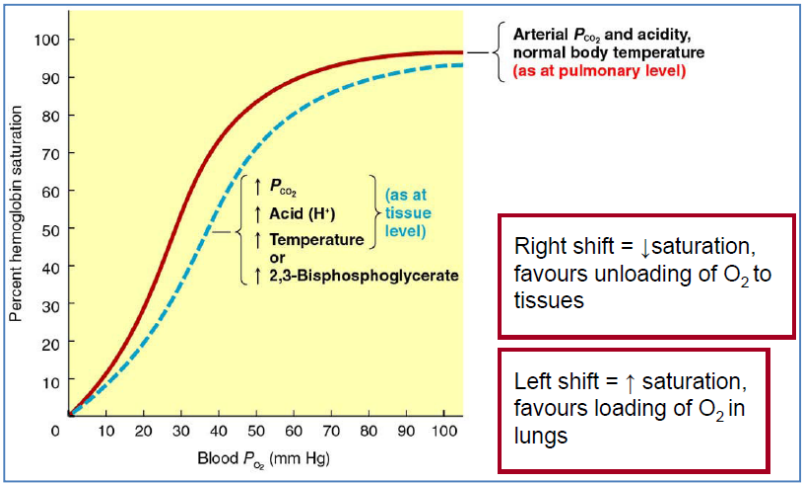
- **3. O_2-Hb-Dissociation Curve:**
  - **Plateau Region (O_2 Loading Zone):**
    - In the lungs (P_{O2} = high)
    - The P_{O2} Range where pulmonary capillaries are *Loaded* with O_2.
    - NB: Normal P_{O2} in pulmonary capillaries ≈ 100mmHg, however the plateau region extends way below that (to ≈ 60mmHg).
      - This allows blood from lungs → Systemic circulation → Tissues, before releasing its oxygen.
      - I.e. The Plateau = safety margin for O_2 *Carrying.*
      - Enables you to maintain blood-O_2 saturation even when P_{O2} falls markedly.

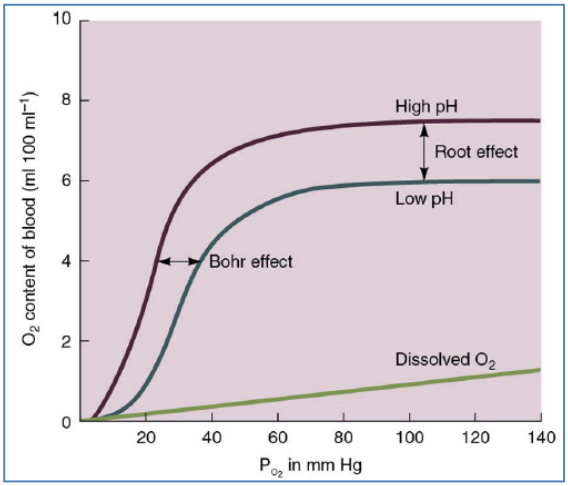


  - **Steep Region (O_2 Un-Loading Zone):**
    - In Systemic Capillary Beds (P_{O2} = low)
    - The P_{O2} Range where Capillary beds *Unload* their O_2 → Tissue cells.
    - NB: As soon as P_{O2} drops below ≈ 60mmHg, Hb begins to 'Dump' its O_2.
      - I.e. Small ↓ in Capillary P_{O2} → Large ↓ in Blood-O_2 Saturation.
      - Allows Oxygenated blood → Pass O_2 to Metabolizing Tissues.



- ***Shifting The Curve:***
  - *Remember the *Things that Change Hb's Shape/Functional Properties* (see above)
    - Such changes shift the O_2-Hb-Dissociation Curve.
  - **Right Shift:**
    - Favours *Unloading* of O_2 to Tissues
    - Reduces Hb's Affinity for O_2 → Stabilises 'T-Conformation'.
    - Hb-Saturation Decreases
    - **Causes:**
      - ↑Temperature (eg. exercising muscles)
      - ↑ DPG (from Glycolysis)
      - ↑ P_{CO2} (causes ↑Carbonic Acid →↓*affinity* for O_2) →*Bohr Effect*
      - ↑ Acid (H^+) (↓*ability*$_{(not\ affinity)}$ to bind O_2) →*Root Effect*





  - **Left Shift:**
    - Favours *Loading* of O_2 to Tissues
    - Increases Hb's Affinity for O_2 → Stabilises 'R-Conformation'.
    - Hb-Saturation Increases.
    - **Causes:**
      - Opposites of Above
  - **Way to Remember:**
    - **Curve shifts to *Right* in an *Exercising Muscle*.**

An exercising muscle is:	•Factors that favour a right shift:
• hot	•Increasing temperature
•acidic (lactic acid)	•Decreasing pH
•has high P_{CO_2}	•Increasing P_{CO_2}
•undergoing rapid glycolysis (lots of DPG)	•Increasing DPG

Opposite of these will *Left shift* the curve

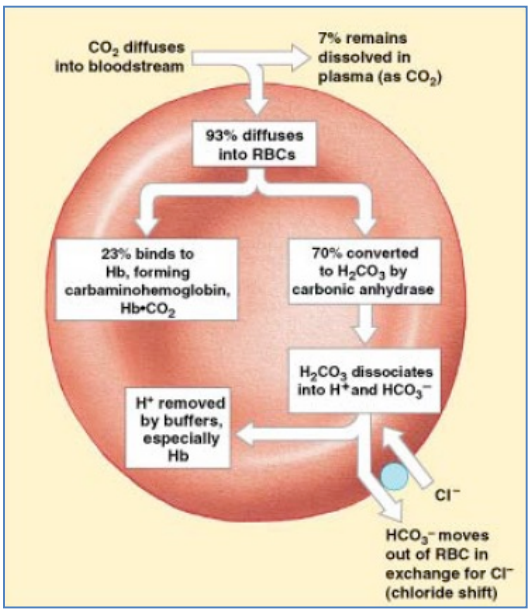
Right shifts favours unloading

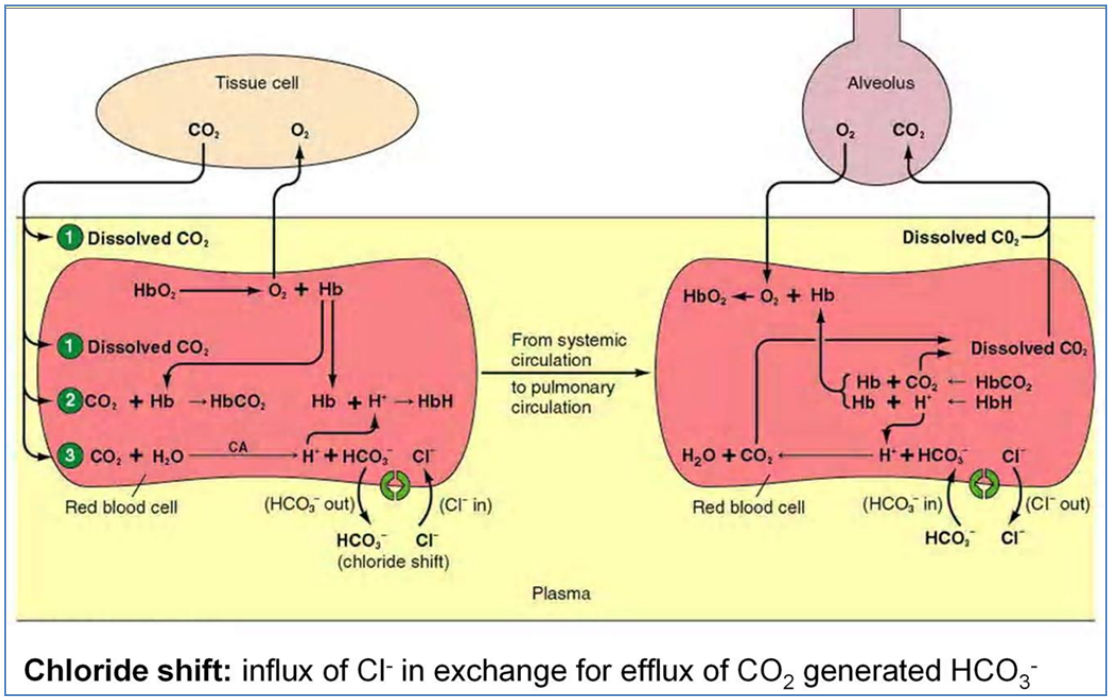
Left shift favour loading

Opposites of these factors → Left Shift

Mechanisms of CO_2 Transport

- CO_2 produced by metabolising cells
- Produced in Mitochondria
- Diffuses into blood.
- **3 Routes To The Lungs:**
  - **1. Dissolved In Plasma:**
    - Tissue CO_2 → Dissolved Plasma CO_2 → Pulmonary Capillaries → Diffusion to Alveoli
    - 5-10% of Total Body-CO_2
  - **2. Bound to Hb:**
    - Tissue CO_2 → Dissolved RBC CO_2 → CO_2 + Hb → $HbCO_2$ → Pulmonary Capillaries (P_{CO2} ↓as dissolved CO_2 diffuses to Alveoli) → Dissolved RBC CO_2 → Diffusion to Alveoli
    - 25-30% of Total Body-CO_2
    - NB: at a different site to O_2
  - **3. In Bicarbonate-Ion Form:**
    - Tissue CO_2 → Dissolved RBC CO_2 → H_2CO_3 → HCO_3 → Exits RBC to Plasma →Pulmonary Capillaries → Re-Enters RBC from Plasma → Dissolved RBC CO_2 → Diffusion to Alveoli
    - 60-70% of Total Body-CO_2
    - Converted to Bicarb by ***Carbonic Anhydrase:***
      - $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3$

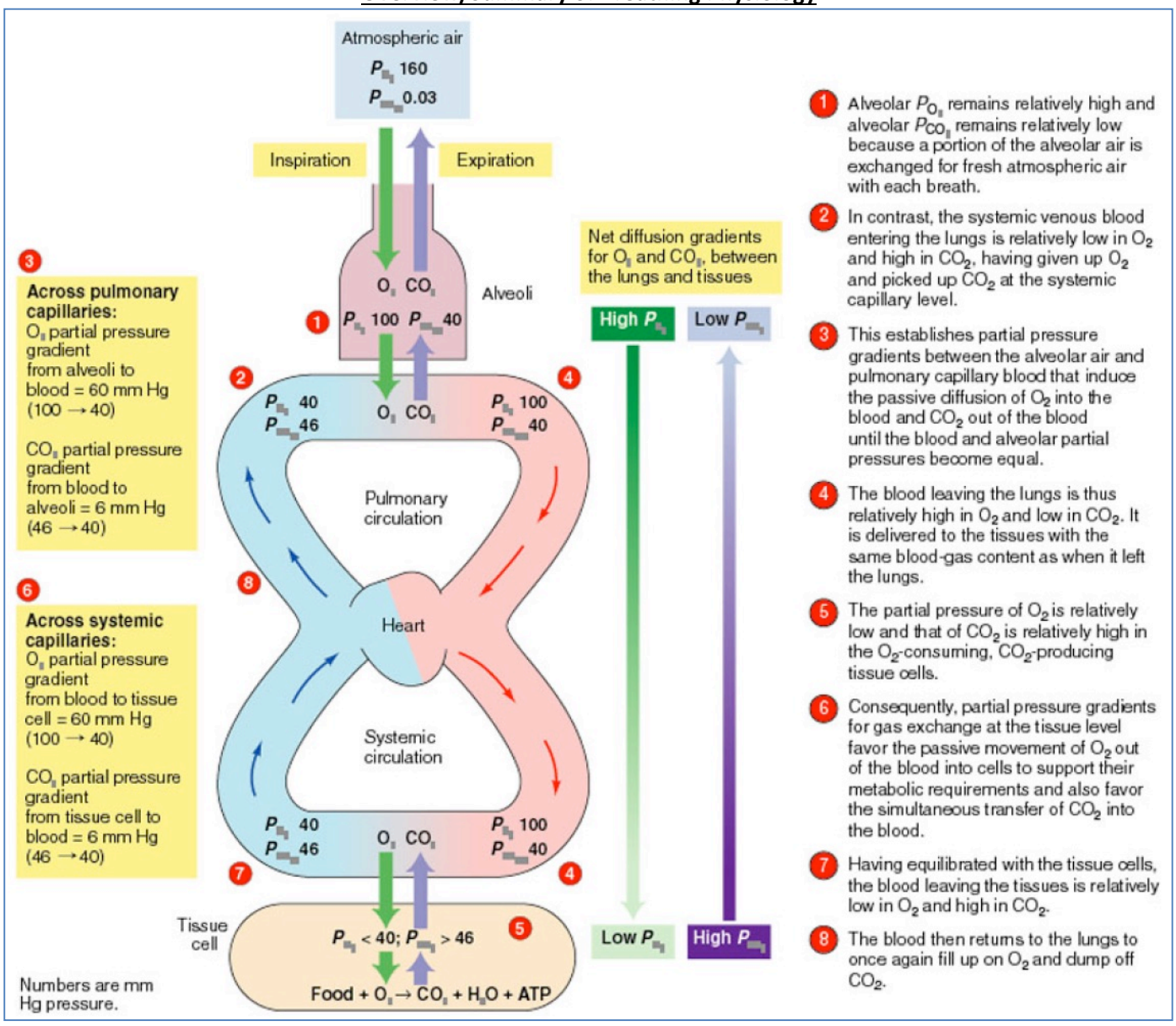




Chloride shift: influx of Cl^- in exchange for efflux of CO_2 generated HCO_3^-

- **Factors Altering CO_2 Transport Efficiency:**
  - **Bohr Effect:**
    - Not only does ↑ P_{CO2} cause ↑Carbonic Acid →↓*affinity* for O_2 →Unloading of O_2.....
  - **Haldane Effect:**
    - But Unloading of O_2 *also Favours* binding of CO_2.
    - (Deoxy-Hb binds CO_2 *more readily* than Oxy-Hb)

Overview/Summary of Breathing Physiology



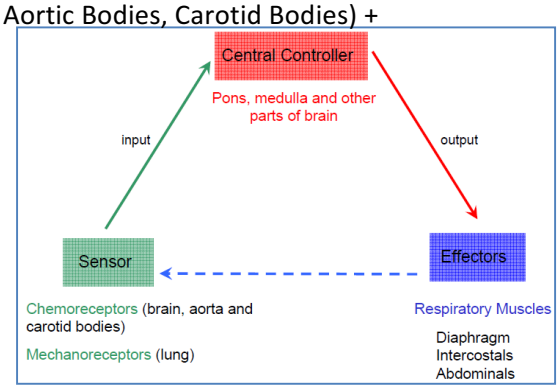
Respiratory Medicine Notes
Control Of Breathing

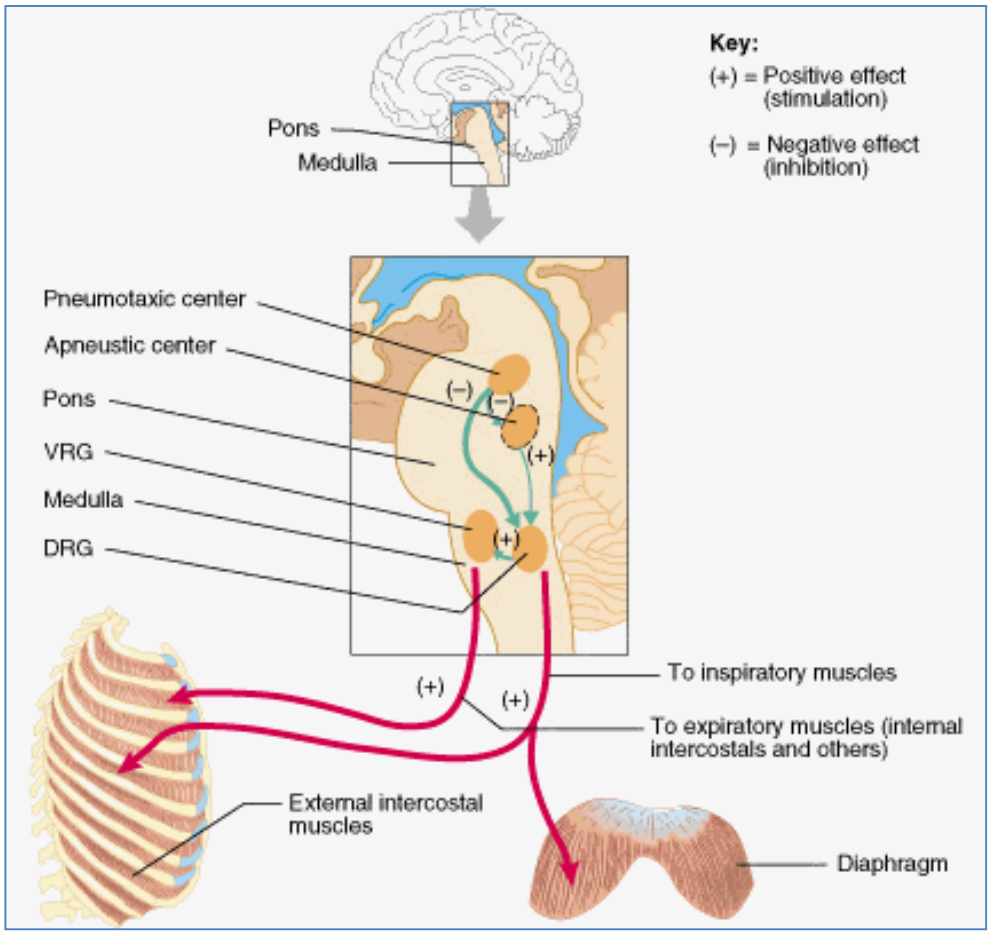
Control Of Breathing:

- **Why?**
  - To Match Alveolar Ventilation with Metabolic Demand.
  - Keeps Arterial P_{O2} & P_{CO2} Very Stable – Even During Severe Exercise.
  - NB: *Venous* gas levels do change markedly.
- **Where?**
  - "Respiratory Centre" of the Brain. (Medulla & Pons of Brainstem)
- **What it Does:**
  - Produces *Uninterrupted Rhythmic* Breathing Activity Throughout Life.
  - Automatically Adjusts Breathing to meet Changing Demands.

Overview of Central Regulation:

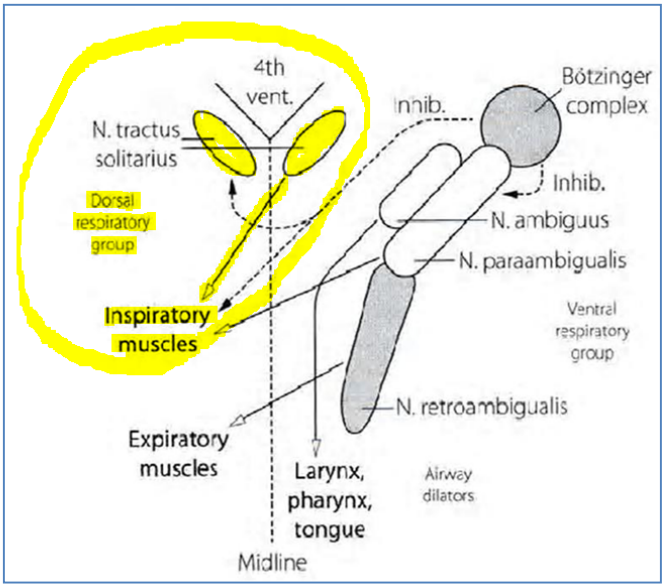
- **Input From:**
  - Chemoreceptors (Chemosensitive area of Medulla, Aortic Bodies, Carotid Bodies) +
  - Mechanoreceptors (Stretch)(Lung)
- **The Respiratory Centre:**
  - Medulla
    - DRG – Dorsal Respiratory Group
    - VRG – Ventral Respiratory Group
  - Pons
    - PRG – Pontine Respiratory Group
  - Cerebral Cortex
    - Voluntary Override
- **Output To:**
  - Respiratory Muscles – (Diaphragm, Intercostals, Abdominals)

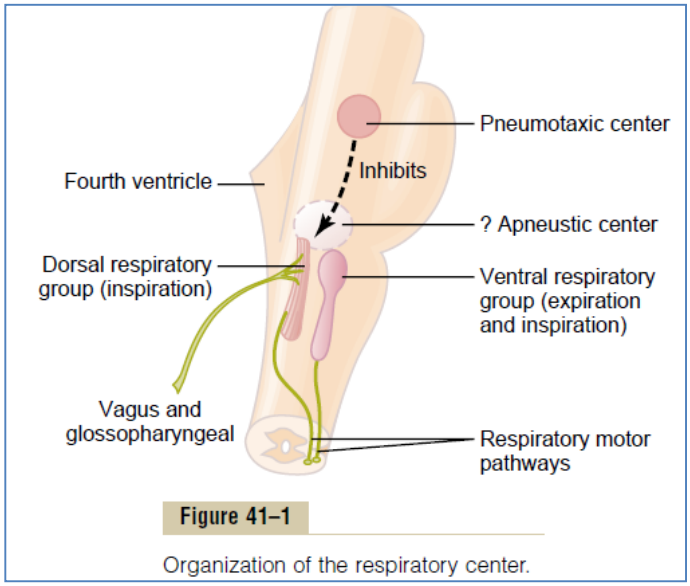




The Respiratory Centre (Brainstem – Medulla/Pons):

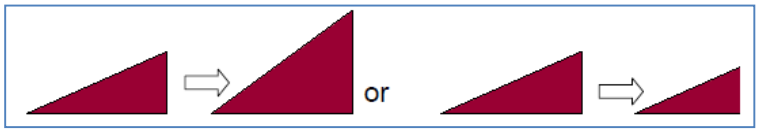
- **Medulla:**
  - ****Dorsal Respiratory Group (DRG):**
    - **Location:**
      - Bilaterally in Dorsal Portion of Medulla
      - In Close Relation to the ***'Nucleus Tractus Solitarius'***.





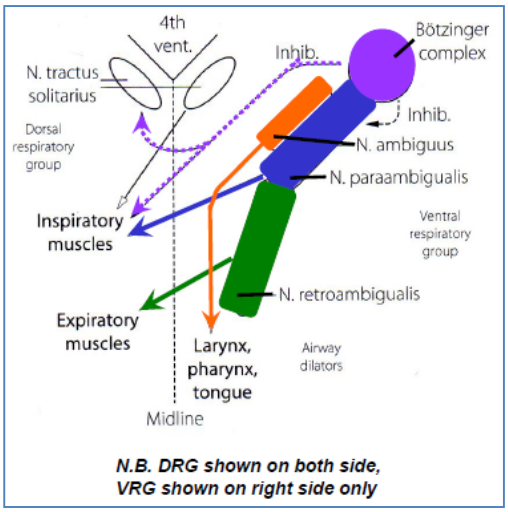
- **Main Function = INSPIRATION:**
  - Initiates the *Respiratory Rhythm.*
  - Determines *Timing* of Respiratory Cycle
  - Via ***"Inspiratory Ramp Signals"*****:**

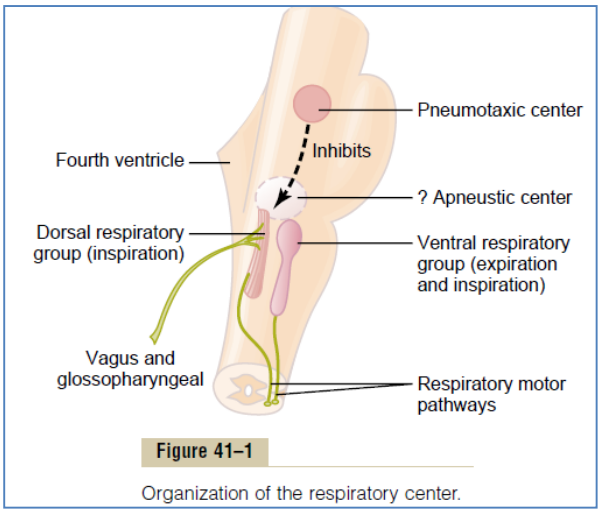
    - (Mechanism Unclear)
    - Signal isn't On/Off
    - Instead it Starts Weak, then Steadily *Increases* for ≈ 2sec.
    - Signal Ceases for ≈ 3sec. → Allows passive Exhalation. (Elastic Recoil)
    - **Signal Can Be Modified** to Alter *Speed* & *Rate* of Inspiration:
      - ↑Speed – By Increasing Ramp-Signal *Gradient*.
      - ↑Rate – By Terminating Ramp-Signal Early. (Pneumotaxic Centre)



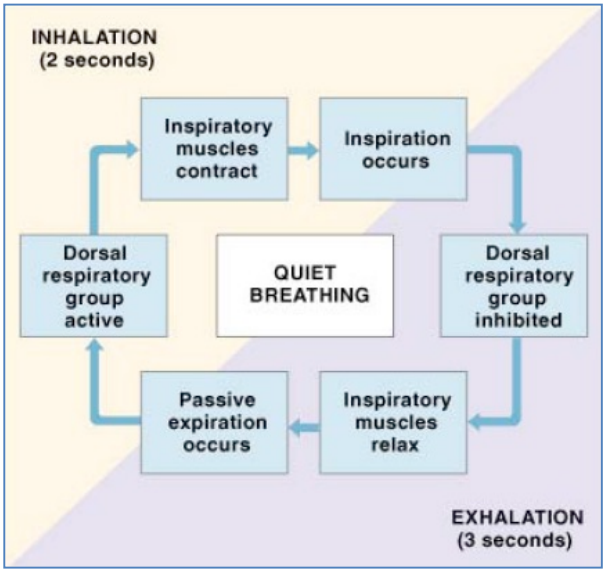
- **Input From:**
  - **Peripheral Chemo/Baro/Mechano-Receptors:**
    - Glossopharyngeal Nerves (CN-IX)
    - Vagus Nerves (CN-X)
- **Output From DRG:**
  - **Motor Neuron Cell Bodies (in Spinal Cord):**
    - Impulse → Phrenic Nerve (C3-C5)→ Diaphragm
    - Impulse → Intercostal Nerves (T1-T11)→ Intercostal Muscles

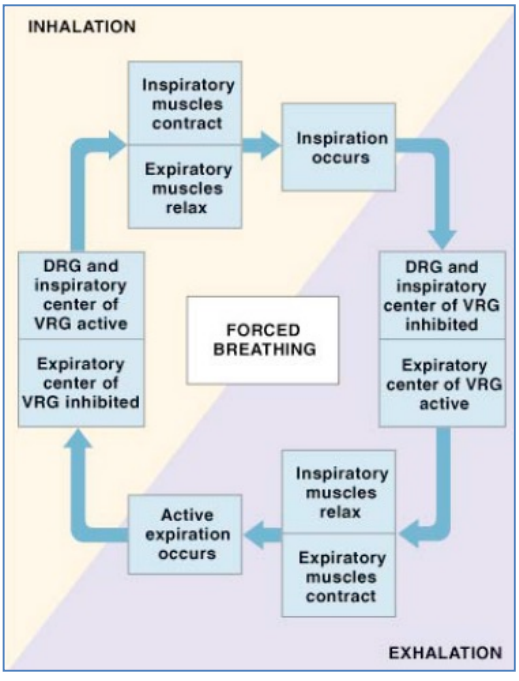
- **Ventral Respiratory Group (VRG):**
  - **Location:**
    - In Each Side of Medulla, Lateral to DRG.





  - **Main *Overall* Function = EXPIRATION$_{(FORCED)}$:**
    - **Important for *Active* Expiration
      - – (Abdominal Muscles + Internal+Innermost Intercostals).
    - Inactive during Normal Quiet Breathing.
    - Has NO ROLE in Respiratory Rhythm
    - Contributes *Extra* Respiratory Drive during ↑↑Demand.
      - Inspiratory &
      - Expiratory.
  - **4 Functional Parts:**
    - **Botzinger Complex:**
      - Both Inspiratory & Expiratory Functions (Much Unknown)
    - **Nucleus Ambiguus:**
      - Controls Airway Patency
      - (Dilator Functions of Larynx, Pharynx & Tongue)
    - **Nucleus Paraambigualis:**
      - Contraction of *Inspiratory Muscles* on Opposite side of body.
    - ****Nucleus Retroambigualis:**
      - Contraction of *Expiratory Muscles* on Opposite side of body.





- **Pons:**
  - **Pontine Respiratory Group (PRG):**
    - **2 Parts:**
      - **Pneumotaxic Centre:**
        - **Location:**
          - Upper Pons
        - **Function:**
          - Controls "Off-Switch" for DRG-Inspiratory-*Ramp-Signal*.
          - Ie. Terminates *Ramp-Signal* Early
          - - **Limits Inspiration
          - - Increases Breathing Frequency
          - - Decreases Tidal Volume
      - **Apneustic Centre:**
        - **Location:**
          - Lower Pons
        - **Function:**
          - Prolongs *Ramp-Signal* (Ie. Terminates Signal Later)
          - - **Prolongs Inspiration
          - - Decreases Breathing Frequency
          - - Increases Tidal Volume

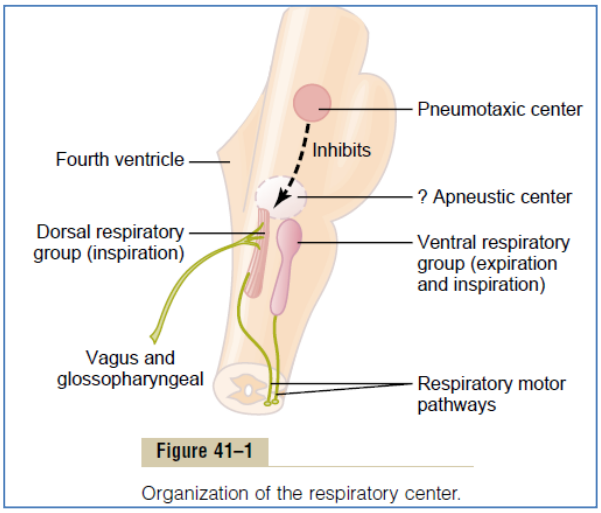


Figure 41–1
Organization of the respiratory center.

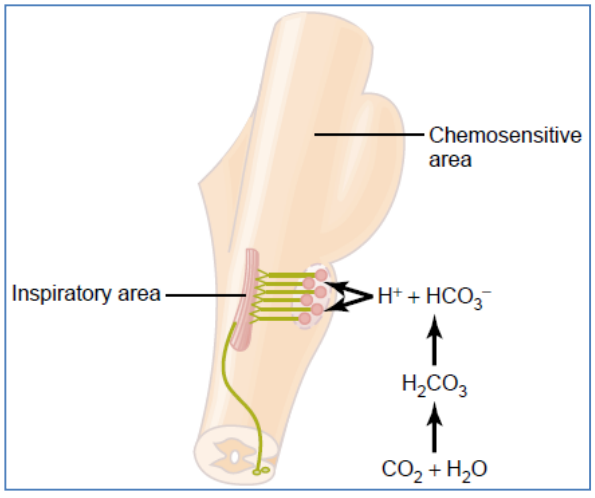
- **Cerebral Cortex:**
  - **Conscious Override:**
    - Of All of the Above. (To an extent)
    - - By bypassing Medulla-Respiratory Centres → Act *Directly* on Respiratory Muscles.
  - **Important For:**
    - Speech
    - Singing
    - Sniffing
    - Coughing
    - Wind Instruments
  - Mechanism Is Very Complicated → Don't need to know.

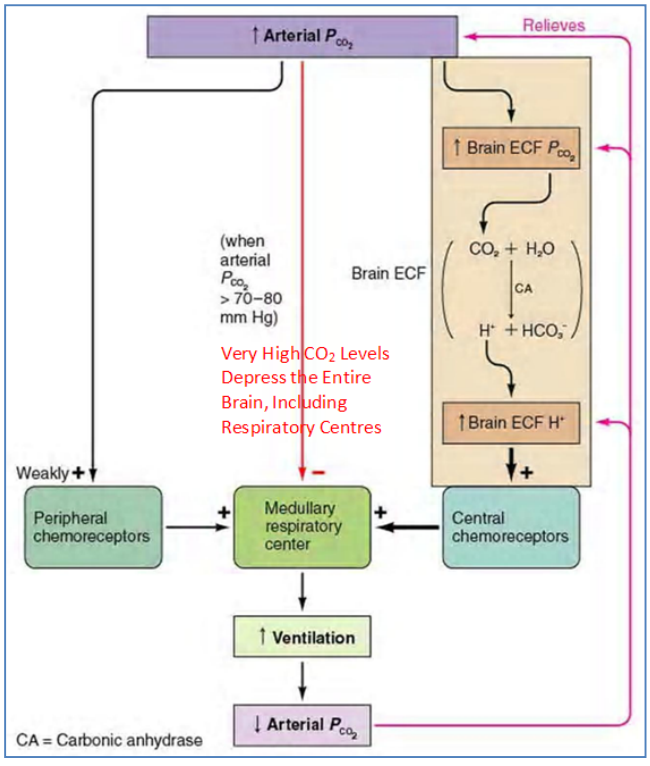
Peripheral Input:

- **Upper Respiratory Tract Reflexes:**
  - Eg. Cough/Sneeze Reflexes. – Don't Know Details
  - Receptors in Nose/Pharynx/Larynx
    - Respond to Toxins/Irritants/Temperature

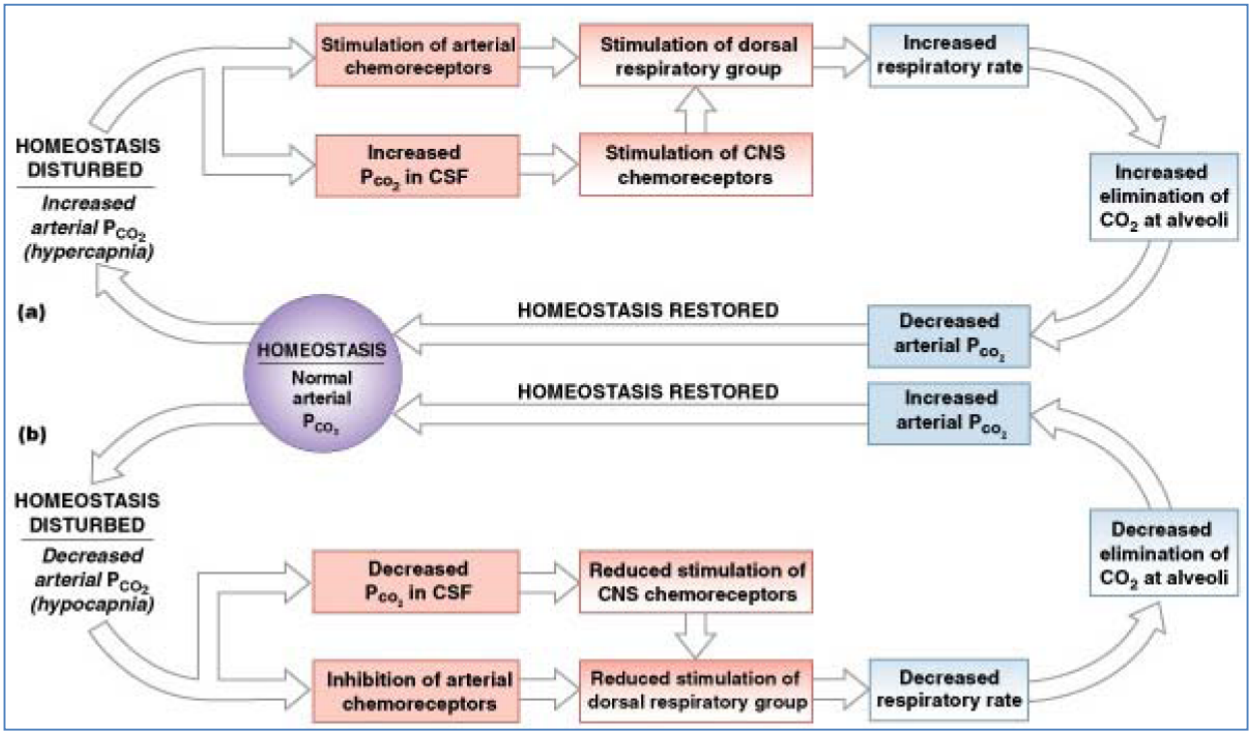
- **Lung Reflexes:**
  - **Pulmonary Stretch Receptors:**
    - **Slowly Adapting Stretch-Receptors (SARs):**
      - Sensitive to Inflation/Deflation.
      - Ie. Lung-Volume Sensors
      - Located in Airways
    - **Rapidly Adapting Stretch-Receptors: (RARs):**
      - Sensitive to Tidal Volume, Frequency, Or Lung Compliance.
      - Also Nociceptive & Chemosensitive.
  - ***Inflation Reflex: ("Hering Breuer Reflex"):**
    - Prevents *Over*-Inflation
    - - By Turning Off the Inspiratory-Ramp-Signal. (Similar to Pneumotaxic Centre)
    - - Activated in response to ↑Pulmonary 'Stretch'
    - - Signal Carried Via *VAGUS*-Nerve →DRG
  - **Deflation Reflex:**
    - Prevents Lung *Collapse* (*Over*-Deflation)
    - - Stimulates Inspiration when Lung-Volume is too Low.

- **Chemical Control of Respiration:**
  - ***↑Arterial PCO_2:**
    - **Central Chemoreceptors – (Chemosensitive Area of Medulla):**
      - ****↑Arterial PCO_2 → ↑*CSF*-[H^+]** (Cerebro-Spinal Fluid)
      - ↑CSF-[H^+] Acts Directly on *Chemosensitive Area on Medulla.*
      - ↑CSF-[H^+] Stimulates Respiratory Centre
        - NB: H^+ = the *Only* important Stimulus, However, H^+ can't cross Bl.Br.Barrier.
        - Therefore, [H^+] is determined by Arterial PCO_2 (which can diffuse into CSF)
          - $CO_2 \rightarrow HCO_3 + H^+$ … Via the Bicarbonate-Buffer System.
      - **POTENT, BUT INDIRECT**

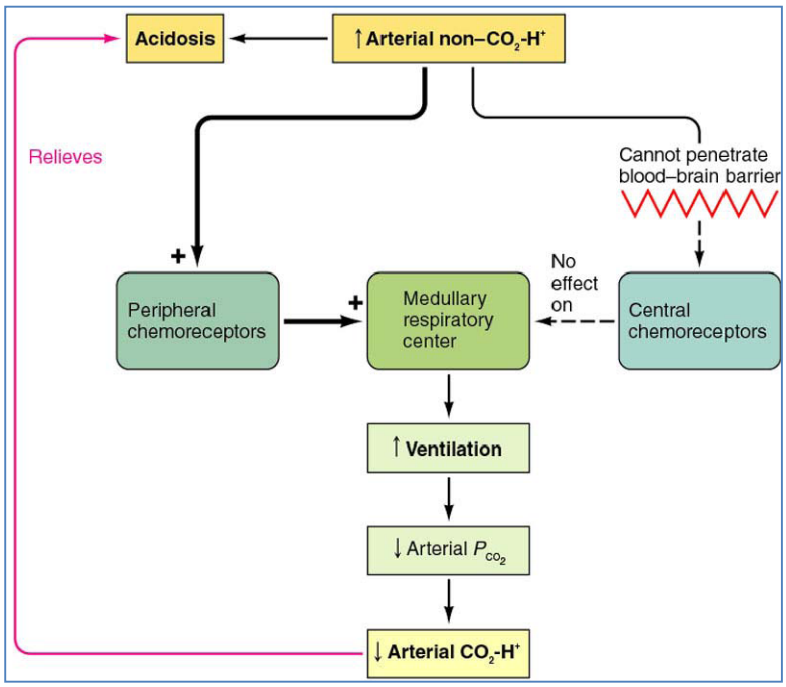


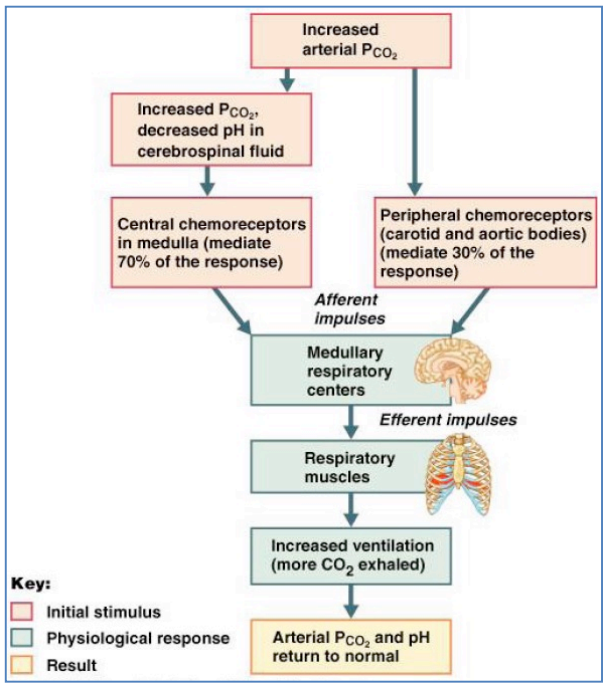


- **Peripheral Chemoreceptors – (Aortic & Carotid Bodies):**
  - **↑Arterial PCO_2 → ↑*Arterial*-[H^+]**
  - ↑Arterial-CO_2→HCO_3 + Arterial-H^+ … Via the Bicarbonate-Buffer System.
    - ↑H^+ Stimulates Ventilation
    - ↓H^+ Depresses Ventilation
  - Very Important in Acid-Base Control → Respiratory Compensation for ΔpH.

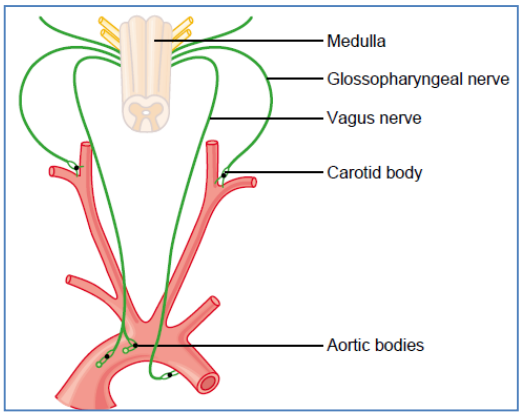


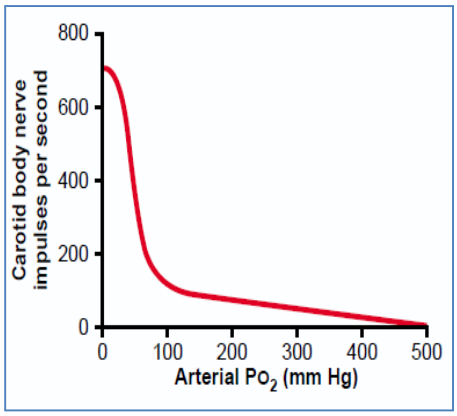
- **Arterial Non-CO_2 [H^+]:**
  - **Peripheral Chemoreceptors – (Aortic & Carotid Bodies):**
    - **↑Non-CO_2-Generated [H^+] → ↑Arterial-[H^+]**
      - **NB:** Non-CO_2-Generated [H^+] = Lactic-Acid/Keto-Acids/Etc.
      - ↑H^+ Stimulates Ventilation
      - ↓H^+ Depresses Ventilation
    - Very Important in Acid-Base Control → Respiratory Compensation for ΔpH.

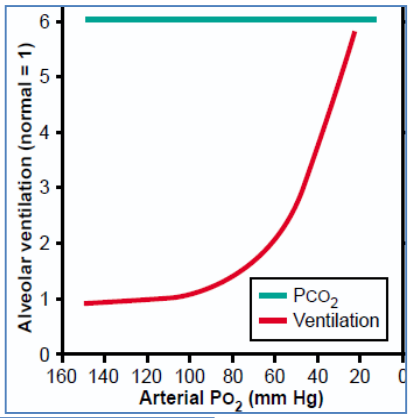


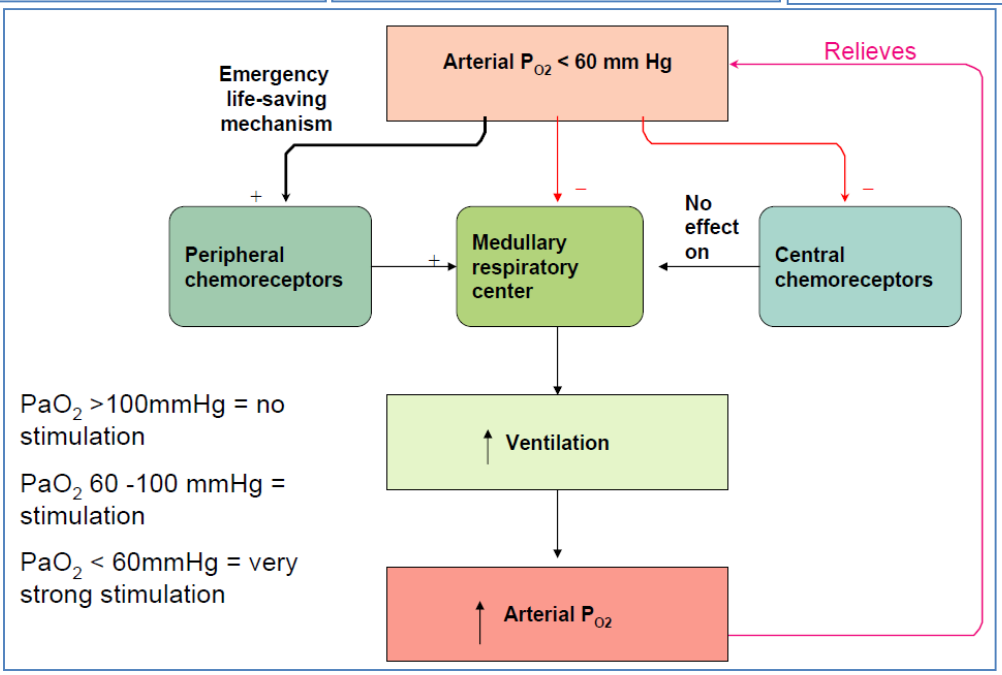


- **↓Arterial O_2:**
  - **Peripheral Chemoreceptors – (Aortic & Carotid Bodies):**
    - ↓Arterial-O_2 (to below ≈100mmHg) → Strong Respiratory Stimulation
      - Increased Breathing Rate
      - Increased Breathing Depth
    - NB: these receptors have their own blood supply, with *extreme* blood flow → Ensures that the receptors don't alter the gas levels of the arterial blood that they're measuring.
    - **NB: Acclimatization:**
      - In Low O_2 environments (mountain climbing), the Central Respiratory Centres lose sensitivity for CO_2. Therefore, Low-O_2 takes over as the #1. Respiratory Driver.





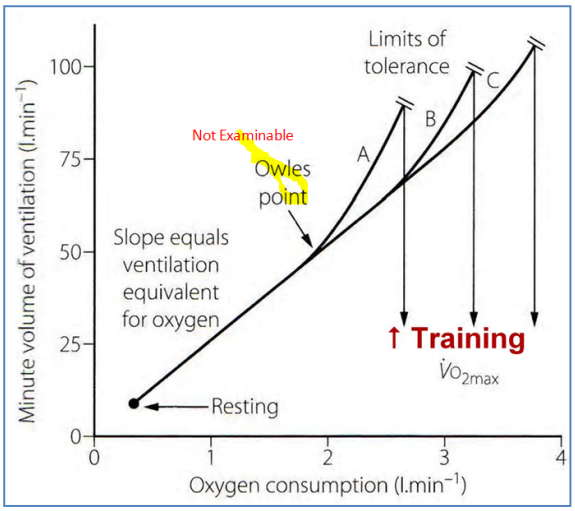


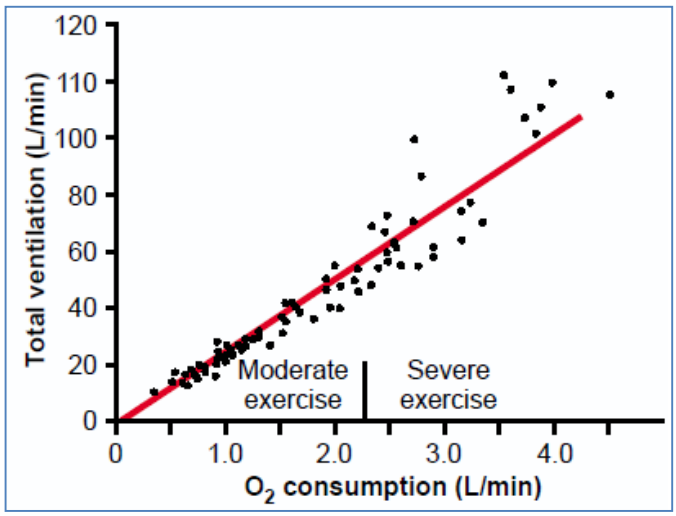


- **Mechanical Stimulation:**
  - **Baroreceptor Reflexes:**
    - ↓BP → ↑Respiratory Rate
    - ↑BP → ↓Respiratory Rate
  - **Lung 'J'-Receptors:**
    - Sensory Nerves in Alveolar Walls, Juxtaposed to the Pulmonary Capillaries.
      - (hence 'J'-receptors)
    - Stimulated when Pul.Capillares are engorged with blood & During Pul.Oedema.
    - Function – Unclear!

Ventilatory Response To Exercise:

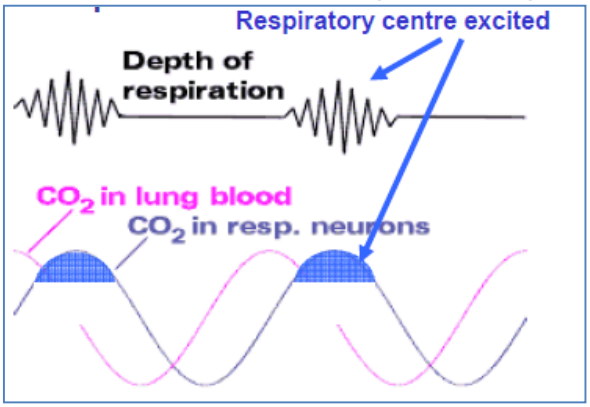
- NB: Gas levels remain stable during exercise – (Ventilation is well matched to O_2 Consumption)
- **During Light-Moderate Exercise:** – Linear Relationship between O_2 Demand & Ventilation.
- **During Severe Exercise:** - O_2 Consumption Exceeds Body's ability to supply it → Anaerobic Metabolism:
    - Lactic Acid Buildup → Lactic-Acidosis → Hyperventilation.

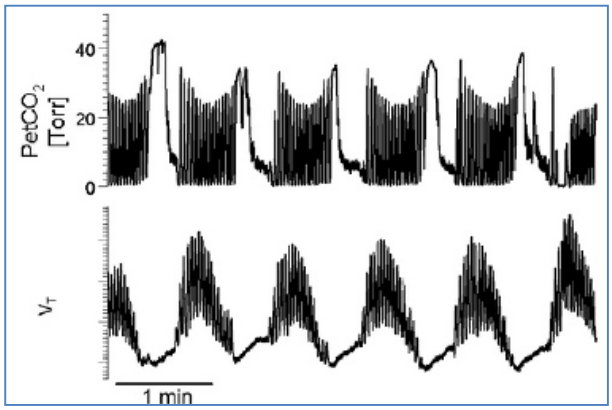




Respiratory Disorders:

- **Odine's Curse:**
    - **AKA:** "*Primary Alveolar Hypoventilation Syndrome*"
    - **Patient has to *REMEBER* to Breathe.**
        - Due to Defect in Automatic Respiratory Control.
        - Require Ventilation when Sleeping to Keep Breathing.
- **Cheyne-Stokes Respiration:**
    - 1. Person Overbreathes,
        - -Blowing off too much CO_2 from *Pulmonary Blood*
        - –At the same time, increasing O_2
    - 2. Something delays time for oxygenated pulmonary blood to reach brain
        - (which delays inhibition of ventilation.)
    - 3. By this time, person has already overventilated.
    - 4. Oxygenated blood finally reaches brain, over-depressing respiratory centre.
    - 5. Person Underbreathes,
        - – Blood CO_2 increases
        - – Blood O_2 decreases
    - 6. This 'depleted' blood takes a while to reach brain and stimulate ventilation.
    - 7. When this blood finally reaches brain, it over-stimulates respiratory centre → Cycle starts again.
    - **Factors leading to Cheyne-Stokes Breathing:**
        - When a *long delay* occurs between transport of blood from lungs to brain. – (Eg. Cardiac Failure)
        - Increased Negative Feedback Gain in Respiratory Control areas (ie. A change in blood CO_2 or O_2 causes a far greater change in ventilation than normal)



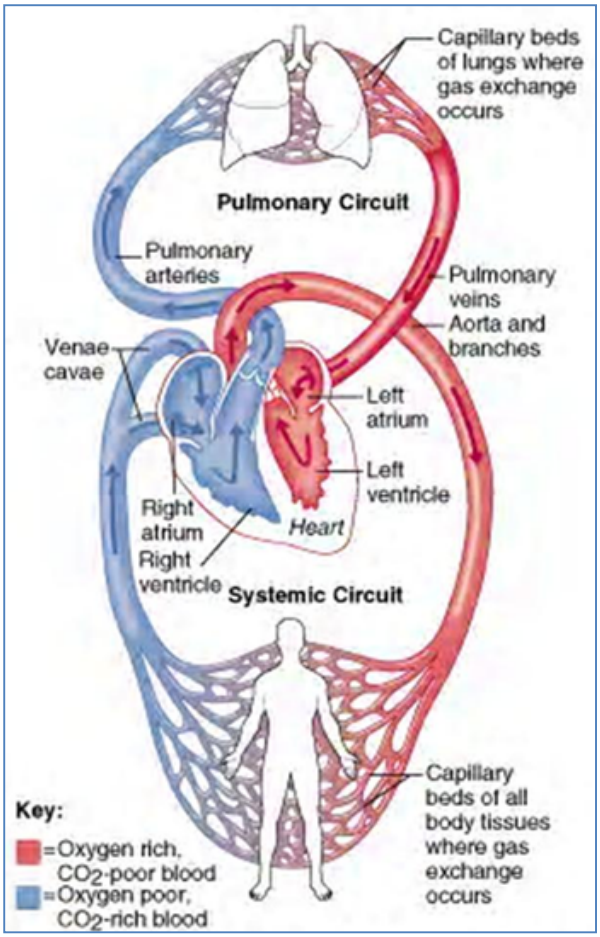


- **Sleep Apnoea:**
    - NB: Apnoea = Absence of Spontaneous Breathing
    - **Obstructive Sleep Apnoea:**
        - Temporary Cessations of breathing due to airway obstruction or compromised airway patency. (Respiratory effort continues)
    - **Central Sleep Apnoea:**
        - Temporary cessations of breathing due to lack of respiratory drive from Dorsal Respiratory Group. (No Respiratory Effort)

Respiratory Medicine Notes
Respiratory Physiology

The Oxygen Cascade:

- **1. Air into Lungs**
- **2. O_2 Diffusion from air → Red Blood Cells**
- **3. Circulation of Red Blood Cells → Periphery**
- **4. O_2 Diffuses from RBCs → Mitochondria of Peripheral Cells**
- **5. Used in Aerobic Production of ATP → CO_2**
- **6. CO_2 Diffuses from Mitochondria → Blood**
- **7. Deoxygenated Blood → Lungs**
- **8. CO_2 Diffuses from Blood → Lungs**
- **9. High [CO_2] Air Exhaled.**

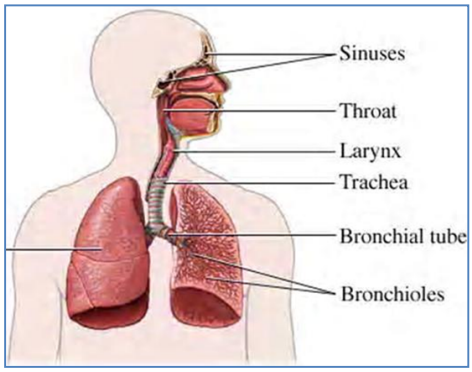


Respiration:

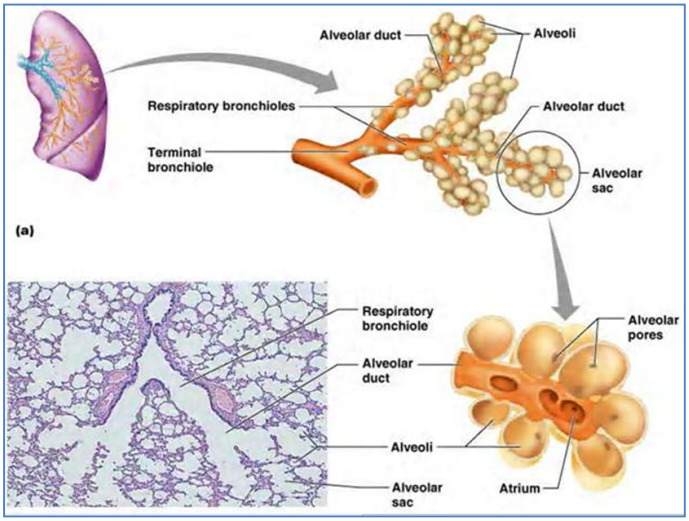
- **External:**
  - Steps involved in getting O_2 down to the Mitochondria (Includes Ventilation)
  - Ie. The exchange of O_2 & CO_2 between the Body & External Environment.
    - Pulmonary Ventilation (breathing)
    - Gas Diffusion
    - Gas Transport (Circulatory System)
- **Internal:**
  - AKA. Cellular Respiration.
  - Ie. The chemical reactions within the Mitochondria.
    - Conversion of O_2 → CO_2

Pulmonary Ventilation (Breathing):

- The physical *movement* of air into/out of respiratory tract.
- Different from respiration.
- AIM: To Maintain adequate *alveolar* ventilation
- **Conducting Zone:**
  - No Gas Exchange
  - Allow Air movement → Alveoli
  - Filter particulate matter in air (such matter in alveoli ↓-effectiveness of gas transfer)
    - Nose/mouth/nasopharynx
    - Trachea
    - Bronchi
    - Bronchioles
  - Must be kept open (Patent) to breath.
  - **Patency Maintained by:**
    - Cartilage Rings – Trachea
    - Cartilage Plates – Bronchi
    - Transmural Pressure + Radial Traction of surrounding tissues – Bronchioles
  - **Patency Problems:**
    - Snoring
    - Sleep Apnoea



- **Respiratory Zone:**
  - Gas Exchange
    - Respiratory Bronchioles
    - Alveolar Ducts
    - Alveoli (Extensive blood supply)
  - **Patency Maintained by:**
    - ˉve Intrapleural Pressure
    - Surface Tension of Alveolar Fluid
  - **Patency Problems:**
    - Emphysema
    - Asthma
    - Infant Respiratory Distress Syndrome

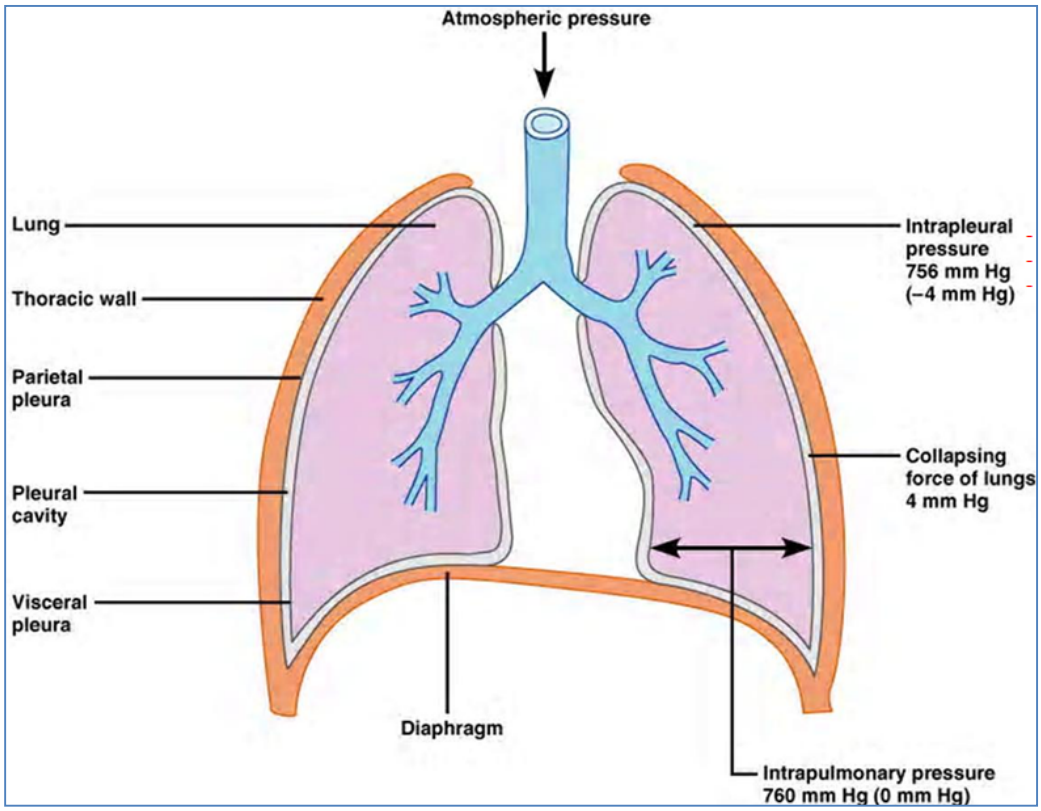


The Physics Of Breathing:

- **Boyle's Law:**
  - At a constant temperature, the pressure of a gas is *inversely proportional* to its volume.
  - Ie. Gases move from High Pressure → Low Pressure
  - So where do these pressure changes occur?.....The Pleura & The Alveoli:

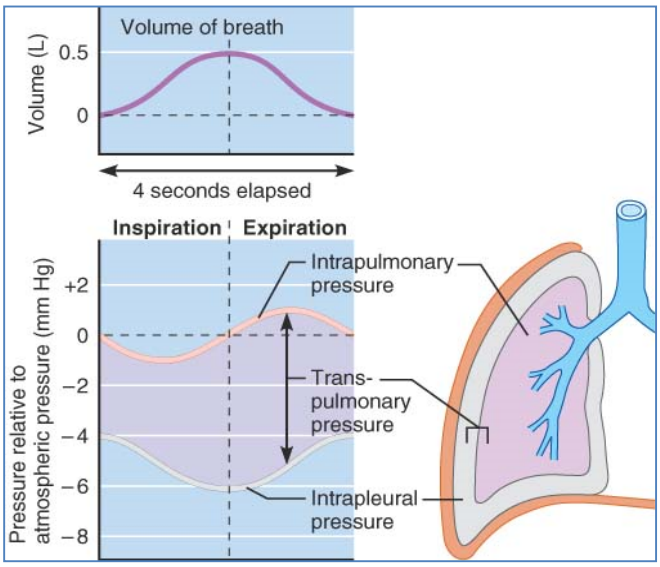
- **Pressure Changes:**
  - **Intrapleural Pressure:**
    - Negative Pressure between Visceral & Parietal Pleural Membranes....*Due To 2 Forces:*
      - Elastic Recoil of The Lungs
      - Surface Tension of *Alveolar Fluid* – acts to shrink alveoli to smallest possible.
    - **Always Subatmospheric (Negative):**
      - Becomes *more* subatmospheric during inhalation
      - Becomes *less* subatmospheric during exhalation
    - Due to serous fluid in Intrapleural space:
      - Secures the pleurae together + Anchors lungs to thoracic wall.
      - ***Ensures **negative pressure** gradient in pleural cavity.* ***(INTRAPLEURAL PRESSURE)***
        - ***Prevents lung from collapsing*
        - *Sucks the lung outwards towards chest wall*
        - *Aids in passive recoil of the lung during expiration.*
      - **NB: PneumoThorax:** Accumulation of air in the pleural cavity → Intrapleural pressure dissipates → lung collapses.
        - Traumatic (Penetrating/Non-penetrating)
        - Spontaneous (Disease complication)

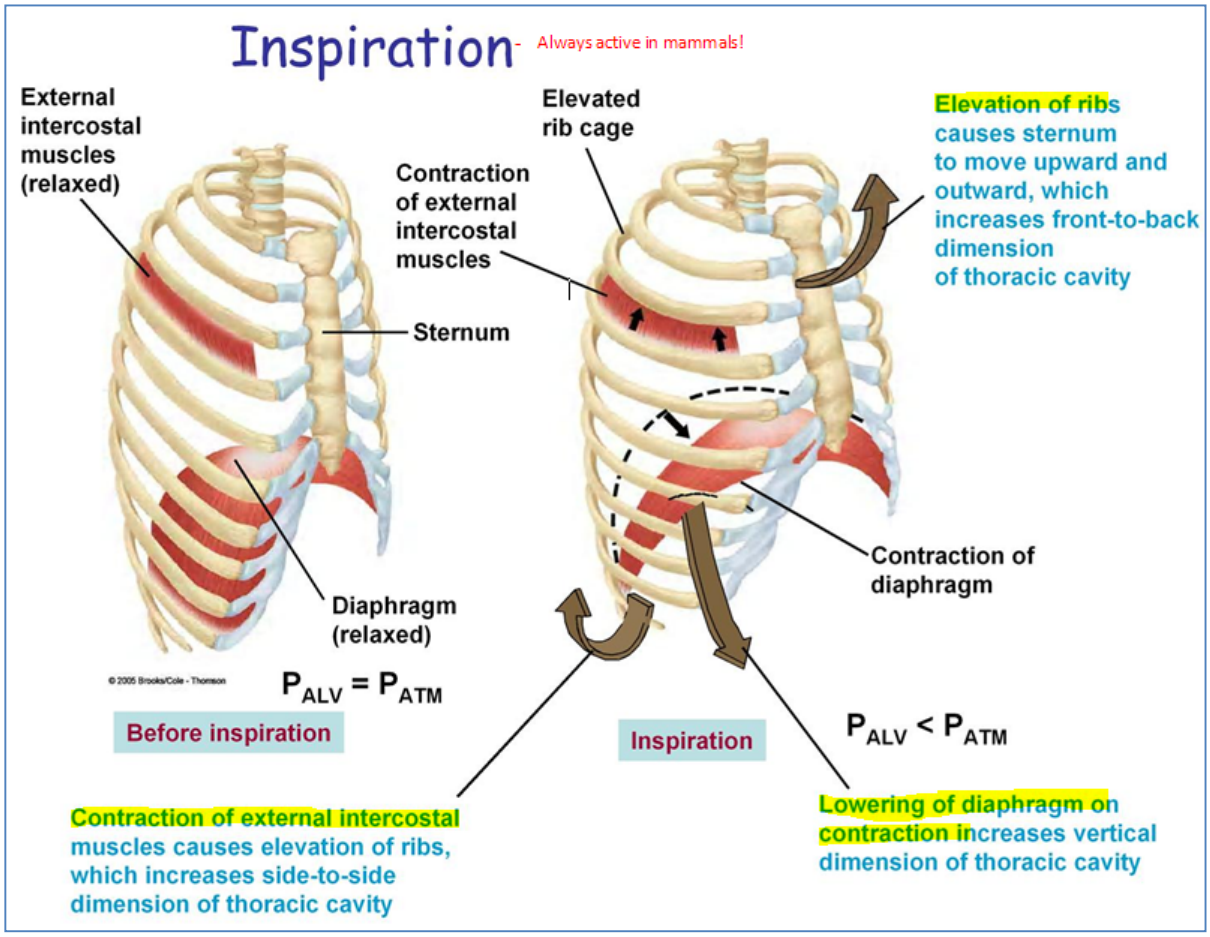
  - **Intrapulmonary Pressure:**
    - Pressure in the Alveoli
    - **Alternates between Positive & Subatmospheric (Negative) Pressures.**
      - *Negative* pressure during Inhalation
      - *Positive* pressure during Exhalation

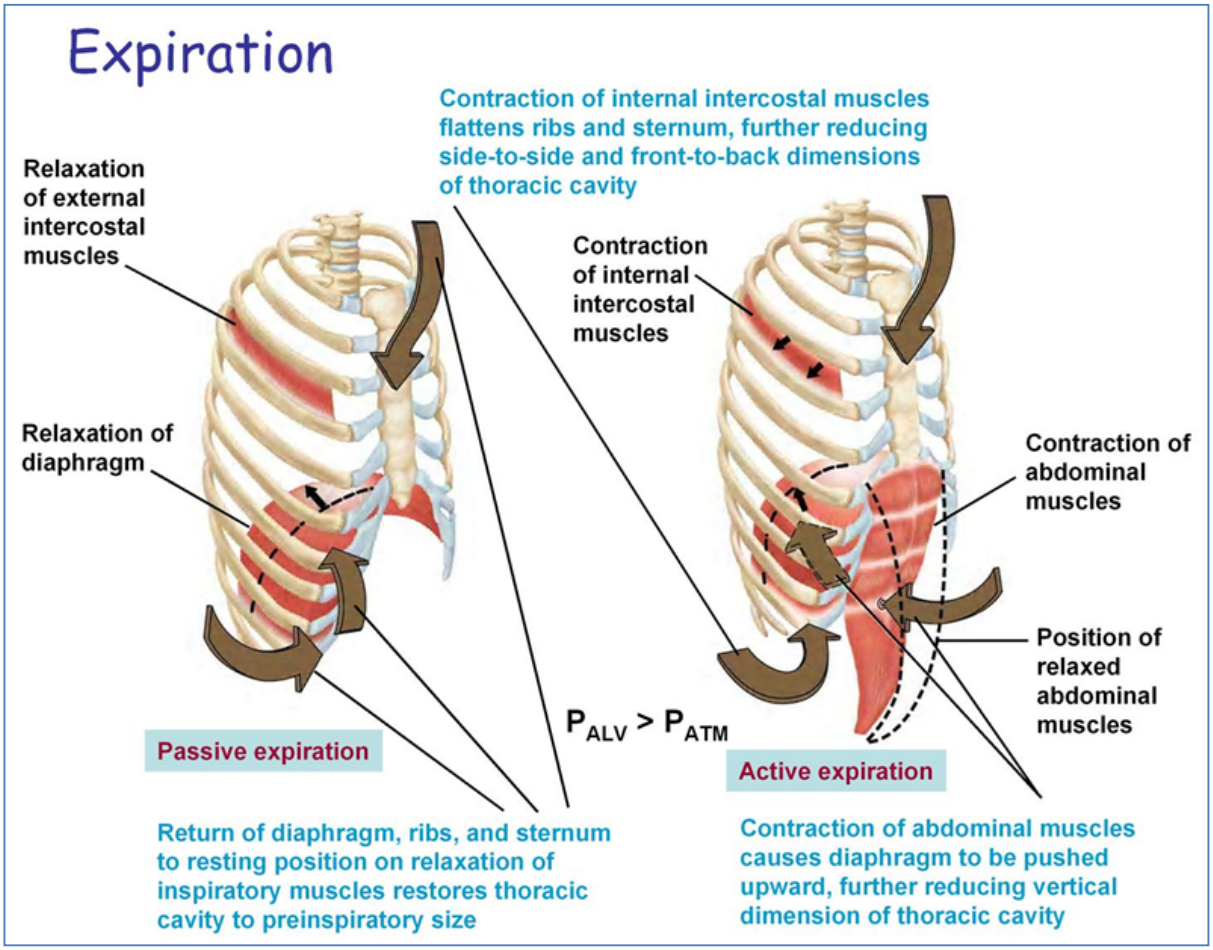


- **Inhalation:**
  - **Diaphragm:**
    - Contracts
    - Moves inferiorly
  - **External Intercostals:**
    - Contract
    - Move ribs out & up (bucket & pump handle mov'ts.)
  - **Accessory Muscles (If Forced):**
    - Scalenes
    - Sternocleidomastoids
    - Pectoralis MInors
  - **Lung Volume:**
    - Increases
  - **IntraPleural Pressure:**
    - Becomes *more* subatmospheric (more negative)
  - **IntraPulmonary Pressure:**
    - Becomes *negative.* (relative to P_{atm})
  - **Air:**
    - Flows In
- **Expiration:**
  - **Diaphragm:**
    - Relaxes
    - Moves superiorly
  - **External Intercostals:**
    - Relax
    - Rib cage descends due to recoil of costal cartilages
  - **Accessory Muscles (If Forced):**
    - Abdominal Wall Muscles (Transverse & Oblique)
    - Internal Intercostals
  - **Lung Volume:**
    - Decreases
  - **IntraPleural Pressure:**
    - Becomes *less* subatmospheric (more positive)
  - **IntraPulmonary Pressure:**
    - Becomes *positive.* (relative to P_{atm})
  - **Air:**
    - Flows Out

NB: Quiet Breathing = Eupnea
Forced Breathing = Hyperpnea




Inspiration
Always active in mammals!
External intercostal muscles (relaxed)
Elevated rib cage
Elevation of ribs causes sternum to move upward and outward, which increases front-to-back dimension of thoracic cavity
Contraction of external intercostal muscles
Sternum
Contraction of diaphragm
Diaphragm (relaxed)
© 2005 Brooks/Cole - Thomson
$P_{ALV} = P_{ATM}$
Before inspiration
Inspiration
$P_{ALV} < P_{ATM}$
Contraction of external intercostal muscles causes elevation of ribs, which increases side-to-side dimension of thoracic cavity
Lowering of diaphragm on contraction increases vertical dimension of thoracic cavity

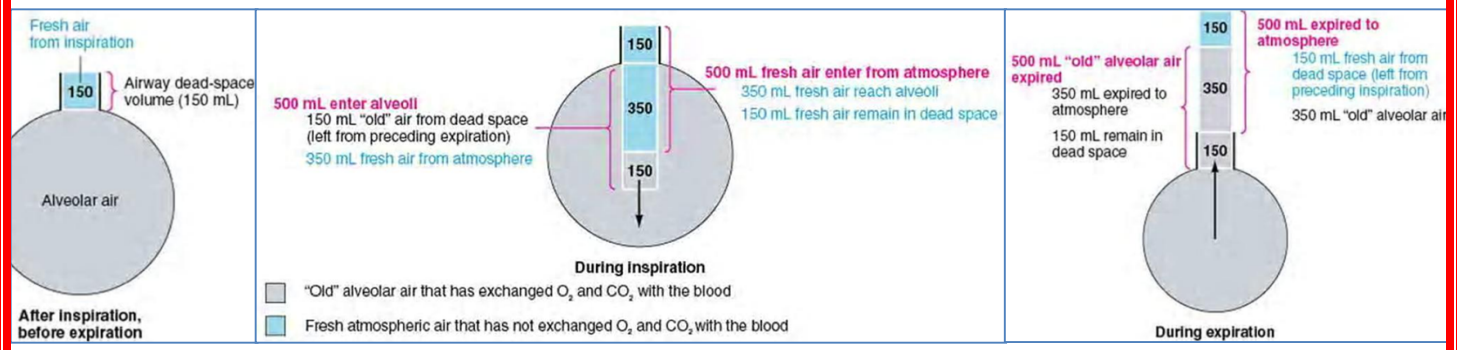

Expiration
Contraction of internal intercostal muscles flattens ribs and sternum, further reducing side-to-side and front-to-back dimensions of thoracic cavity
Relaxation of external intercostal muscles
Contraction of internal intercostal muscles
Relaxation of diaphragm
Contraction of abdominal muscles
Position of relaxed abdominal muscles
$P_{ALV} > P_{ATM}$
Passive expiration
Active expiration
Return of diaphragm, ribs, and sternum to resting position on relaxation of inspiratory muscles restores thoracic cavity to preinspiratory size
Contraction of abdominal muscles causes diaphragm to be pushed upward, further reducing vertical dimension of thoracic cavity

Respiratory Rates:

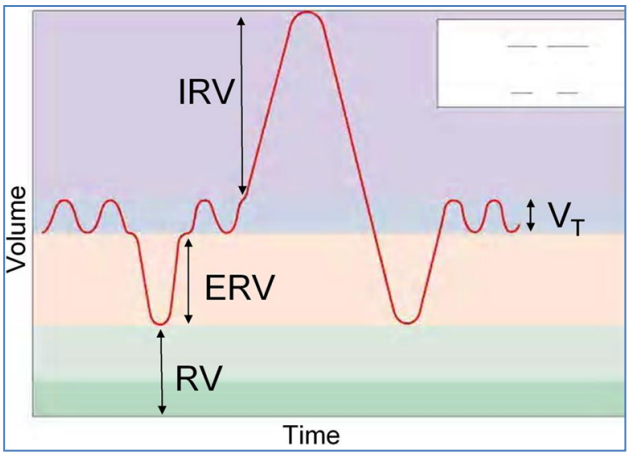
- **Respiratory Rate:** (f)
  - Breathing Frequency
- **Respiratory Minute Volume (Minute Ventilation Rate):** ($\dot{V}_E$)
  - Amount of air moved *via Tidal Ventilation* Each Minute.
  - **$\dot{V}_E = V_T \times f$**
    - Minute Ventilation Rate = Tidal Volume x Respiratory Rate
  - NB: the dot means a 'rate'.
  - NB: The Same Minute Ventilation Rate can be achieved by Different Combos of V_T & *f.*
- **Alveolar Ventilation:** ($\dot{V}_A$)
  - Amount of air *reaching the Alveoli each minute*
  - **$\dot{V}_A = (V_T - V_D) \times f$**
    - Alveolar Ventilation = (Tidal Volume – Dead Space) x Frequency
  - NB: High V_T & Low f. *maximizes Alveolar Ventilation*, but is Energetically Expensive.
    - High f. & Low V_T are Energetically Cheap, but have *low Alveolar Ventilation* due to Increased Dead Space.

Respiratory Volumes:

- **Tidal Volume:** (T_V)
  - Volume of air *inhaled* OR *exhaled during 1x Normal Breath.*
- **Dead Space:** (V_D)
  - Amount of air in *Conducting Zone* that doesn't take part in Gas Transfer.
  - There is always a small volume of air from the previous breath that will re-enter the alveoli.

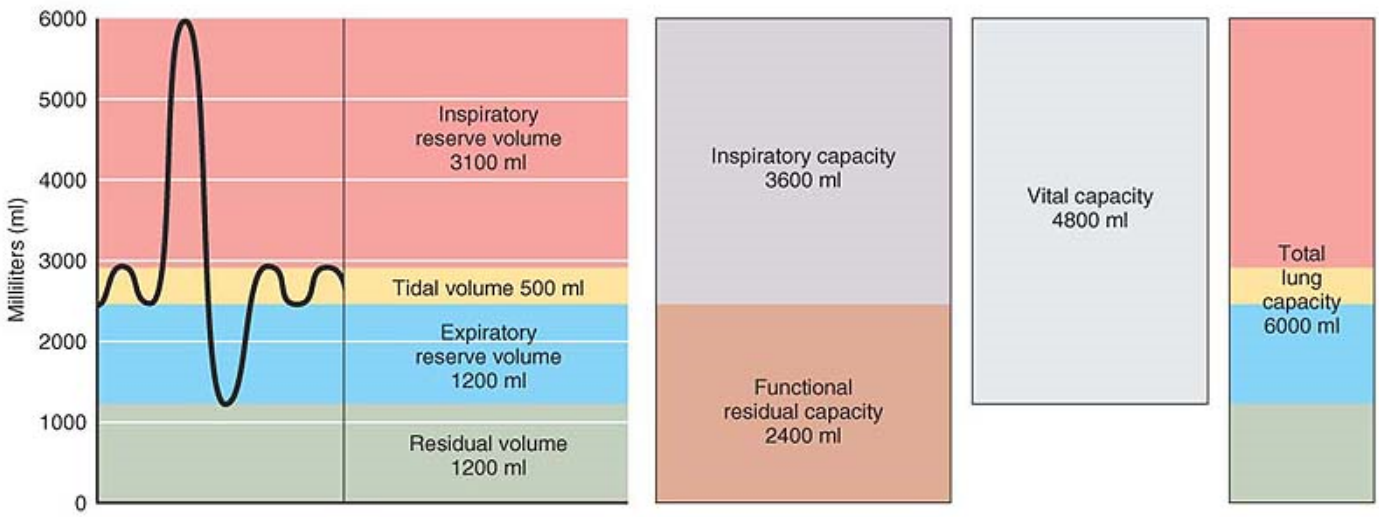


- **Expiratory Reserve Volume:** (ERV)
  - Volume of Additional air that can be EXPIRED *After A Normal Quiet Expiration*
  - Ie. Beyond Tidal Volume.
- **Inspiratory Reserve Volume:** (IRV)
  - Volume of Additional air that can be INSPIRED *After A Normal Quiet Inhalation*
  - Ie. Beyond Tidal Volume.
- **Residual Volume:** (RV)
  - Air left in lungs after *Maximum Forced Expiration*.
  - Ie. Air that *can't* be breathed out (Therefore Cannot be seen/measured on a Spirometer)



Respiratory Capacities:

- **Inspiratory Capacity:** (IC)
  - Volume of air that can be INSPIRED *After A Normal Quiet Expiration*
  - Ie. Tidal Volume + Inspiratory Reserve Volume
  - **IC = V_T + IRV**
- **Functional Residual Capacity:** (FRC)
  - Total Air Remaining *After A Normal Quiet Expiration*
- **Vital Capacity:** (VC)
  - Max Air you can Move Into OR Out of your lungs.
  - Ie. Expiratory Reserve + Tidal Volume + Inspiratory Reserve
  - **VC = ERV + V_T + IRV**
- **Total Lung Capacity:** (TLC)
  - Total Air in Lungs *After A Forced Inspiration*
  - Ie. Residual Volume + Expiratory Reserve Volume + Tidal Volume + Inspiratory Reserve Volume.
  - **TLC = RV + ERV + V_T + IRV**



(a) Spirographic record for a male

	Measurement	Adult male average value	Adult female average value	Description
Respiratory volumes	Tidal volume (TV)	500 ml	500 ml	Amount of air inhaled or exhaled with each breath under resting conditions
	Inspiratory reserve volume (IRV)	3100 ml	1900 ml	Amount of air that can be forcefully inhaled after a normal tidal volume inhalation
	Expiratory reserve volume (ERV)	1200 ml	700 ml	Amount of air that can be forcefully exhaled after a normal tidal volume exhalation
	Residual volume (RV)	1200 ml	1100 ml	Amount of air remaining in the lungs after a forced exhalation
Respiratory capacities	Total lung capacity (TLC)	6000 ml	4200 ml	Maximum amount of air contained in lungs after a maximum inspiratory effort: TLC = TV + IRV + ERV + RV
	Vital capacity (VC)	4800 ml	3100 ml	Maximum amount of air that can be expired after a maximum inspiratory effort: VC = TV + IRV + ERV (should be 80% TLC)
	Inspiratory capacity (IC)	3600 ml	2400 ml	Maximum amount of air that can be inspired after a normal expiration: IC = TV + IRV
	Functional residual capacity (FRC)	2400 ml	1800 ml	Volume of air remaining in the lungs after a normal tidal volume expiration: FRC = ERV + RV

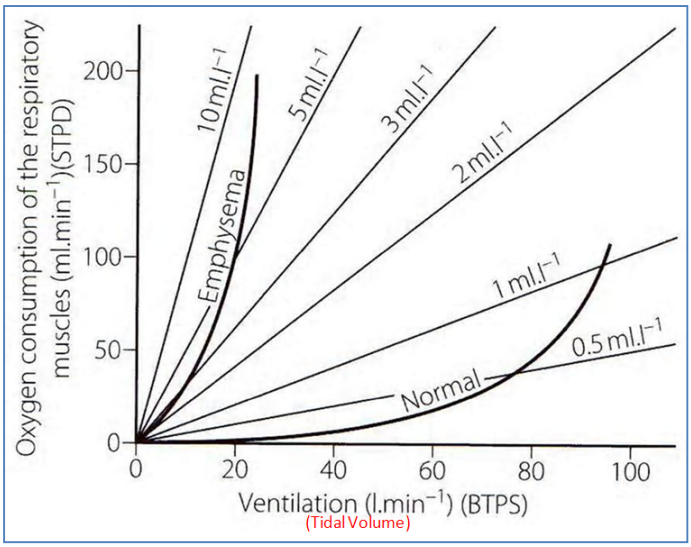
(b) Summary of respiratory volumes and capacities for males and females

Lung Compliance:

- Ease of Expansion of Lungs
- Ie. Pressure change needed to *create* Volume Change
    - Low Compliance – Requires greater force to expand lungs (opposite for high compliance)
- **Factors:**
    - **Pulmonary Conn. Tissue:**
        - Increase in Conn. Tissue (scarring/cirrhosis) → Decreases Compliance
    - **Surfactant:**
        - Prevents pulmonary epithelial surfaces from adhering during exhalation.
        - Low Surfactant → Decrease Compliance
    - **Thoracic Cage Mobility:**
        - Decrease in Thoracic Cage Mobility → Lower Compliance
        - Ie. Arthritis/scoliosis/etc.

Energetic Cost of Ventilation:

- Resting Ventilation ≈ 3-5% of Body's Energy Demands
- **Cost of Ventilation Increases When:**
    - **V_T Increases**:
        - Ie. Exercise
    - **Compliance Decreases:**
        - From: Decrease surfactant/
        - Increase in Conn. Tissue (scarring/cirrhosis) → Decreases Compliance
        - Decrease Thoracic Mobility
    - **Airway Resistance Increases:**
        - From broncho-constriction
        - Eg. Asthma/Emphysema
        - NB: Airway Diameter is an EXTREMELY POWERFUL FACTOR OF FLOW RATE.
- **NB:** Some Path. Conditions Increase the cost of breathing so significantly that the respiratory muscles alone consume more oxygen than they bring in.



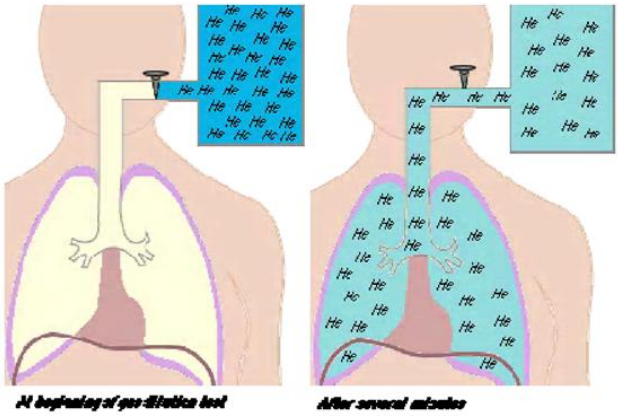
Station B: Determination of Functional Residual Capacity, Residual Volume and Total Lung Capacity Using the Helium Dilution Method

The functional residual capacity is the volume of air that remains in the lungs at the end of each normal expiration. Its value changes markedly in some types of respiratory disease. It cannot be measured directly by a spirometer, because the residual volume of the lungs cannot be expired into a spirometer. It can however be determined using the closed circuit helium dilution method (Refer to Guyton page 476 for more information).

A spirometer of known volume is filled with air mixed with helium at a known concentration. Before starting to breathe from the spirometer, the person exhales normally (therefore the volume of air in the lungs is equivalent to the functional residual capacity). At this point, the subject begins to breathe from the spirometer, and the gases of the spirometer begin to mix with the gases of the lungs, as a result the helium becomes diluted by the functional residual capacity gases and, when equilibrium is reached as a result of rebreathing, it is possible to calculate the functional residual capacity from the degree of dilution of the helium.

$$FRC = \left(\frac{Ci_{He}}{Cf_{He}} - 1 \right) Vi_{spir}$$

Where FRC is the functional residual capacity, Ci_{He} is the initial concentration of helium in the spirometer, Cf_{He} is the final concentration of helium in the spirometer, and Vi_{spir} is the initial volume of the spirometer. This is a manipulation of the Law of conservation of mass:



Conservation of mass: $C_1V_1 = C_2(V_1+V_2)$

In addition, total lung capacity (TLC = FRC + IC) and residual volume (RV = FRC – ERV) may be calculated.

From the following data, calculate the functional residual capacity, the total lung capacity and the residual volume.

Respiratory Medicine Notes
Ventilation vs. Perfusion

Bronchial Circulation:

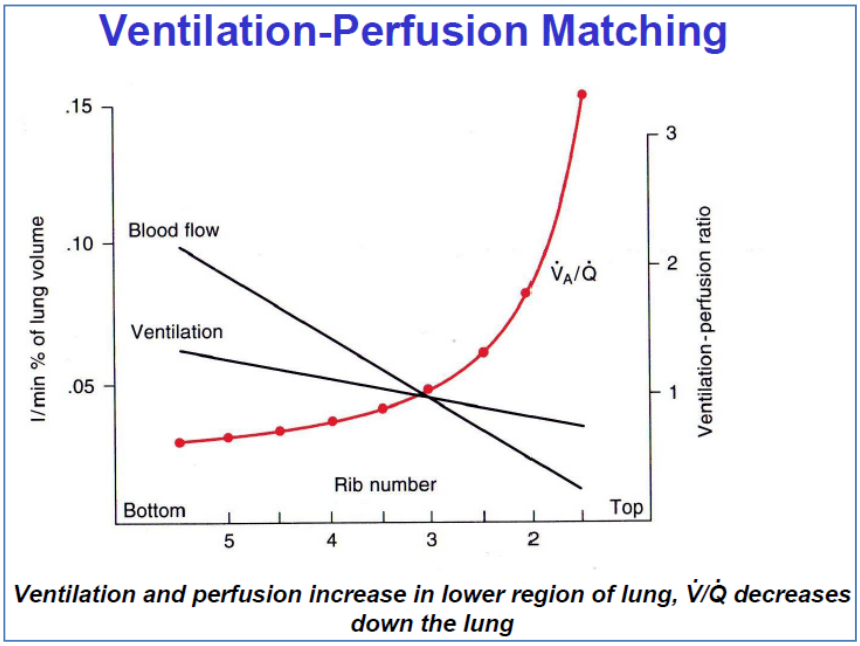
- O_2/Nutrient-Rich blood supply →Lung Tissues
- Originates from *Systemic Circulation*
- Via small *Bronchial Arteries*.
- Blood empties into *Pulmonary Veins* → Left Atrium
    - NB: because of this, Venous Return to L-Atrium is *More* than R-Ventricular Output.

Pulmonary Circulation:

- **Features:**
    - Much shorter than systemic circulation
    - Artery lumens are larger than systemic..Due to:
        - *Thin* walls (1/3 of aorta)
        - *Distensible* Walls:
            - Stretch to maintain low BP
            - Prevents rupture of microvessels.
- **Pressures:**
    - *Pressure & Resistance - MUCH LOWER THAN SYSTEMIC CIRCUIT*
    - *Prevents rupture* of *Microvessels*
    - **Pulmonary Artery:**
        - Systolic = 25mmHg
        - Diastolic = 8mmHg
    - **Pulmonary Capillary Pressure:**
        - ≈ 7mmHg
    - **Pulmonary Vein:**
        - ≈ 2mmHg
- **Resistance:**
    - Much lower than systemic
    - Extra-Alveolar vessels have Low Resistance @ High Lung Volumes – Due to Radial Traction
    - However, as lung approaches full volume, Transmural Pressure overcomes Radial Traction → Decreases Vessel Diameter → Increases Resistance
- **Blood Volume:**
    - Average = 450-500mL (9% Total Blood Volume)
    - Only 70-100mLs of this is involved in Gas-Exchange at any one time.
    - ≈70mLs of blood is replaced each heart-beat
    - Varies Greatly in different Circumstances:
        - **Physiologically:**
            - **Eg. Blowing Trumpet** → ↑Thoracic Pressure → may expel 250mL blood
            - **Eg. Acute blood loss** → ↓ Total Blood Volume → affects Pulmonary Blood Volume
            - **Eg. Posture**: Supine or Standing – standing ↓ B-Volume by 10%
            - **Eg. Systemic Vascular Tone:** ↑Systemic Vascular Tone – Squeezes blood into Pulmonary Circuit.
        - **Pathologically:**
            - **Eg. L-Heart Failure** → Blood backs up in Pul-Circuit → ↑Pulmonary Blood Volume.
- **Blood Flow:**
    - Pulmonary Blood Flow = Cardiac Output
    - Anything affecting CO, will equally affect P-Blood Flow (HR/SV/Contractility/Venous Return)
- **PO_2 Vs. Blood Flow: (*HYPOXIC VASOCONSTRICTION*):**
    - Alveolar Blood is *Directed To* areas of the lungs that are *Best Oxygenated (Best Ventilated)*.
        - Opposite to systemic circulation
    - If $P_{A\text{-}O2}$ (Alveolar O_2 Partial Pressure) Decreases, adjacent blood vessels constrict for a few minutes.
        - -Restricts blood flow to poorly ventilated alveoli.
    - ***Ie. Automatic Mechanism*** that ***Matches Blood Flow with Ventilation***

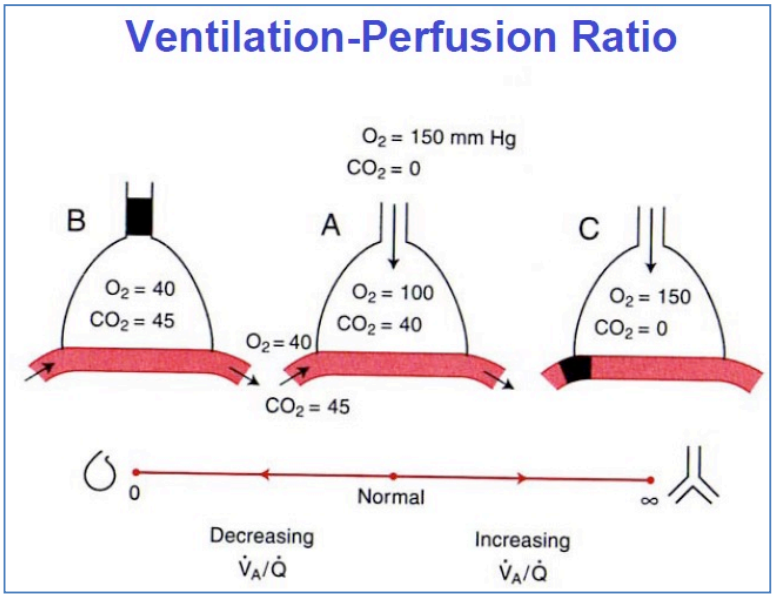
Regional Pulmonary Blood Flow:

- **Ventilation-Perfusion Matching:**
  - Not All Alveoli are Perfused or Ventilated equally.
  - Even in a normal lung, there will be an imbalance of Perfusion & Ventilation.
    - This Imbalance is ***quantified* by** a ***Ventilation-Perfusion Ratio***.
    - This ratio ***changes depending on location within lung***.
      - *Blood Flow Rate increases toward Base of Lung.*
      - *Ventilation Rate increases toward Base of Lung.*(To a Lesser Degree than Blood Flow)

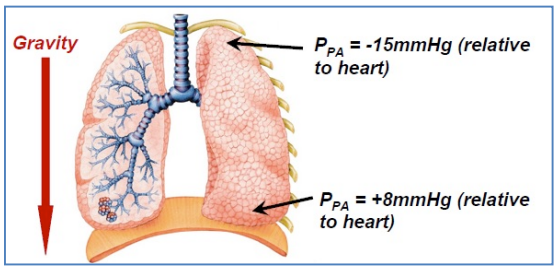


Ventilation and perfusion increase in lower region of lung, V̇/Q̇ decreases down the lung

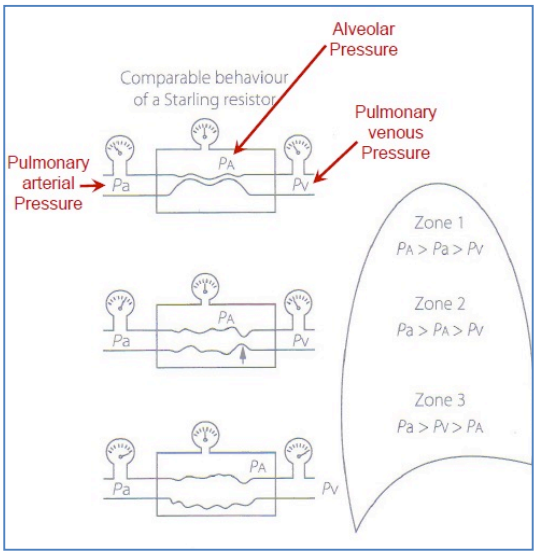
  - **Ventilation-Perfusion Ratios:**
    - $\dot{V}_A/\dot{Q}$ (Alveolar Ventilation *Rate* / Blood Flow *Rate*)
    - **Approaching Zero:**
      - When Ventilation = 0, but there's still Perfusion, $\dot{V}_A/\dot{Q} = 0$
      - No fresh gas coming into lung →
      - Partial Pressures in Alveolus will equalise with Capillary Partial Pressures.
    - **Approaching Infinity:**
      - When Adequate Ventilation, but *No Perfusion*, $\dot{V}_A/\dot{Q}$ = Infinity
      - No blood supply to alveolus →
      - Partial Pressures in Alveolus will equalise with Atmospheric Partial Pressures.

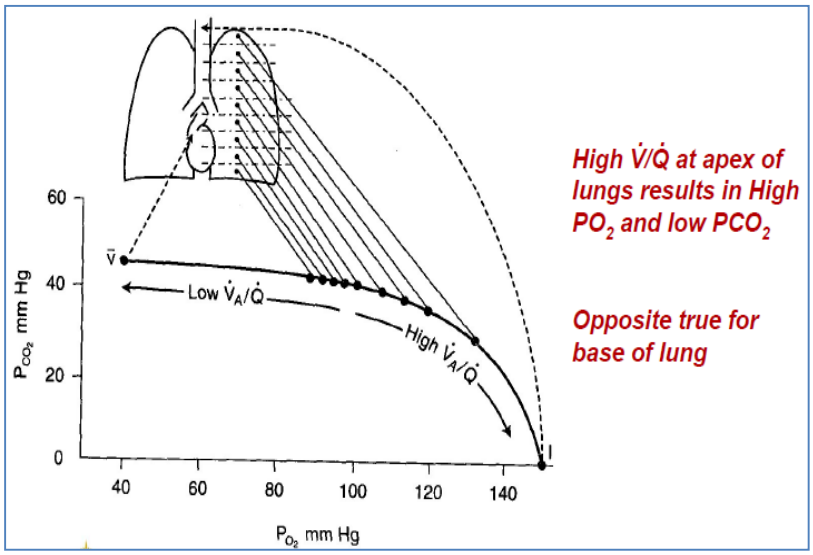


- **Affect of Gravity:**
  - **P_a (Arterial Pressure):**
    - Pressure at top – Lower
    - Pressure at bottom – Higher
    - Pressure difference ≈ 23mmHg between Top & Bottom.
  - **When Standing:** Little flow @ Top, 5x Flow @ Bottom.



  - **Blood Pressure Vs. Alveolar Air Pressure (TRANSMURAL PRESSURE):**
    - Capillaries are distended by internal BP.
    - But, are also compressed by Alveolar Air Pressure
      - The ***net result*** between these 2 pressures, **determines perfusion (**vessel patency)
    - **Lung is divided into 3 zones based on the 3 possible *net results* of BP vs. Alv.Air Pressure.**
- **3 Zones:**
  - **Zone 1:**
    - Capillary Pressure never exceeds Alveolar Air Pressure.
    - No Blood Flow at all.
    - V/Q Ratio → Infinity
  - **Zone 2:**
    - Capillary Pressure only exceeds Alveolar Air Pressure during Systole.
    - Intermittent Blood Flow (Flow during systolic pressure)
    - V/Q Ratio = Normal
  - **Zone 3:**
    - Capillary Pressure always exceeds Alveolar Air Pressure.
    - Constant Blood Flow.
    - V/Q Ratio → Still Normal, but lower.
  - NB: Zone 1 is generally only seen under Abnormal Condtions. Normal Lung = usually Zone 2 & 3.



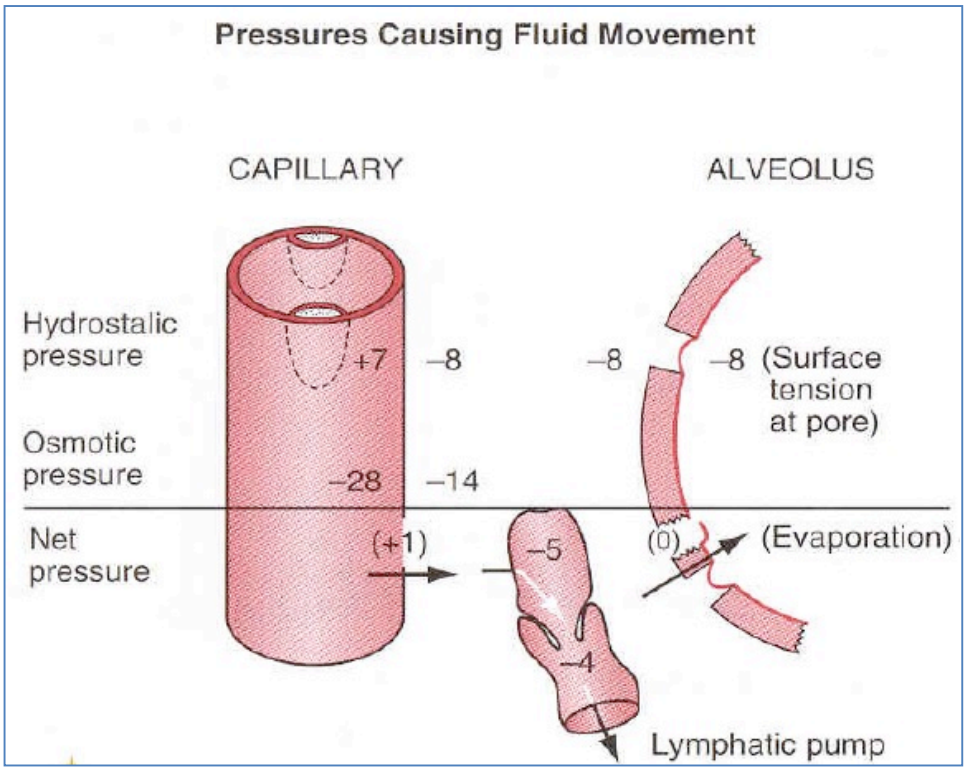


Effect of Exercise on Blood Flow:

- Blood Flow through lungs increases 4 – 7 Times!
- However, Rise in $BP_{Pulmonary}$ Must be kept low to stop microvessel rupture.
- Extra Flow Accommodated for in 3 Ways:
    - Distension of Capillaries.
    - Increasing *number* of O*pen* Capillaries
    - For Blood Flow to be maintained, Pulmonary Arterial Pressure must Be Increased.

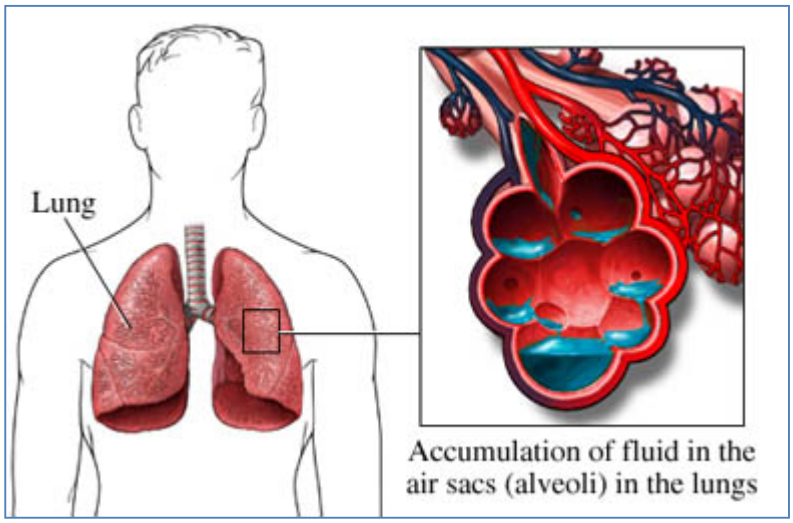
Pulmonary Capillaries:

- **Dynamics:**
    - Blood Transit Time through Capillaries ≈ 0.8 sec.
    - During Exercise, CO↑ → Capillary Transit time shortens to ≈ 0.3 sec.
        - NB. If less than 0.3 sec. Blood doesn't have time for adequate Gas Exchange.
- **Fluid Exchange:**
    - **Same Forces as Systemic Capillaries:**
        - Hydrostatic Pressure
        - Colloid-Osmotic Pressure
    - **But Different Magnitudes:**
        - **Hydrostatic:**
            - **≈ 7mmHg**
            - Pul.Capillary Hydrostatic Pressure Lower Than Systemic
            - Slightly Negative Interstitial Hydrostatic Pressure
                - Keeps alveoli 'dry'
        - **Colloid-Osmotic Pressure**
            - Cap. Osmotic Pressure Higher than Interstitium.
                - **≈ -28mmHg**
                - Draws Fluid back into Capillaries
                - Opposes Hydrostatic Pressure.
            - Pul.Capillaries – relatively leaky to proteins → some proteins move to Interstitium.
                - Interstitial Osmotic Pressure > Alveolar Osmotic Pressure
                - Draws Alveolar Fluid → Interstitium
                - Prevents build-up of fluid in alveoli.
                - NB: if too leaky, proteins in Interstitium can cause Oedema.



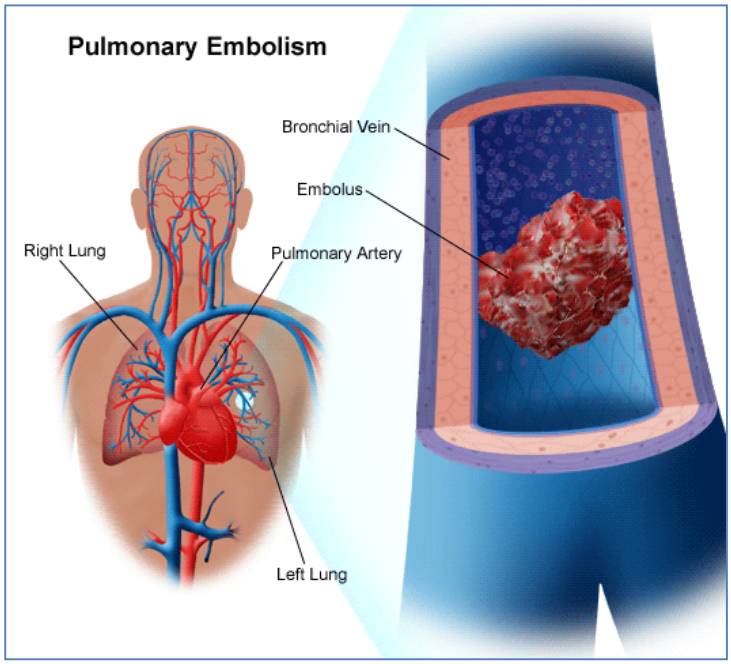
Preventing Pulmonary Oedema:

- **Negative Interstitial Pressure:**
  - Slightly Negative Interstitial Hydrostatic Pressure
  - Keeps alveoli 'dry'
  - Fluid in Alveoli is sucked into Interstitium → Lymphatics
  - NB: If Interstitial Fluid Pressure was +ve, Oedema would occur.
- **Lymphatic Vessels:**
  - Extend from all tissues of lungs.
  - Actively pump Interstitial Fluid → Blood Vessels
- **Oedema Safety Factor:**
  - For oedema to occur, Pul.Cap-Pressure must rise above Colloid Osmotic Pressure.
    - Pul.Cap-Pressure ≈ 7mmHg
    - C.Osmotic Pressure ≈ -28mmHg
  - Therefore a +21mmHg rise in Pul.Cap-Pressure is needed.
    - If this occurs, lethal oedema may occur within *hours!*
  - Chronic elevated Pul.Cap-Pressure → Expanded Lymph Vessels.



Pulmonary Embolism:

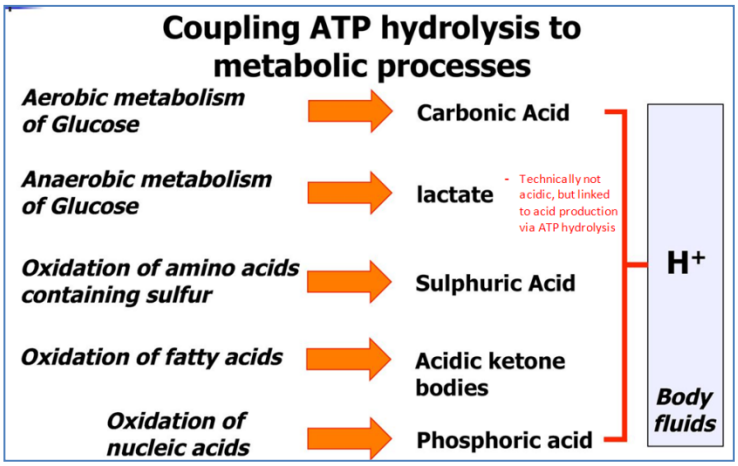
- Foreign fragments blocking a blood pulmonary vessel.
- Often due to Blood Clot (Thrombus)
- Blockage of vessel in lung will impact/prevent effective oxygenation of blood.



Respiratory Medicine Notes
Body Acid-Base Balance

Acid Production:

- **The Body *turns over* up to 150*Moles* of H^+ per day – THAT'S A LOT!!**
- **Where does it come from?**
  - **Metabolic Processes:**
    - **Most H^+ comes from *Hydrolysing ATP* (ie. *Aerobic Metabolism*)**
      - $ATP + H_2O \rightarrow ADP + P_i + H^+$
      - NB: The Body turns over ≈40kg of ATP *per day!*
    - **Much H^+ also comes from:**
      - Anaerobic Glucose Metabolism
      - Amino Acid Metabolism
      - Fatty Acid B-Oxidation.
      - Nucleic Acid Metabolism.



- **Despite LOADS OF H^+ produced, *Body pH* is *Finely Regulated.***
  - Ie. Very small pH changes observed in body.

What is pH?:

- pH = the *negative log* of the *H^+ ion concentration.*
- ***pH* = -log [H^+]**
- **Remember:**
  - **Acid:** Proton (H^+) *Donor*
  - **Base:** Proton (H^+) *Acceptor*

Physiological pH Values:

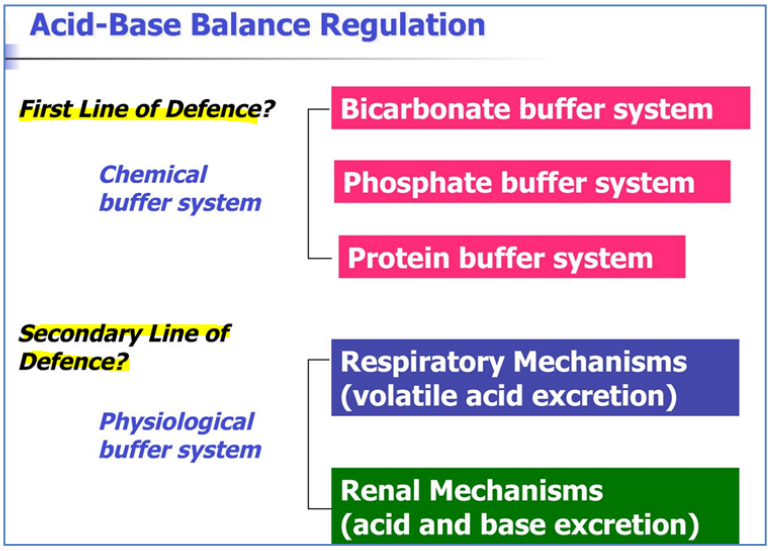
- **Arterial pH = 7.40**
  - NB: pH of <6.9 can be lethal
- **Venous pH =** **7.35** - more acidic due to *higher HCO_3* (ie. Higher P_{CO2})
- **Urine pH =** 4.5 to 8.0
- **Stomach pH =** 0.8 - requirement of chemical digestion & activation of digestive enzymes.
- **Bile pH =** 7.8 to 8.6 - needs to be alkaline to break down fats.

Acid-Base Homeostasis Regulated By:

- **Buffers:**
  - **What are they?:**
    - Solutions of A Weak Conjugate Acid & A Weak Conjugate Base.
    - Resist changes in pH
  - **pK of A Buffer:**
    - Mathematically → The –log of the Equilibrium Constant (K_{eq} **= [Products] ÷ [Reactants]**)
    - The pH of the Buffer Solution where both the Conjugate Acid & Base are at **50% dissociation**.
    - It is the pH that the Buffer Solution wants to be at.
    - Hence – yields Max. Buffering Power.
      - Ie. If an experiment required a pH of 7.4, you would conduct it in a buffer of pK=7.4
  - **Isohydric Principle:**
    - There are many H^+ buffers in the body...
    - All *Buffers* in a *Common Solution* are in *Equilibrium* with the *Same* $[H^+]$
    - Thus, All Buffers in the Body Work Together.
    - **Isohydric Principle =**

    "When $[H^+]$ Changes, the *Balance* of all buffer systems changes at the same time."

- **Acid-Base Balance Lines of Defence:**
  - **1. Chemical Buffer Systems:**
    - #1.Bicarbonate Buffer System
    - Phosphate Buffer System
    - Protein Buffer System
  - **2. Physiological Buffer Systems:**
    - Respiratory Mechanisms
    - Renal Mechanisms



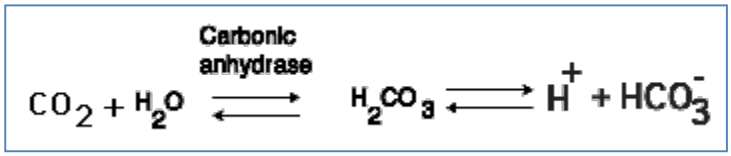
-1st Line Of Defence: Chemical Buffer Systems:

- **#1. Carbonic-Acid-Bicarbonate Buffer System:**
  - The most important Body Buffer System
  - Occurs **within the Red Blood Cell**
    - ***Carbonic Anhydrase*** (in RBC) catalyses: **($CO_2 + H_2O \rightarrow H_2CO_3$)**
  - Operates **in conjunction with the respiratory system**.
    - Ie. Blowing off CO_2 shifts eq. To the left → Less $[H^+]$ → pH increases.

  - **Clinical Assessment of Acid/Base:**
    - **3 Factors Required:**
      - 1. Blood pH
      - 2. Blood P_{CO2}
      - 3. Plasma Bicarbonate

  - **When the ratio of $[HCO_3^-]/[H_2CO_3]$ = 20:1, The blood pH will be *normal* = pH 7.4**
    - Ie. The [Bicarbonate] : [Carbonic Acid] = 20:1
    - Ie. The [Bicarbonate] : [Carbon Dioxide]= 20:1

    - **Changing this ratio – Changes Blood pH:**
      - **pH ↑ When:**
        - [Bicarbonate]↑ (Pushes Equation to the Left)
        - [Carbon Dioxide]↓ (Pushes Equation to the Left)
      - **pH ↓When:**
        - [Bicarbonate]↓ (Pushes Equation to the Right)
        - [Carbon Dioxide]↑ (Pushes Equation to the Right)



$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^- (pK\ 6.11)$$

Carbon Dioxide Carbonic Acid Bicarbonate Ion

Simplified Equation

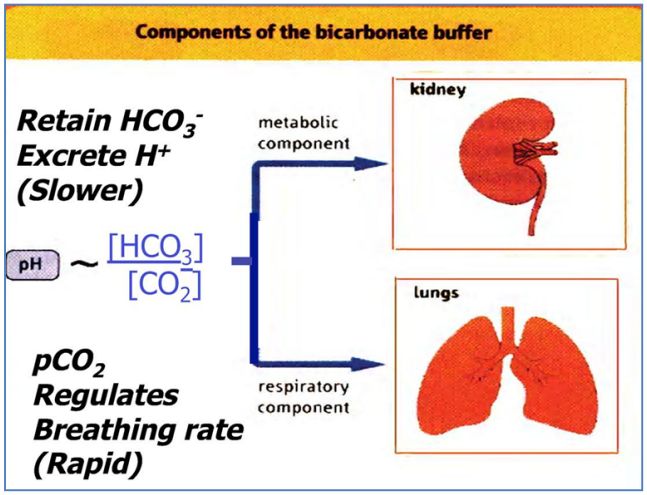
$$\text{Net } CO_2 \text{ (dissolved)} + H_2O \leftrightarrow H^+ + HCO_3^- (pK\ 6.11)$$

- **#2. Phosphate Buffer System:**
  - Second most important Body Buffer System
  - Operates in the internal fluid of all cells.

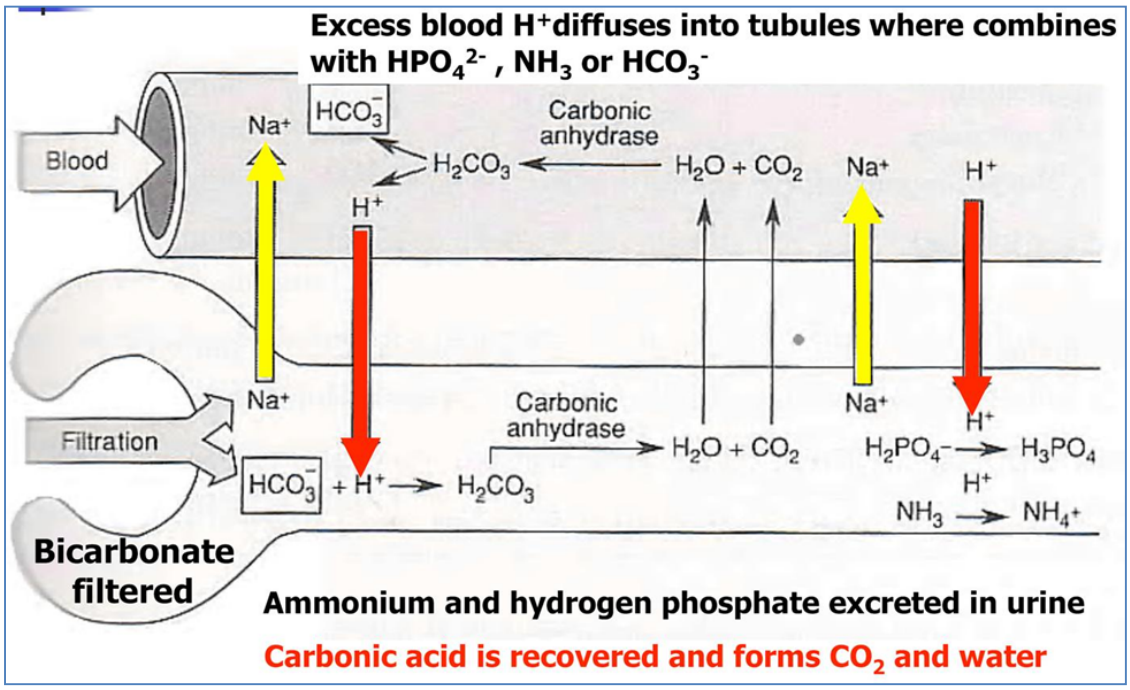
$$H_2PO_4^-(aq) \rightleftharpoons H^+(aq) + HPO_4^{2-}(aq)$$

- **#3. Protein Buffers (in RBCs & Intracellular Buffers)**
  - Both intracellular and extracellular **proteins have negative charges and can serve as H^+ buffers**.
  - However, because most proteins are inside cells, this primarily is an **intracellular** buffer system.
    - Eg. Haemoglobin (Hb) is an excellent intracellular buffer because of its ability to bind H^+.
    - Forms a *weak acid + carbon dioxide (CO2).*
    - After O_2 is released (in the peripheral tissues), Hb binds CO2 and H^+ ions.
    - As blood reaches the lungs these actions reverse themselves →Hb binds O_2, releasing the CO_2 and H^+ ions.
    - The H^+ combines with bicarbonate (HCO_3) → carbonic acid (H_2CO_3). The H_2CO_3 breaks down to form water (H2O) and carbon dioxide (CO2) which are excreted via expiration through the lungs. Therefore respirations help maintain pH.

- 2nd Line Of Defence: Physiological Buffer Systems:

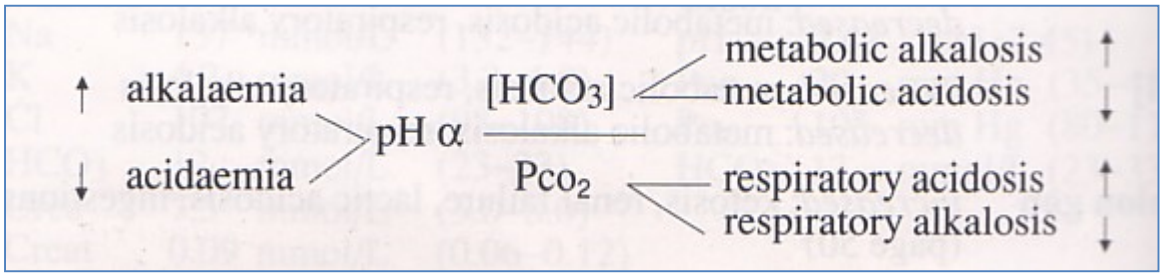


- **Respiratory System – Short Term:**
  - (CO_2 Excretion)
  - CO_2 constantly produced during Metabolic Processes
  - Eliminated by lungs.
  - If not eliminated from body, pH would quickly become *Acidic* (Bicarb-Buffer Eqn. Shifts to Right)
  - **CO_2: The Controller Of Ventilation:**
    - CO_2 is the main controller because H^+ can't cross the *Blood-Brain-Barrier.*
    - **ΔP_{CO2} → ΔpH of Cerebro-Spinal Fluid → Sensed by Medulla (respiratory centres)→ ΔResp's**
      - ↑P_{CO2} Increases Ventilation Rate + Depth (eg. Exercise)
      - ↓P_{CO2} Decreases Ventilation Rate + Depth (eg. After Hyperventilating)
- **Kidneys – Long Term:**
  - **Kidneys Control Acid/Base by excreting either:**
    - Acidic Urine
    - Basic Urine
  - **Mechanism:**
    - **HCO_3^-** Filtered → Renal Tubules →Combined with H^+ → Carbonic Acid → $H_2O + CO_2$ → Blood
    - **H^+** Filtered → Renal Tubules → Combines with HCO_3 →Carbonic Acid →$H_2O + CO_2$ → Blood
      → Combines with HPO_4^{2-} or NH_3 → Excreted in Urine**.**
    - In Short:
      - Carbonic Acid is recovered → CO_2 & H_2O → Blood
      - Ammonium & Hydrogen Phosphate → Excreted in Urine.



Metabolic Vs. Respiratory pH Disturbances:

- **Metabolic –**
  - **– Acidosis:**
    - Due to ↓[HCO_3]
    - (Due to inability of the body to form bicarbonate (HCO_3^-) in the kidney)
    - (Or, Due to Lactic/Keto Acid build-up)
  - **– Alkalosis:**
    - Due to ↑[HCO_3]
    - (Due to Loss of H^+ in Urine or Vomiting)
    - (Or, Due to Retention of Bicarbonate (HCO_3))
- **Respiratory –**
  - **– Acidosis:**
    - Due to ↑P_{CO2}
    - (Due to decreased ventilation of the pulmonary alveoli, →elevated P_{CO2}).
  - **– Alkalosis:**
    - Due to ↓P_{CO2}
    - (Due to increased alveolar respiration (hyperventilation) →decreased plasma [CO_2])



- **Compensatory Mechinisms:**
  - In either Metabolic or Respiratory Acidosis/Alkalosis, the compensatory mechanism will always be the other system.
    - Ie. If Metabolic Acidosis, the Compensatory Mech. Will be the Respiratory System (viseversa)
  - NB: Regulation of breathing – normally via P_{CO2} (because H^+ can't cross Blood-Brain Barrier). However, in *Metabolic Acidosis*, the P_{CO2} is already lower than normal (due to right-shift in equil.) and therefore can't stimulate breathing. *Instead,* the Primary Factor would be *Blood pH* on *Peripheral Chemoreceptors*.

Anion Gap:

- **What is it?:**
  - The Difference between Plasma Concentrations of *Measured* Anions & Cations, Minus *Unmeasured* Cations.
  - Anion Gap = (Na^+ – (HCO_3^- - Cl^-)) – Unmeasured Cations
- **Background Info:**
  - Plasma concentrations of Anions & Cations must be *Equal* – to maintain electrical neutrality.
  - However, only certain ions (Na^+, Cl^- & HCO_3^+) are measured in the Lab.
  - Therefore, there are other *Unmeasured Ions* that contribute charge to the solution, resulting an 'imbalance' in the Anion Gap Equation.
    - This magnitude of this 'Imbalance' can indicate concentrations of *Unmeasured Ions*:
      - Eg. Lactic Acid
      - Eg. Keto Acids
    - Therefore useful in.....
- **An important tool for Evaluating The *Type* of Metabolic Acidosis:**
  - **If Patient is in Metabolic Acidosis, and Their Anion Gap is Normal:**
    - The ↓[HCO_3^-] has likely been balanced by ↑[Cl^-]
    - Therefore – *Hyperchloraemic* Metabolic Acidosis
  - **If Patient is in Metabolic Acidosis, and Their Anion Gap is High:**
    - Due to ↑[Lactic Acid] → *Lactic* Acidosis.....OR
    - Due to ↑[Keto Acids] → *Keto* Acidosis.

Question To Ponder:

- **Q. If you are doing a lab experiment, you choose a buffer with a pK as close as possible to the pH of the solution to get maximal buffering. Therefore, how is the Bicarbonate Buffer System still an effective buffer, even though it has a pK of 6.1 (over 1 pH unit less than blood pH (7.4))?**
    - A. The Bicarbonate Buffer System would be an inefficient buffer in the lab (Closed system). However, our body is different to a lab experiment in that it is an open system that is exchangeable with the environment. Ie. By actively breathing off CO_2 into the air, we shift the equilibrium to the left, keeping our blood pH at an acceptable level.
    - The advantage is that this system is convenient and fits in with our metabolic cycles.
    - The disadvantage is that our blood pH is *directly* linked to breathing, and if we stop breathing, even for a minute, our blood pH can reach dangerous (lethal) levels.

Respiratory Medicine Notes
Hyperbaric & Hypobaric Conditions

Basics of Hyper/Hypo-Baric Conditions:

- ***Barometric Pressure Decreases Greatly With Altitude***
  - NB: The *Percentage* of Oxygen is the same at any Altitude (21%)
  - NB: The *Partial Pressure* of Water Vapour is the same at any Altitude (47mmHg)
- ***Barometric Pressure Increases Greatly With Depth (Underwater)***
  - NB: Every 10 metres you go down, the pressure increases by 1xAtmosphere (760mmHg).

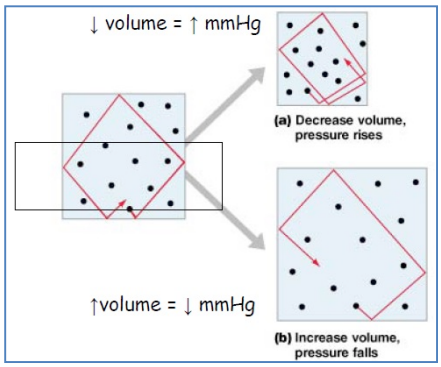
Revision of The Gas Laws:

- **Dalton's Law of Partial Pressures:**
  - The total pressure of a mixture of gasses is the combined sum of each gas's partial pressure, which is proportional to its abundance (%age) in the mixture.

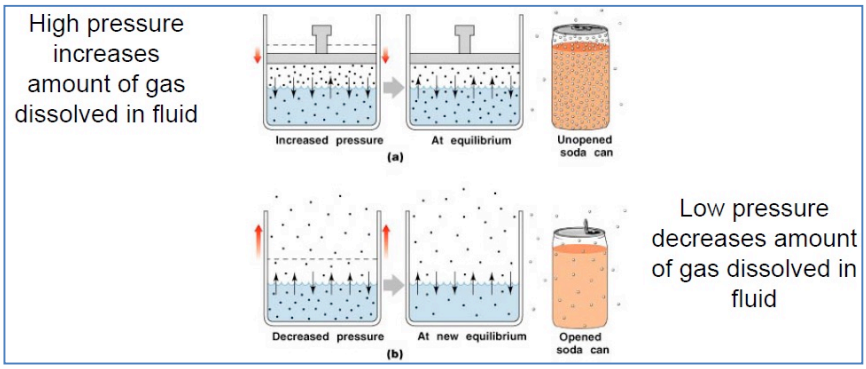
Abundance in air:	Collisions:	Partial Pressure:
78.6% N_2 (Nitrogen)	78.6% N_2	N_2 78.6% x 760 = 597 mmHg
20.9% O_2 (Oxygen)	20.9% O_2	O_2 20.9% x 760 = 159 mmHg
0.5% H_2O (Water)	0.5% H_2O	H_2O 0.5% x 760 = 3.8 mmHg
0.04% CO_2 (Carbon dioxide)	0.04% CO_2	CO_2 0.04% x 760 = 0.3 mmHg

$$P_{N_2} + P_{O_2} = P_{H_2O} + P_{CO_2} = 760 \text{ mmHg}$$

- **Boyle's Law of Pressure Vs. Volume:**
  - At a constant temperature, the pressure of a gas is inversely proportional to its volume.



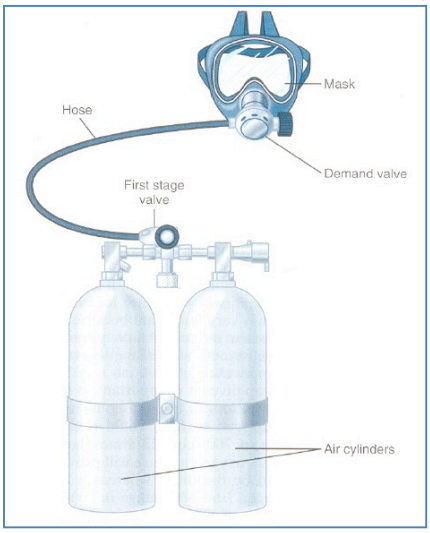
- **Henry's Law of Dissolved Gasses:**
  - At a constant temperature, the amount of gas dissolved in a solution is proportional to the Partial Pressure and solubility of that gas in that liquid.



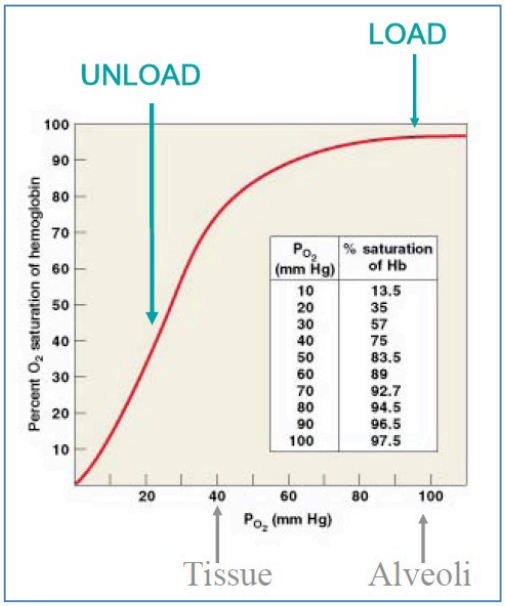
Hyperbaric Conditions (Ie. SCUBA Diving):

- **Relevant Gas Laws:**
  - **Dalton's Law:** Increase in Pressure → Increases the Partial Pressures by the same amount.
  - **Boyle's Law:** Increase in Pressure Decreases Gas Volumes.
  - **Henry's Law:** Increase in Pressure Forces More Gas into Solution.

- **The Breathing Apparatus:**
  - Tanks of Compressed Air (Needs to be compressed to inflate the lungs underwater)
  - Regulator 'steps down' the pressure.
  - Mouthpiece + Valve
  - Hose – Must have the smallest possible Dead-Space (to avoid re-breathing expired CO_2)



- **Effects of High Partial Pressures (of O_2):**
  - **Haemoglobin Saturation Curve:**
    - Normally, all of the Blood's O_2 is bound to Haemoglobin (little/none in simple solution)
    - However, since SCUBA air is delivered at high pressure, lots of O_2 will dissolve in the blood.
    - As a result, the O_2 Partial Pressures in the Blood far exceed Hb's Functional Range.
    - This renders Haemoglobin useless and it remains 100% saturated.



P_{O_2} (mm Hg)	% saturation of Hb
10	13.5
20	35
30	57
40	75
50	83.5
60	89
70	92.7
80	94.5
90	96.5
100	97.5

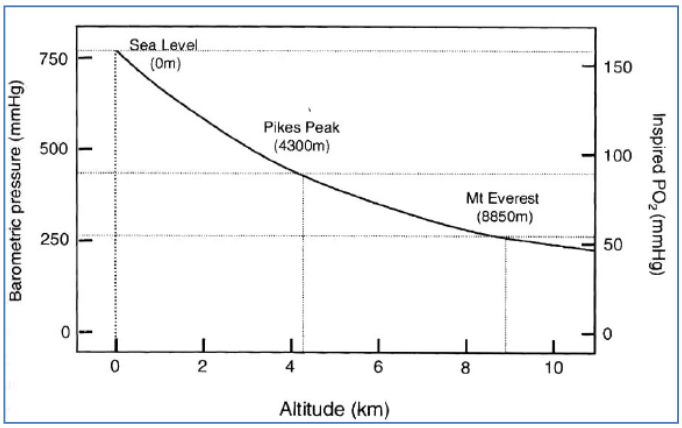
  - **Acute Oxygen Poisoning:**
    - If the diver descends more than ≈ 80m, he will be breathing O_2 at 1500mmHg.
    - A P_{O2} of 1500mmHg may lead to Oxygen Poisoning.
    - A P_{O2} of 3000^{+}mmHg will cause Seizures & Coma. (Brain is particularly sensitive)
    - Also, excess oxygen converts to O_2-Free Radicals → Cellular Damage

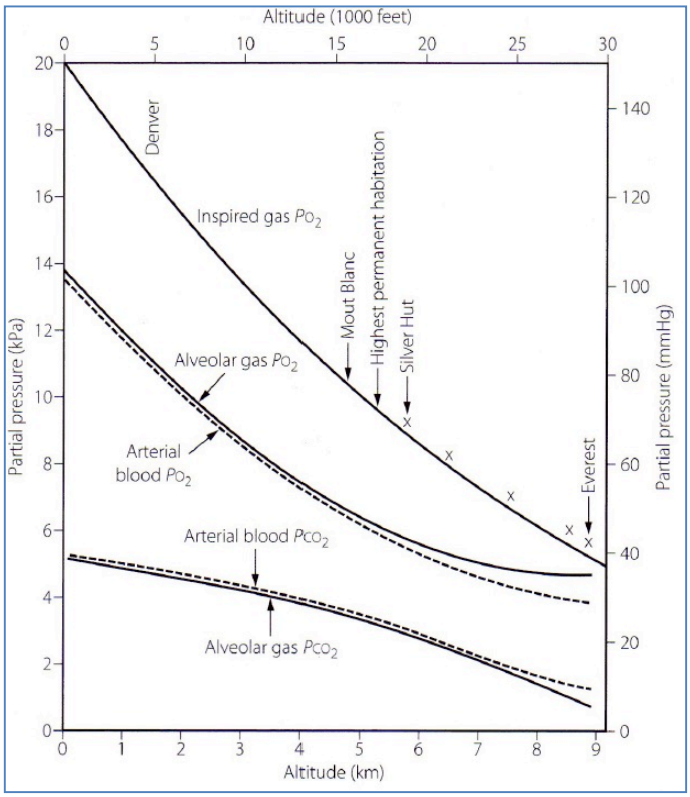
- **Effects of High Partial Pressures (of CO_2):**
  - CO_2 is Less of a Problem than O_2 & N_2.
    - Because [blood CO_2] is determined by metabolism, not the Environment.
    - Therefore, P_{CO2} will be constant provided the Diver exhales normally.
  - However, if CO_2 builds up in the "Dead Space" of the Apparatus & is Re-Breathed, CO_2 Levels will rise.
    - Diver may become Hypercapnic (High CO_2)
    - A Diver may tolerate a P_{CO2} of up to 80mmHg by increasing Respiration.
      - Beyond 80mmHg, Respiratory Acidosis results.

- **Effects of High Partial Pressures (of N_2):**
  - NB: N_2 is not metabolised. Therefore it remains in the body until P_{aN2} decreases →Removed by Lungs
  - **Nitrogen Narcosis:**
    - Nitrogen is Highly Lipid Soluble.
    - High Amounts of Dissolved N_2 → 'Nitrogen Narcosis' (aka. "Raptures of the Deep")
    - Similar to Alcohol Intoxication
    - Effects increase dramatically with increased depth. (Similar Stages to Alcohol Intoxication)
  - **Decompression Sickness (The Bends):**
    - If a diver ascends too quickly, the pressure decreases, causing N_2 to fall out of solution.
    - → N_2 Bubbles
    - These bubbles amalgamate → Bigger & Bigger → Block Larger Vessels ("Air Emboli")
    - **May Lead to:**
      - Tissue Ischaemia/Death
      - Pains in Joints
      - Pains in Muscles
      - Paralysis
      - Unconsciousness
      - The Chokes (Some Air-Emboli can rupture lung capillaries →Bleeding into the lungs)
    - **Treatment:**
      - Diver placed in Hyperbaric Decompression Chambers (Pressurized Tank)
  - **Mechanical Hindrance to Breathing:**
    - Nitrogen has a High Density under Pressure.
    - Makes it physically harder to breath

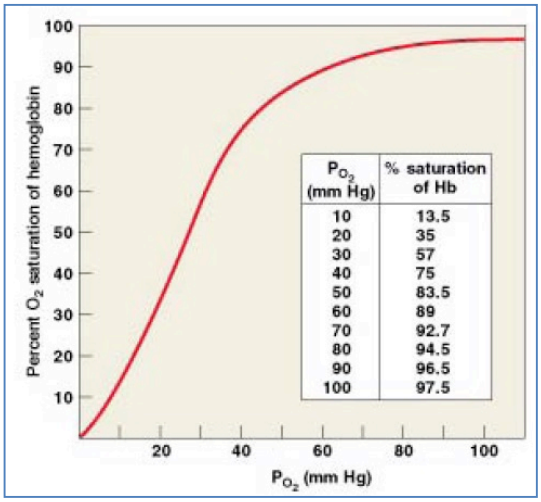
Hypobaric Conditions (Ie. Mountain Climbing):

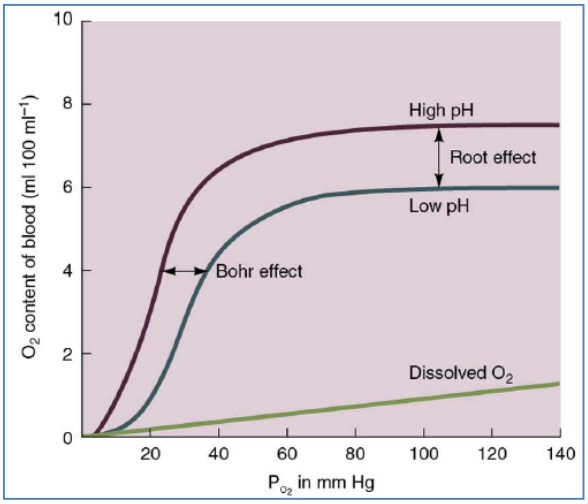
- **Challenges to Altitude:**
  - ****Hypoxia:**
    - NB: At High Altitude, the Air Pressure (& therefore the Oxygen Partial Pressure) Decreases.
    - Therefore by decreasing *Inspired* P_{O2} , The *Alveolar & Arterial* O_2 pressures decrease as well.
    - This leads to Hypoxia.
    - NB: Alveolar & Arterial P_{CO2} decreases slightly @ High Altitude.





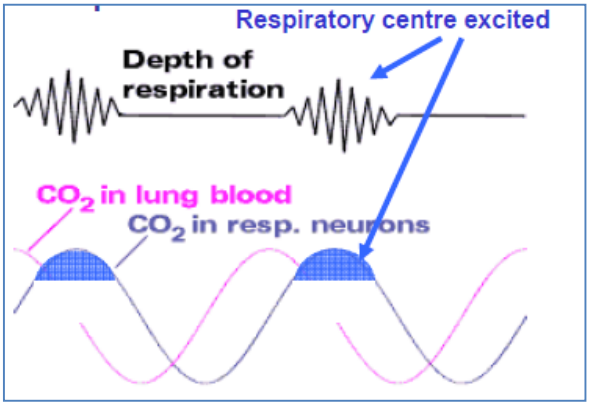
- **Hb-Oxygen Saturation:**
  - At Sea-Level, $P_{O2} \approx 160mmHg$ → $Hb_{sat} = 95\%$
  - At 10,000ft, $P_{O2} \approx 110mmHg$ → $Hb_{sat} = 90\%$
  - Any higher, P_{O2} Falls Rapidly → Hb_{sat} Falls Rapidly
  - **NB:** At high altitudes, **water vapour** accounts for a *relatively larger proportion* of the inspired gas than at sea-level → Decreases the proportion of pressures of the other gasses → Further decreases the P_{O2} as Altitude Increases.

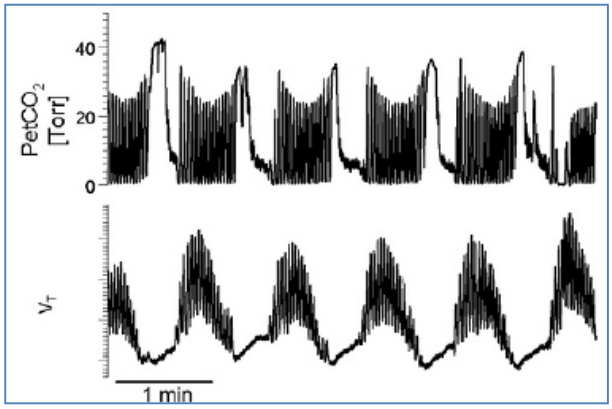




- **NB:** Once Hb_{Sat} reaches ≈60-65%, it remains fairly stable despite further increases in altitude (And subsequent decreases in P_{O2}).
- Why? Because the increased ventilation → Respiratory Alkalosis (↑pH)→ "Root Effect" (Left Shift of Hb_{sat} Curve) → Favouring Increased Oxygen-Loading.

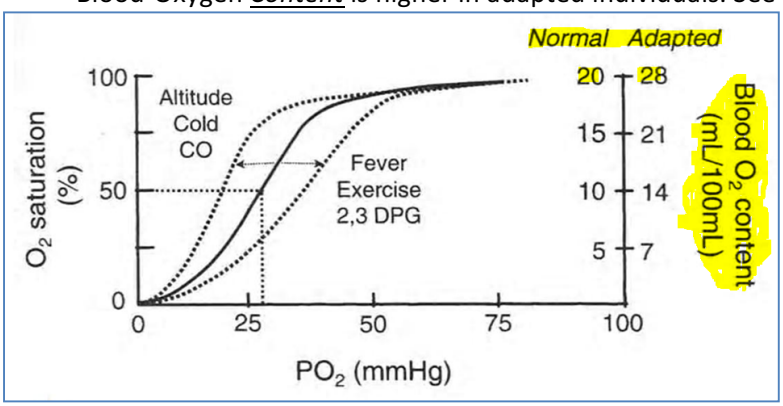
- **Cheyne-Stokes Breathing @ Altitude:**
  - 1. Low Oxygen Levels (<60mmHg) Stimulate Peripheral O_2 Chemoreceptors.
    - Stimulates the Respiratory Centre to hyperventilate.
  - 2. Increased respirations blow off too much CO_2 → Respiratory Alkalosis.
    - Depresses Central Chemoreceptors (On the Medulla)
    - → Depresses Respiratory Centre
  - 3. Arterial Oxygen Levels fall to <60mmHg again → Cycle Starts Again.



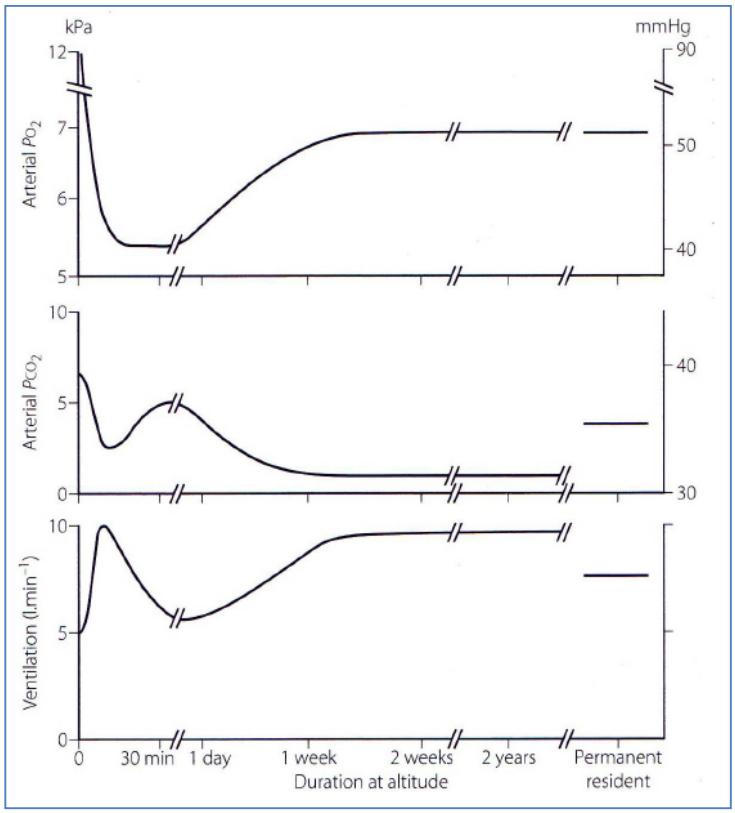


- **Effects of Hypoxia:**
  - **Begin @ ≈12,000ft:**
    - Impaired Mental Function/Judgement
    - Impaired Memory
    - Impaired Motor Function
    - Drowsiness
    - Lassitude
    - Fatigue
    - Nausea
    - Euphoria
  - **@ ≈ 18,000ft:**
    - Twitching
    - Seizures
  - **@ ≈ 23,000ft:**
    - Coma
    - Death

- **Acclimatization:**
  - Body Compensates for Low O_2 Levels over a Prolonged Time by:
    - Increasing Ventilation
    - Increasing RBC Production (Therefore ↑O_2 Carrying Capacity of Blood)
    - Rapid Angiogenesis in Lungs → Increase Diffusing Capacity
    - Rapid Angiogenesis in Tissues → Allows ↑ Perfusion.
    - Fine-Tuning the Efficiency of Aerobic Metabolic Processes.
  - Blood-Oxygen *Content* is higher in adapted individuals. See below:



- **Process of Acclimatization:**
  - Initially, there is a sharp increase in Respiratory Rate, decreasing P_{CO2} and Slowing the onset of Hypoxia. This initial Hyperventilation quickly subsides & P_{CO2} returns to normal.
  - Within a few days, Hyperventilation returns and continues for the long term. This partially restores the P_{O2}, however P_{CO2} falls again → Respiratory Alkalosis.
  - Over the long term, the Kidneys compensate for the Respiratory Alkalosis by excretion of Bicarb.



- **Mountain Sickness:**
  - **(AMS) Acute Mountain Sickness:**
    - Occurs in those who ascend Too High Too Fast.
    - Will die if not given O_2 or Removed to Lower Altitude.
    - Requires Immediate Descent.
    - **Manifestations:**
      - **(HACE) High Altitude Cerebral Oedema:**
        - Build-Up of Fluid In the Brain – Due to Vasodilation of the Cerebral Vessels in response to Hypoxia
        - → Headache
        - → Decreasing Consciousness
        - → Hallucinations
        - → Psychotic Behaviour
      - **(HAPE) High Altitude Pulmonary Oedema:**
        - Pulmonary Vessel Constriction due to Hypoxia → Increased Pulmonary Pressure → Fluid Build-up in the Lungs.
        - → Persistent Productive Cough
  - **(CMS) Chronic Mountain Sickness:**
    - Occasionally occurs in those at altitude for a long time.
    - **Symptoms:** Due to ↑Red Blood Cells – Sluggish Blood:
      - **Pulmonary Hypertension**
      - **Myocardial Hypertrophy → Heart Failure**

- **Low-Humidity & Temperature:**
  - **High Respiratory Water & Heat Loss:**
    - Due to humidification of cold, dry air by the nasal turbinates.
    - → Dehydration
    - → Dry Mouth
    - → 'Burning' Throat
  - **Khumbu Cough:**
    - Extreme Irritation of Bronchi & Respiratory Membranes
    - → Powerful, Dry Cough (May tear respiratory muscles / Break Ribs)
    - → Damaged epithelial lining can slough off and be coughed up.

Respiratory Medicine Notes
Airway Hypersensitivity & Asthma

Airway Smooth Muscle:

- Regulates airway diameter by Bronchoconstriction/Bronchodilation
- Exists in all airways.
- Makes up most of non-cartilaginous airways. (eg. Bronchioles = almost entirely smooth muscle)
- If this muscle spasms, airway diameter will Decrease.

Autonomic Effects on Smooth Muscle:

- **Sympathetic: → Broncho*dilation***
  - *β-Adrenergic* Receptors (on Smooth Muscle) → Bronchodilation
    - (ie. Ventalin = β-adrenergic *AGONIST*)
  - Most of the Sympathetic drive comes from ***Adrenaline*** as Innervation of Airways is Sparse

- **Parasympathetic: → Broncho*constriction***
  - *M_3-Muscarinic Cholinergic* Receptors (on Smooth Muscle) → Bronchoconstriction
  - Most of the Parasympathetic drive comes from Vagus Innervation.

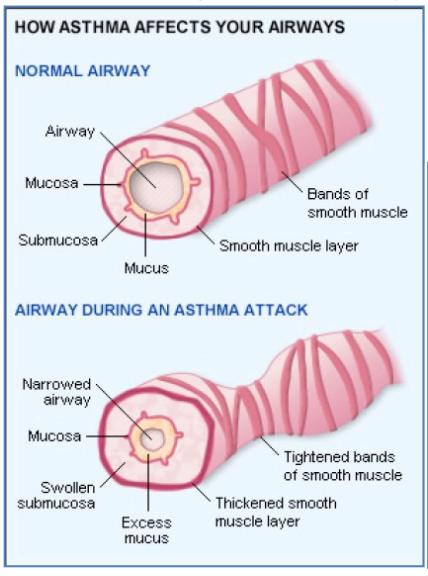
Immune-System Effects on Smooth Muscle:

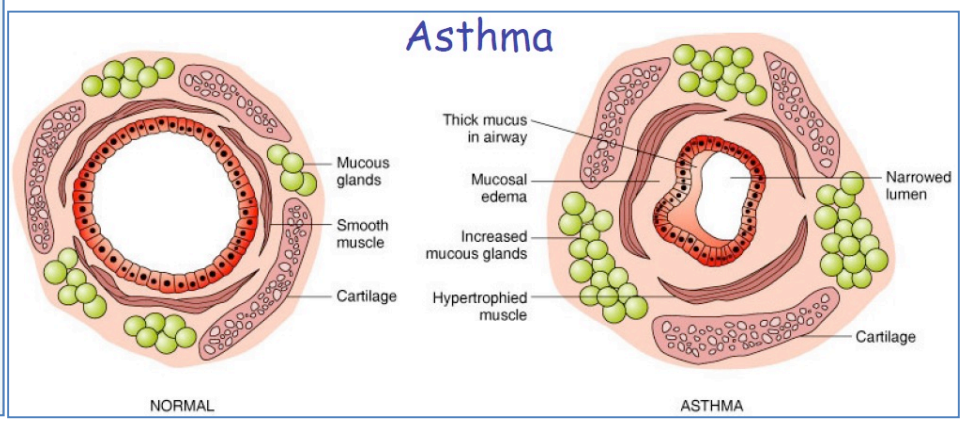
- **Inflammatory Chemicals Can → Bronchoconstriction**
  - (Leukotrienes, Histamines, etc.)
- **Inhaled Irritants Can Directly → Bronchoconstriction**
  - (Dust, haydust, sawdust, perfume, smoke, etc.)

Asthma:

What is Asthma?:

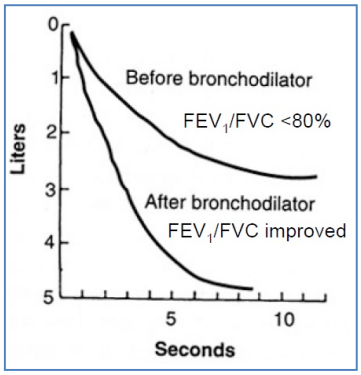
- Hypersensitivity of Airways to Various Stimuli → Inflammation → Constriction of Airways.
- Ie. A chronic ***Inflammatory Disorder*** → Damage to Airway Epithelium → Amplifies Neural, Inflammatory & Immune responses → Episodic, Reversible Constriction. (Ie. A ***Variable Obstructive PD***)
- **Changes in the Airway:**
  - Narrowed Airway
  - Swollen Mucosa (Mucosal Oedema)
  - Hypertrophied Mucosal Glands → Excess Mucus Production
  - Thicker Mucus
  - Hypertrophied Smooth Muscle → Stronger Spasms
  - Constriction of Smooth Muscle
  - Thickened Smooth Muscle Layer
- **Inevitably leads to Airway *OBSTRUCTION* & ↑Resistance to Airflow.**





Clinical Signs of Asthma:

- Asymptomatic between 'Attacks'.
- **'Attacks' of Severe "Dyspnoea"** (Shortness of Breath) Due to Bronchospasm. (Constriction)
  - Coughing
  - Wheezing
- **'Attacks' Triggered by:**
  - Exposure to Allergen (Pollens/Dust/Animal Dander)
- **Dynamic Airway Compression:**
  - Bronchoconstriction + Oedema + Inflammation of Airway → ↑Reliance on Forced Expiration
  - Equal Pressure Point moves into lower (Unsupported) airways.
- **↓FEV_1** (Forced Expiratory Volume in 1 sec) – Due to being an Obstructive condition.
- **↓PEFR** (Peak Expiratory Flow Rate) – Due to ↑Frictional Resistance
- **↑RV** (Residual Volume) – Due to EPP moving lower → Airway Compression → Gas Trapping → Hyperinflation of Lungs.
- **↓Arterial P_{O2}**: - Due to Poor Ventilation (↓V/Q Ratio)
- **Response to Bronchodilators:**
  - Asthma ***IS*** responsive to Bronchodilators
  - However, Chronic Bronchitis & Emphysema are ***NOT*** responsive.
    - Ie. Expiratory Flow Measurements Increase with Bronchodilators.
  - *This is a useful Diagnostic Tool for Determining Chronic & Variable Obstructive Conditions.*
  - **NB: Bronchodilators may also have a Vasodilator Effect:**
    - Leading to slightly↓ P_{aO2} – due to ↑perfusion of poorly ventilated areas.
    - However the benefits of ↑Ventilation outweigh the slight ↓ P_{aO2}



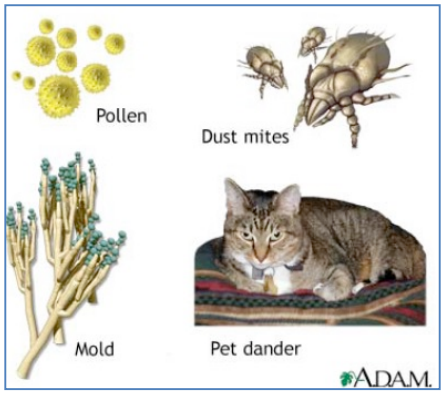
- **NB: "*Status Asthmaticus*":** Acute Asthma Unresponsive to Bronchodilators/Corticosteroids. (Can be Fatal)

Types of Asthma:

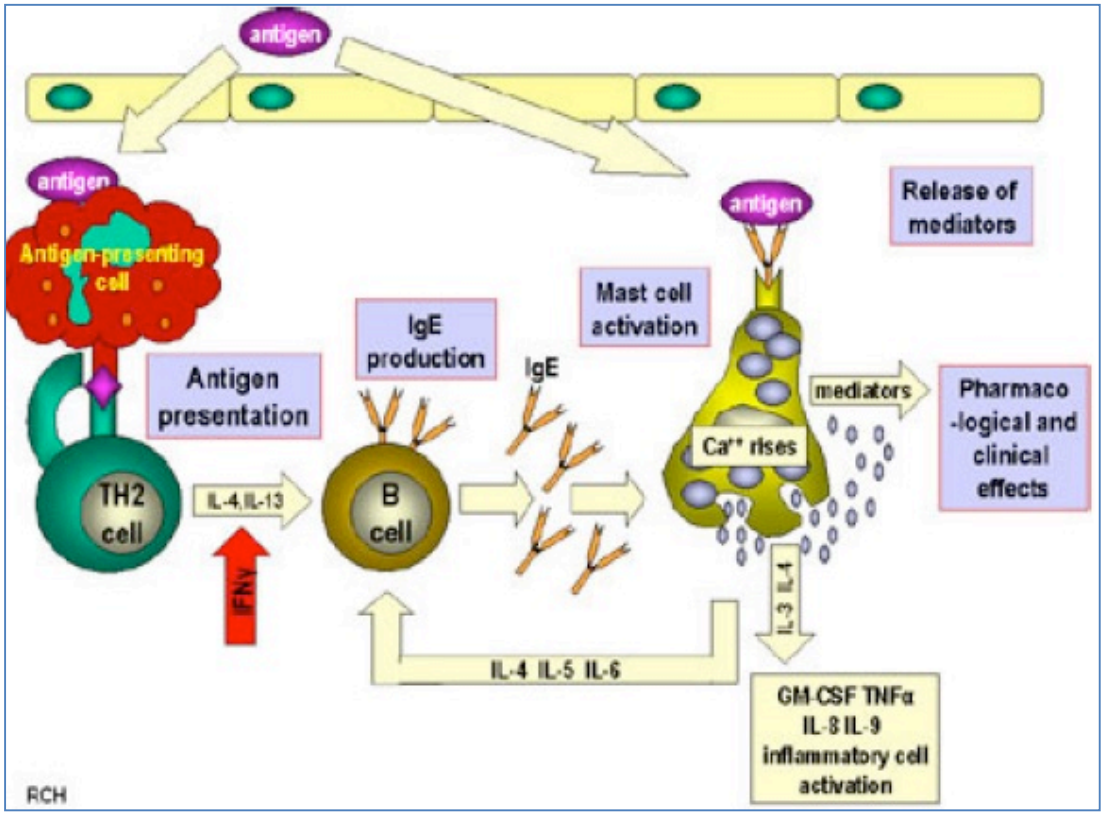
- **Intrinsic Asthma:**
  - We have no idea what triggers it.
- **Extrinsic (Environmental) Asthma:**
  - Most Common
  - **Includes:**
    - **Atopic** (Allergic) Asthma
    - **Non-Atopic** Asthma (Viral-Induced/Drug-Induced/Occupational)
  - Results from a ***Type 1 Hypersensitivity Reaction***.
    - Triggered by Extrinsic Allergens. (Ie. By Environmental Factors)

Extrinsic (Environmental) Asthma

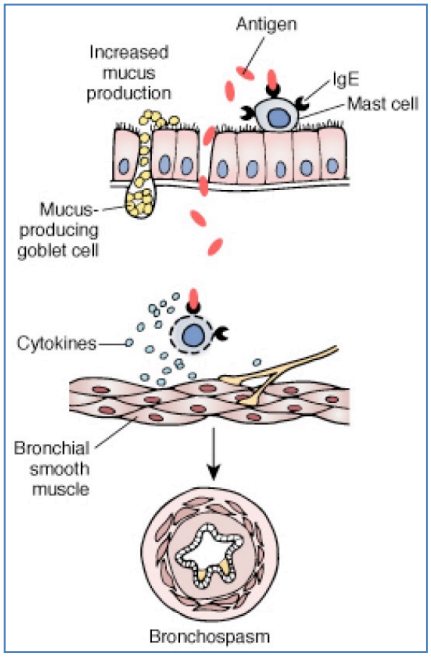
Atopic (Allergic) Asthma:

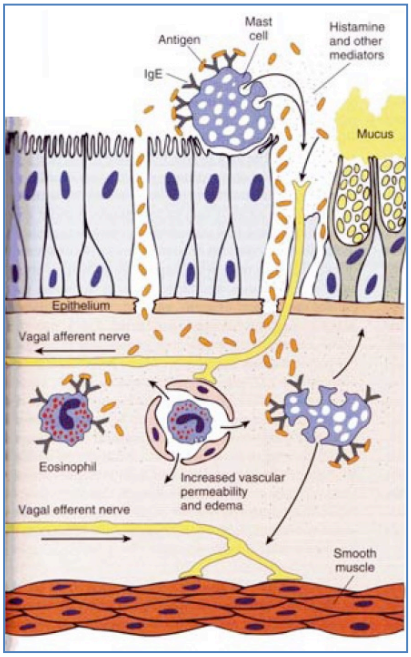


- The Commonest form of *Extrinsic Asthma*.
- Triggered by Environmental Allergens
  - Dust
  - Pollen
  - Dander
  - Mould
  - Smoke
  - Pollution
  - Perfume
  - Cold Air
- Family history of Allergic Reactions is Common.
- Often Preceded by Allergic Rhinitis, Hives or Eczema.
- Results from a ***Type 1 Hypersensitivity Reaction***:
- **Type 1 Hypersensitivity Reaction:**
  - Rapid immune reaction to a Previously-Sensitised Antigen.
  - Occurs when Antigen is Re-Exposed to a sensitized Mast-Cell/Basophil →*Degranulates* 'Mast Cells'
    - → Releasing Inflammatory Mediators of Type-1-Hypersensitivity Reactions.
  - **Sensitization:**
    - 1. Antigen enters the body.
    - 2. 'Antigen-Presenting Cell' Presents the Antigen to 'Type-2 Helper-T-Cells' (TH2-Cells)
    - 3. TH2-Cells Produce Cytokines → Activate B-Cells
    - 4. B-Cells Produce IgE-Antibodies
    - 5. IgE-Antibodies attach to Mast-Cells.
  - **Re-Exposure:**
    - 6. Re-Exposure of Antigen → Attaches to Antibody on Mast-Cell → Mast-Cell Degranulates
    - 7. Degranulation Releases Mediators →Type-1-Hypersensitivity Reaction Occurs.
    - **Mediators Include:**
      - Histamine
      - Leukotrienes
      - Prostaglandins

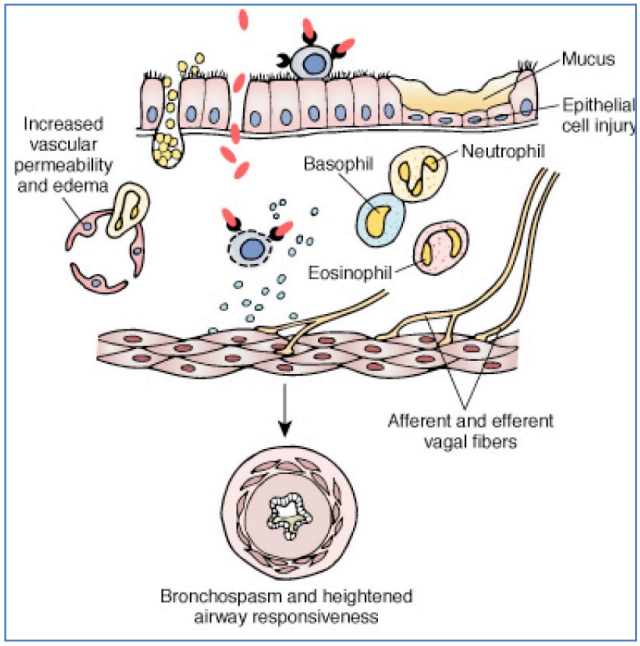


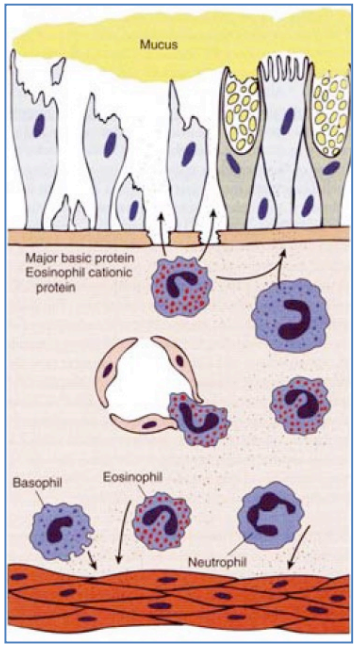
- **Initial (Early) Phase:**
  - Re-Exposure → Mast-Cell Degranulation → Release of Mediators (incl. Histamine)→...
    - ↑Mucus Secretion
    - 'Loosens' the Tight-Junctions between Mucosal Cells → Antigen enters Submucosa.
      - Submucosal Mast-Cells Stimulated→Degranulate.
      - Degranulated Mediators Directly Stimulate Nerve Terminals →…
        - Smooth Muscle Spasm → Bronchoconstriction
    - Vasodilation
    - ↑Vascular Permeability
    - Smooth Muscle Spasm





- **Late Phase:**
  - Release of Inflammatory Mediators Lead to:
    - Influx of Leukocytes, Basophils, Neutrophils & Eosinophils
      - Eosinophils release '*Major Basic Protein*' → Epithelial Damage.
    - Epithelial Damage → Causes Localized Oedema
    - ↓Mucociliary Function → Accumulation of Mucus
    - ↑Airway Responsiveness





Non-Atopic Asthma:

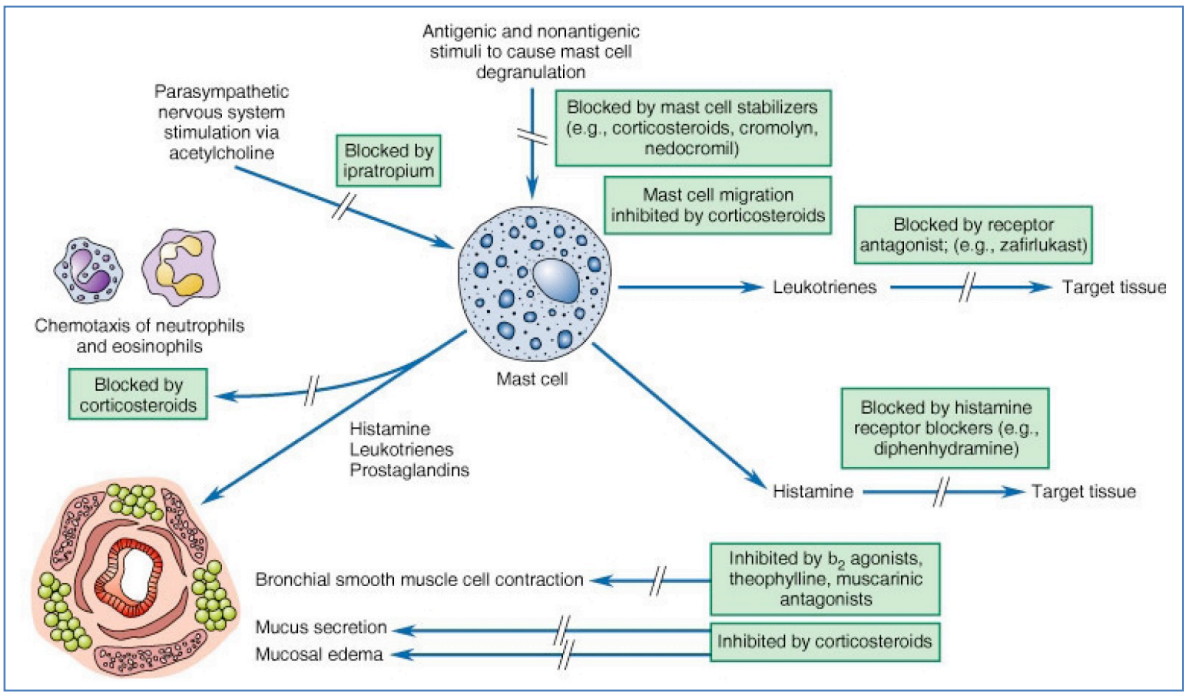
- (Non-Allergic Asthma)
- (Therefore, No Family History & IgE Levels are Normal.)

- **Viral-Induced Asthma:**
  - Asthma triggered by Respiratory-Tract Infections (Mostly Viral)
  - **Pathogenesis:**
    - Believed that Viral-Induced Inflammation of Respiratory Mucosa *Lowers* the Threshold for Stimulation of Sub-Epithelial Vagal (Parasympathetic)Receptors.
      - → ↑Parasympathetic Stimulation
      - → Bronchoconstriction.
- **Drug-Induced Asthma:**
  - Asthma provoked by Pharmacological Agents
  - The Most Common:
    - Aspirin-Sensitive Asthma – (Stimulates Production of Leukotrienes → Bronchoconstriction)
  - Others:
    - Codeine & Morphine – (Stimulate Mast Cells)
    - Mellitin (Bee Venom) – (Stimulates Mast Cells)
- **Occupational Asthma:**
  - Triggered by Minute Amounts of:
    - Fumes
    - Gases
    - Chemicals
    - Dusts
  - Mechanism Varies with Substance:
    - Either: Hypersensitivity Reactions (Similar to Atopic Asthma)
    - Or: Direct release of Bronchoconstrictors (Without a Hypersensitivity Response)
- **NB: Exercise-Induced Asthma:**
  - Believed to be due to Cooling & Drying of the airway.
  - However, the mechanism is still unclear.

Treatment of Asthma: (2 Types)

- **1. Bronchodilators:**
  - To Reverse/Prevent Bronchoconstriction
  - **β_2-Agonists:**
    - **Stimulate β_2-Adrenergic Receptors on:**
      - **Airway Smooth Muscle:**
        - Activated β_2-Adrenergic Receptors → Mimic the Physiological Actions of Adrenaline (A Sympathetic Response) → Bronchodilation
      - **Mast Cells/Neutrophils/Eosinophils:**
        - Activated β_2-Adrenergic Receptors → Inhibits Mediator Release
  - **Anticholinergics:**
    - **Inhibit Muscarinic Receptors on:**
      - **Airway Smooth Muscle:**
        - Acts to inhibit the Parasympathetic effect (Constriction) on Airways.
      - (Blocks Parasympathetic NS Stimulation by blocking Acetylcholine Receptors.)
        - Therefore causes Bronchodilation.
        - NB: they're less effective than β_2-Agonists.
          - But may be useful in conjunction with β_2-Agonists. (Ie. Acting on both Para- & Sympathetic Pathways)
  - NB: β-Agonists are more effective than Anticholinergics because there is more sympathetic innervations in the lung (& heart). This feature is part of the body's failsafe – so that during rest (where parasympathetic NS should dominate, leading to bronchoconstriction), there is enough residual sympathetic innervations to keep airways dilated. Because of this, there are more sympathetic receptors for potential drug action → Equates to ↑ Effectiveness of β-Agonists.

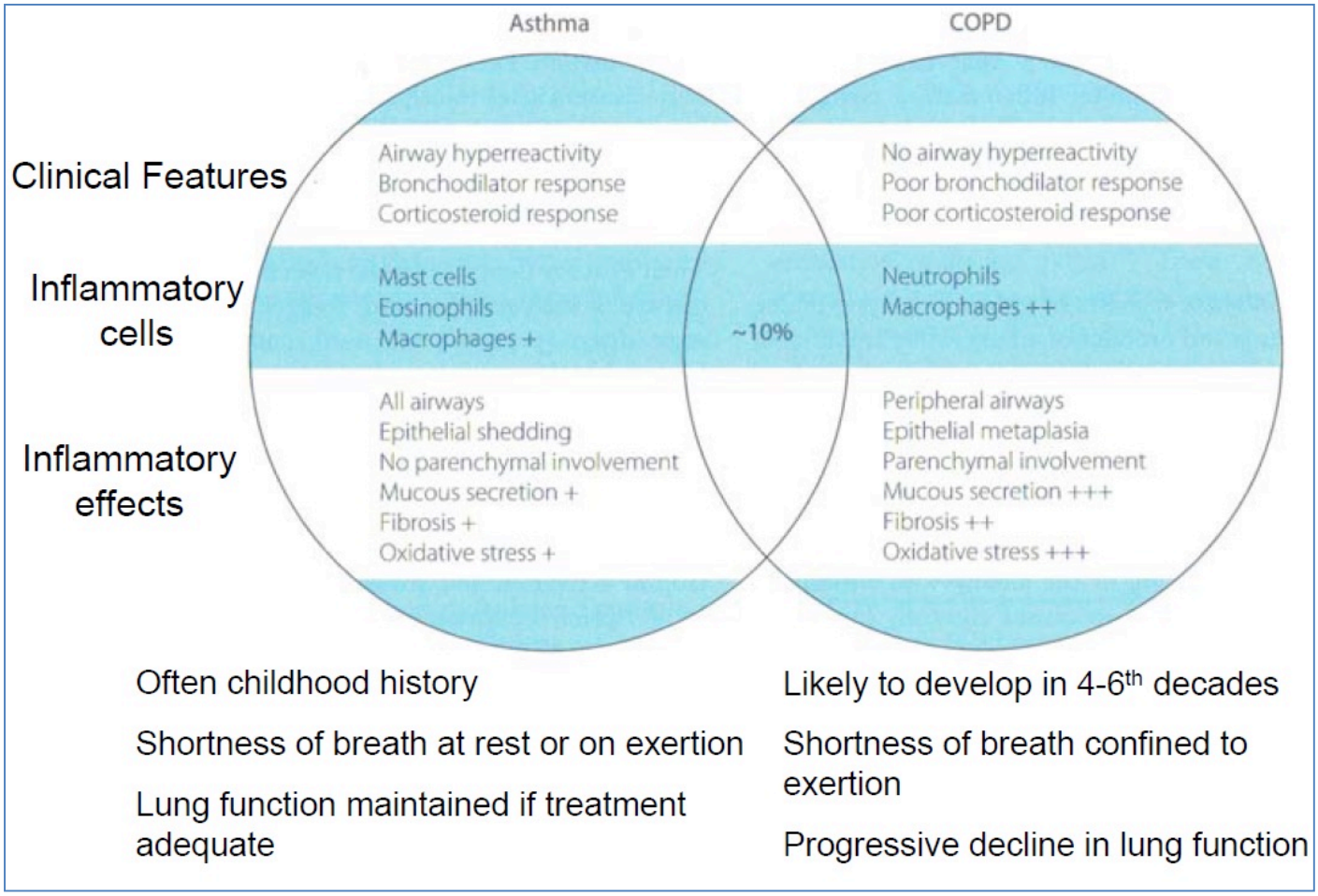
- **2. Anti-Inflammatory Drugs:**
  - To halt Inflammatory Response
  - **Corticosteroids:**
    - Stabilize Mast-Cell Membrane → Prevents Degranulation.
    - Reduce Chemotaxis (Migration) of Mast-Cells, Neutrophils & Eosinophils.
    - Inhibits Mucus Secretion
    - Inhibits Mucosal Oedema
    - Enhances β-Receptor Expression/Function (Amplifies Sympathetic Responses)
    - Disrupt Production of Inflammatory Mediators (Cytokines) from Neutrophils & Eosinophils.
    - Directly Inhibit T-Cells, Eosinophils & Airway Epithelium → Prevents Inflammation



Nebulizer Vs. Inhaler:

- Nebulizers allow higher doses of β-Agonists (Bronchodilators) than a puffer.
- Nebulizers are also easier for the patient during an acute attack.

Asthma Vs. COPD:



Respiratory Medicine Notes
Foetal Lung Development & Transition to Extra-Uterine Life

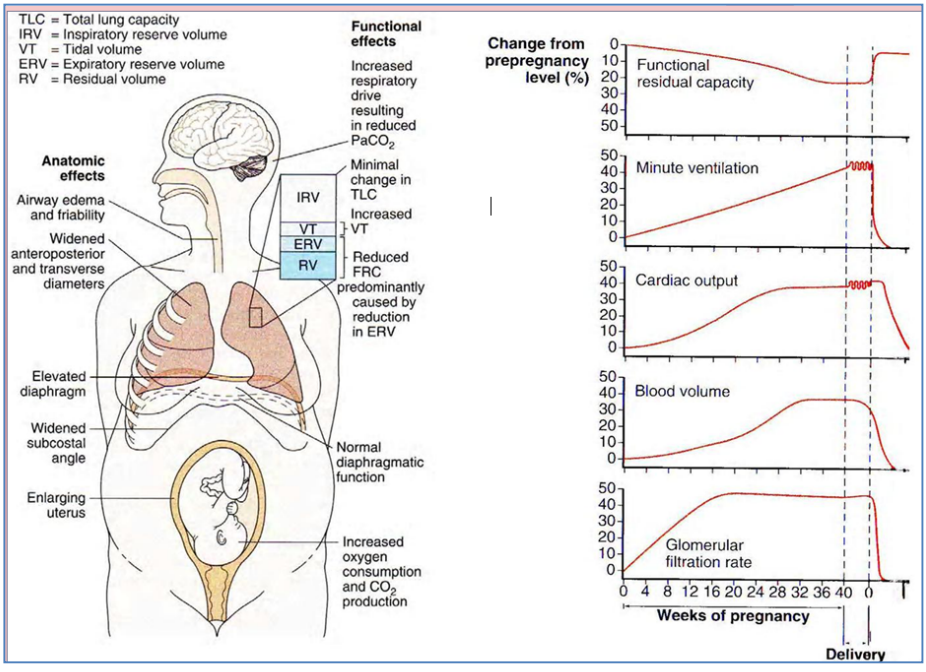
Effects of Gestation on the *Maternal* Respiratory System:

- **High Oestrogen Levels:**
  - Causes Fluid Retention – Increases Blood Volume
  - Causes Oedema of Airway Mucosa
  - Stimulates Mucous Gland Proliferation & Growth

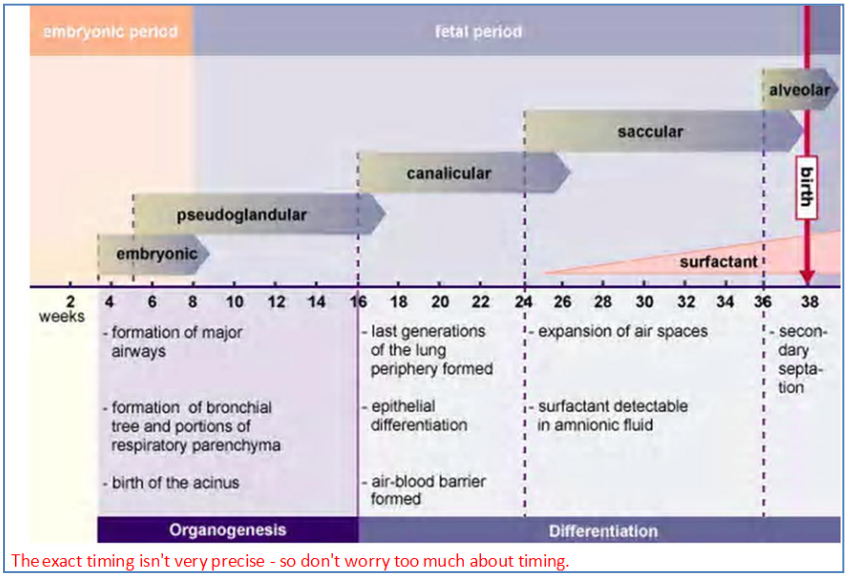
- **High Progesterone Levels:** (6x normal)
  - **Hyper-Sensitizes Central (CO_2) Chemoreceptors:**
    - (Ie. Chemosensitive Area of Medulla becomes hypersensitive to CO_2 Levels)
    - The 'normal' P_{CO2} is reset to a lower P_{CO2} → Stimulates Relative Hyperventilation (40%↑V_{Tidal})
      - "Relative Hyperventilation" = Where the mother breaths more than what *her* metabolic rate would dictate.
      - Why? – To aid clearance of Foetal CO_2
      - How? – Via a 40% increase in Tidal Volume (but no change in Frequency)
    - **↑Respiratory Drive Results in:**
      - ↓Arterial P_{CO2}
      - No change in Arterial P_{O2}
      - ↑pH (Alkalosis).

- **15-30% Increase in Metabolic Rate:**
  - Increase in Oxidative Phosphorylation → ↑O_2 Consumption → ↑Respiratory Rate.

- **Uterus Invades Thoracic Cavity:**
  - Compression of Lungs & Diaphragm by Enlarged Uterus →:
    - ↓Lung Compliance
    - ↓Residual Volume
    - ↓Functional Residual Capacity
    - ↓Expiratory Reserve Volume
    - ↓Inspiratory Reserve Volume
  - Compensated for by:
    - Increased AP-Diameter
    - Increased Transverse-Diameter
    - (Ie. Chest Volume increases to combat the invasion of Uterus into Thoracic Cavity)

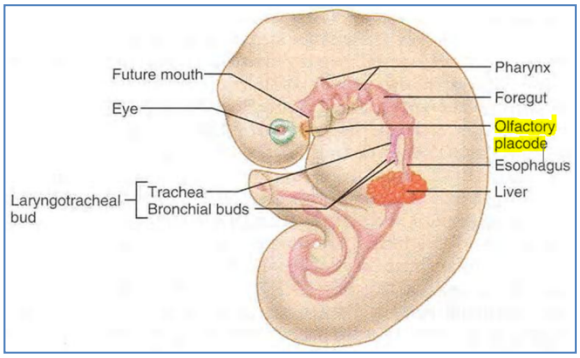


Development of the *Foetal* Respiratory System:

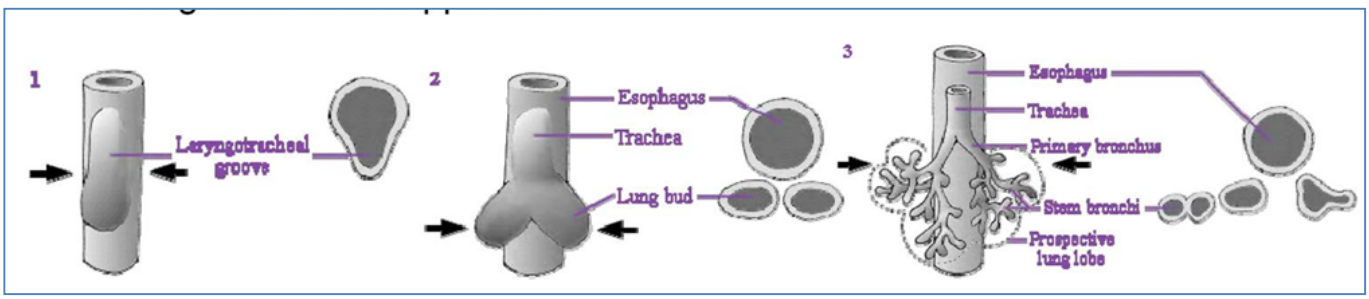


The exact timing isn't very precise - so don't worry too much about timing.

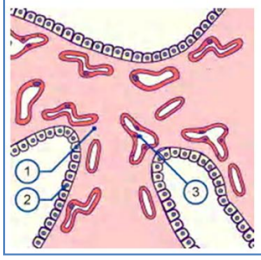
- **1. Embryonic Stage:**
  - Upper Respiratory Structures Develop First, Then Lower Respiratory Structures.
  - **Wk 4: Olfactory Placodes:**
    - Form from Ectoderm (The outermost of the 3 Primary Germ Layers)
    - Olfactory Placodes Invaginate to form Nasal Cavities.
    - Nasal Cavities Extend Posteriorly → Connect with Developing Foregut.



  - **Wk 5: "LaryngoTracheal Bud" (Respiratory Epithelium):**
    - Forms from Endoderm (The innermost of the 3 Primary Germ Layers)
    - Develops as an 'outpocket' of the Foregut Mesoderm → Becomes Respiratory Mucosa:
      - Pharyngeal Mucosa
      - Tracheal Lining
      - Bronchial Mucosa
      - Bronchiole Mucoaa
      - Alveolar Membrane
    - By wk 6/7, all Basic Upper Respiratory Tree is laid down.



- **2. Pseudoglandular Stage:**
  - **Wk 8: Formation of Airway Smooth Muscle/Cartilage/Blood Vessels/Interstitium:**
    - Mesoderm covers the Endoderm-Derived Respiratory Epithelium with Associated Structures.
  - **Wk 8-16: Rapid Proliferation of the Airways:**
    - By wk16, all airway divisions are complete. (Down to the terminal bronchioles)



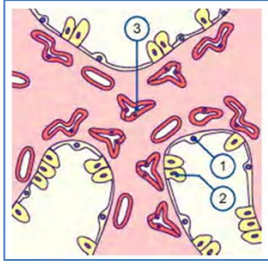
Lung tissue in the pseudoglandular stage.

1 = Lung mesenchyma

2 = Type II pneumocytes

3 = Capillaries

- **3. Canalicular Stage:**
  - **Wk 16-26: Rapid Angiogenesis (Vascular Proliferation):**
    - Respiratory Capillaries forming around Potential Airspaces.
  - **Thinning of the Acinar Walls by Fibroblast Apoptosis:**
    - Fibroblasts undergo Apoptosis → Reduces Acinar Wall Thickness.
    - Brings the Capillaries in closer association with developing air-spaces
    - NB: Both of the above are required for Sufficient Gas-Exchange from Alveoli → Blood.
  - **First Appearance of Surfactant:**
    - Type-II Surfactant-Producing cells (Pneumocytes) appear.
    - ↓Surface Tension of Fluid in Lungs → Draws Acinar Walls Apart → ↑Lung Volume



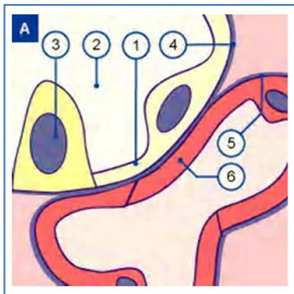
Lung tissue in the canalicular stage.

1 = Type 1 pneumocytes

2 = Type II pneumocytes

3 = Capillaries

- **4. Saccular Stage:**
  - **Wk 25-35: Proliferation of Air-Spaces:**
    - Airspaces develop a sac-like appearance = Become 'Saccules'.
    - Airspaces contain both Type-I & Type-II Epithelial Cells (Type 2 = Surfactant-Producing Cells).
    - NB: By 27 Weeks, the Air-Spaces are sufficient for gas exchange (Ie. A 9 wk premature baby's lungs can support gas exchange)



Lung tissue in the saccular stage.

1 = Type 1 pneumocytes

2 = saccular space

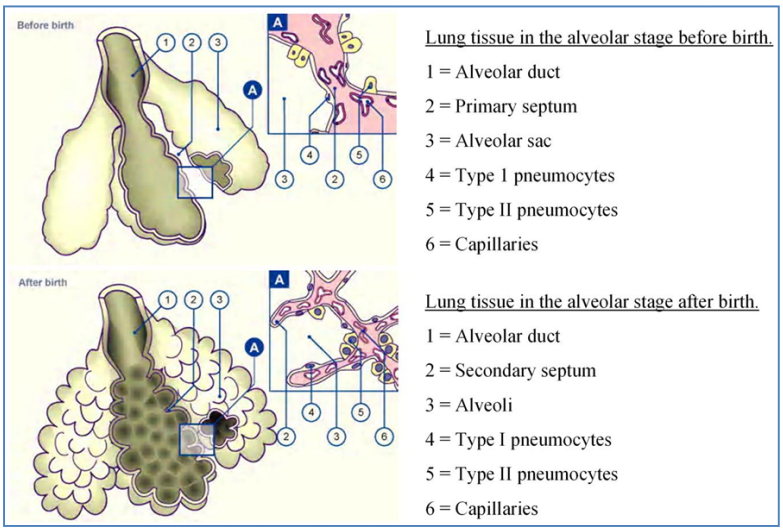
3 = Type II pneumocytes

4 = Basement membrane of air passage

5 = Basement membrane of capillaries

6 = Endothelium of the capillaries

- **5. Alveolar Stage:**
    - **Wk 35 – Term: Rapid Development of Alveoli:**
        - Terminal Saccules Invaginate into Cup-Like Structures = Primitive Alveoli.
        - Thinning of Septal Wall by Type-II Cells giving rise to thinner Type-I Cells.
        - NB: The Above two developments Dramatically Increase Surface Area of Lung.
    - NB: By birth, ≈50Million Alveoli have developed. This increases to around 300million when fully developed at 3yrs old.



Foetal Lung Fluid:

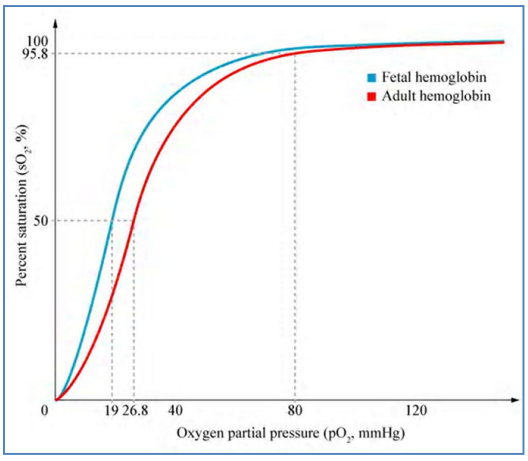
- Type-I Epithelial Cells continuously secrete fluid into the Air-Spaces.
- This fluid flows from airway → Amnotic Fluid (Flushes out debris from the lung)
- Maintains positive pressure within the Air-Spaces Relative to Amniotic Fluid (Prevents Lung Collapse)
    - Also causes lung *expansion* → Stimulates Cell Division/Growth
      → Stimulates Differentiation of Type-II Cells to Type-I Cells

Foetal Respiratory Movements:

- Attempted Respiratory Movements occur *In-Utero*. – Increase in frequency from 22-35wks of gestation.
- However, During the Last Week of pregnancy, Respiratory Movements are Inhibited:
    - To Prevent Lungs Filling with Fluid
    - To Prevent Aspiration of Meconium in the Amniotic Fluid.

Foetal Haemoglobin:

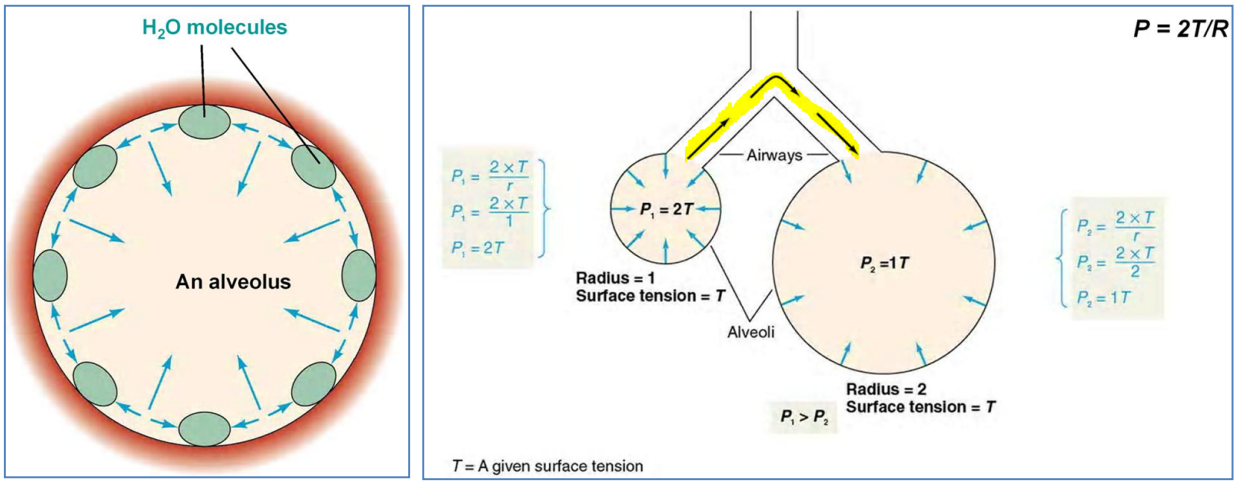
- Foetal-Hb has a different Saturation Curve to Adult-Hb:
    - Left-Shifted Compared to Adult-Hb (Favours O_2 *Loading*)
    - Foetal-Hb has a *Higher Affinity for* O_2 (Ie. It's designed to operate at lower P_{O2})
- NB: These properties are critical for Foetal-Hb to pull O_2 off the Maternal-Hb
    - (Ie. At a particular P_{O2}, the Maternal-Hb will favour *Unloading*, while the Foetal-Hb favours *Loading*.)



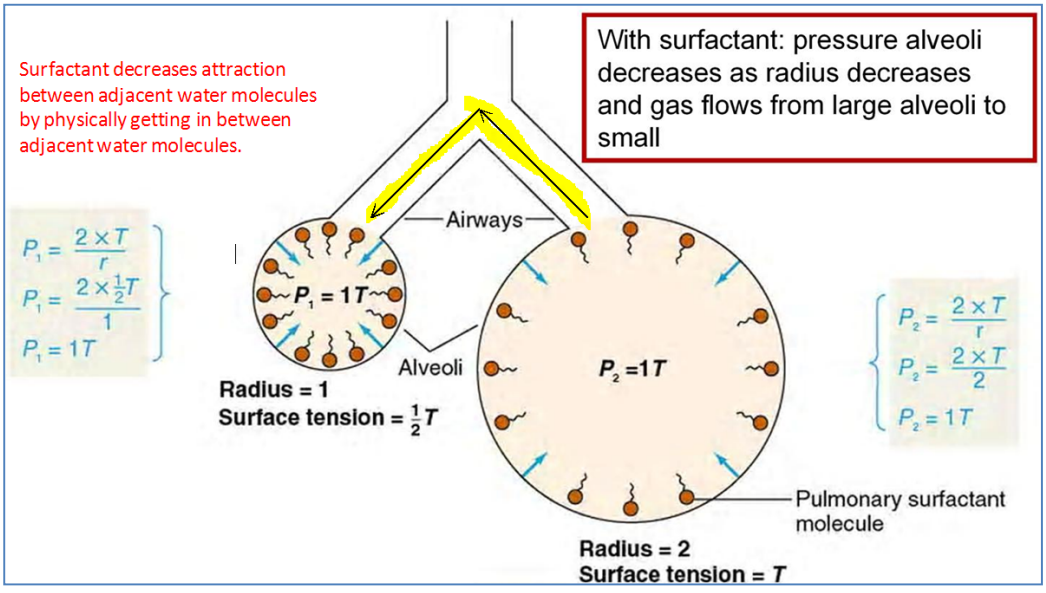
Foetal Hb Replaced by 6mths of Age.

Pulmonary Surfactant:

- **Without Surfactant:**
  - Surface Tension of the Fluid lining the lungs causes the Alveoli to Recoil.
  - – caused by the Attraction between Adjacent H_2O Molecules acting to ↓Surface Area & Alveolar Size
  - NB: Surface Tension of H_2O is so strong that the Alveoli would collapse if the fluid was just H_2O.
    - Without Surfactant, Lung Compliance is 10-20% of Normal.
    - → Requires huge Negative Pressures to maintain Patent Alveoli.
    - Lack of Alveolar Surfactant = Primary Cause of *Infant Respiratory Distress Syndrome* (IRDS)
  - **NB: The *Inward Pressure* of Surface Tension INCREASES as Radius DECREASES.**
    - Therefore, if two alveoli of different sizes were joined by a common airway, the smaller alveolus would collapse into the bigger alveolus (Due to the pressure gradient)

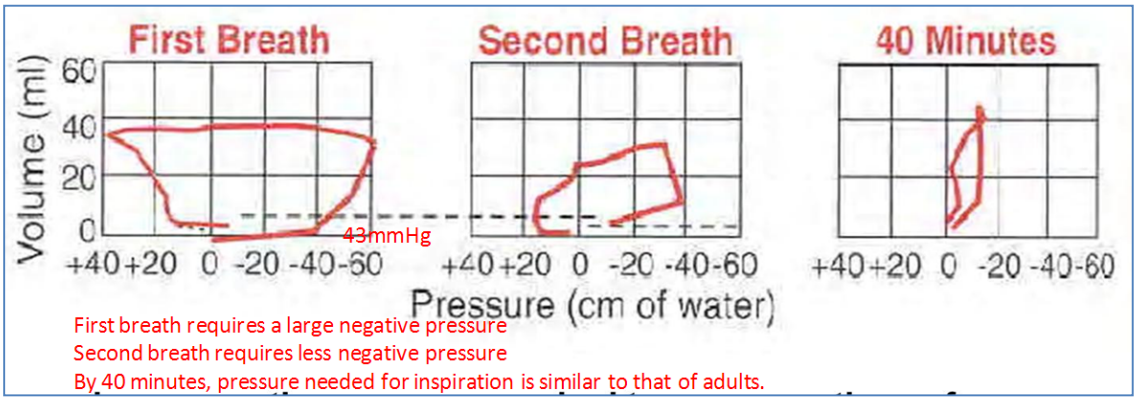


- **With Surfactant:**
  - NB: Pulmonary Surfactants = Mainly Lipids 90% (DPPC), Some proteins & carbohydrates
  - Surfactant Produced by Type-II Alveolar Cells
  - DPPC is responsible for Surfactant's Effect on Surface Tension:
    - ↓Alveolar Pressure
    - ↓Energetic Cost of Ventilation
    - ↓Lung's Tendency to Collapse
  - **With Surfactant, the *Inward Pressure* of Surface Tension DECREASES as Radius DECREASES.**
    - Ie. It Decreases the Surface Tension in Smaller Alveoli MORE THAN the Larger Alveoli.
    - - This Solves the Problem of Small Alveoli Collapsing into Larger Alveoli.



Transition to Extra-Uterine Life:

- **Loss of Placenta:**
  - Loss of Metabolic Support
  - Loss of Respiratory Support → Hypoxia/Hypercapnia → Respiratory Centre → Breathing.
- **Need to Begin Breathing to Survive:**
  - Breathing Triggered by:
    - Hypoxia
    - Touch/Skin-Cooling
    - Possible Chemical/Hormonal Stimuli
  - When?
    - Most take their first-breath within 20s & are breathing normally by 90s after birth.
    - NB: Baby may survive for up to 10mins without breathing, however, after 8mins brain damage occurs.
    - NB: Maternal Anaesthetics can delay Initiation of Breathing.
- **Removing Fluid From Lungs:**
  - At Birth, Alveolar Epithelial Cells switch from Secretion to Absorption of Fluid.
  - Also, Thoracic Compression of Vaginal Delivery → Squeezes some of the fluid in the lung.
- **The First Breaths:**
  - Remaining Fluid in lungs creates High Surface Tension – Requires large –ve Pressure to Inflate.
  - **First Breath:**
    - Between -25mmHg and -40mmHg is needed. (Compared to an Adult's -15mmHg)
    - It is important that the baby doesn't expire fully after taking its first breath – as this would cause the alveoli to collapse again.
  - **Subsequent Breaths:** Require less negative pressure.
  - **By 40 Minutes:** Inspiratory force is similar to Adults.



Circulatory Readjustments:

- **Closure of Foramen Ovale:**
  - Hugh Loss of Vasculature (Through loss of placenta) → Doubles Systemic Vascular Resistance.
    - → ↑Aortic Pressure → ↑L-Atrial & L-Ventricular Pressures.
  - Mechanical Inflation of Lungs → Dilates Pulmonary Vasculature → ↓Pulmonary Vascular Resistance.
    - → ↓Pulmonary Artery Pressure → ↓R-Atrial & R-Ventricular Pressures.
  - – The Combination of the above two pressure changes causes the valve-like Foramen Ovale to Close.
- **Closure of Ductus Arteriosus:**
  - Decrease in Prostaglandins cause muscular wall of Ductus Arteriosus to Contract → Duct Occludes.

Postnatal Lung Growth & Lung Size:

- Foetal Hb Replaced by Adult Hb by 6 months.
- Alveolar number increases (From 50 million @ birth to 300 million in adulthood)
- Alveolar Diameter Increases (From 0.15mm @ birth to 0.3mm in Adult)
- Surface Area Increases (From $4m^2$ @ birth to $100m^2$ in Adult)
- Lung Volume Increases (From 250mL @ birth to 5000mL in Adult)
- Lung Weight Increases (From 50g @ birth to 800g in Adult)

When Things Go Wrong:

- **Infant Respiratory Distress Syndrome:**
  - Typically seen in Premature Infants (around 25wks or less)
  - **Where the baby is born with Insufficient Pulmonary Surfactant**:
    - → ↑Alveolar Surface Tension
    - → ↓Lung Compliance (10-20% of Normal)
    - -- Requires Large Negative Pressures to Keep Alveoli Open.
  - Ie: Premature Infants (with poorly developed inspiratory muscles) must maintain High Negative Pressures just to Breath.
  - Also: The Alveolar Membranes may be damaged due to the sheer stress of trying to breath.
  - **Results in:**
    - Alveolar Collapse ("Atelactasis")
    - ↑Energetic Cost of Breathing
    - Hypoxia & Hypercapnia (↑Energetic Cost of Breathing – Respiratory Muscles consume a lot of the Inspired O_2)
    - Hyaline (Glassy) Membranes
    - Periodic (Cheyne-Stokes) Breathing – due to significant fluctuations in Blood-Gas Levels & due to premature Central-Respiratory Controllers.
  - **Treatment:**
    - Mechanical Ventilation:
      - CPAP – Constant Positive Airway Pressure
      - PEEP – Positive End-Expiratory Pressure
      - NB: Requires a fine balance of Mech.Ventilation as it may damage the lung lining.
    - Exogenous Surfactant – (Artificial/Natural)

- **Sudden Infant Death Syndrome:**
  - **Definition:**
    - "Death of an infant under 1year which remains unexplained – usually occurs while asleep"
  - **Peak Incidence** = 2-3 Months
  - **Contributing Factors:**
    - Premature Birth
    - Low Birth Weight
  - **Causes – Probably Multifactorial:**
    - Central Apnoea – No Respirator Signals due to Poorly Developed Central Control.
    - Abnormal Temperature Control – Overheating may be a cause of SIDS.
    - Prolonged Apnoea during Cheyne-Stokes Breathing (Ie. The stress associated with the period of apnoea prevents re-initiation of breathing)

- **Mother's Water Breaks at 27 Weeks:**
  - Risk of Foetal Infection
  - Lack of Mechanical Protection of baby
  - Baby may be contorted – as there is no room to move with no amniotic fluid.
  - **Effects on Respiratory Development:**
    - Amniotic Fluid Aids in the Development of Lungs – If no fluid → Lung membranes become dry → Don't grow properly → ↓Surfactant Production → IRDS.

- **Meconium Aspiration:**
  - If the baby defecates in-Utero, then inhales it.
  - → Infection

RESPIRATORY SYNTHESIS SESSION CASES:

Respiratory Emergencies:

- **Case 1:**
  - Temperature
  - Otherwise well
  - 100% sats
  - Cough & runny nose
  - **Diagnosis =** Viral Infection
  - **Treament =** Reassurance, rest & fluids

- **Case 2:**
  - Febrile
  - Creps
  - 90% Sats (Hypoxic)
  - Tachypnoeic
  - Mild indrawing & creps
  - **Diagnosis =** Severe Pnemonia (Due to hypoxia)
  - **Treatment =** IV Antibiotics, IV Fluids, Oxygen

- **Case 3:**
  - Knife in man's chest on right hand side of sternum.
  - Breathless
  - Hypotensive
  - JVP not raised
  - **Diagnosis =** Massive Haemothorax (Because his JVP isn't distended → he prob has Hypovolaemia :. The knife has cut a blood vessel and is bleeding into his chest.)
    - Tension Pneumothorax is a possibility also
  - **How would you confirm this?**
    - Clinical assessment
  - **Treatment =**
    - If haemothorax → put a needle (drain) in his chest

- **Case 4:**
  - Attempted hanging
  - Unconscious
  - Stridor
  - **What is the 1st Priority?**
    - Airway Management – Probably use of Endotracheal Intubation (although may be very difficult)
      - Guedel airway is too short
      - If impossible to intubate → Emergency Tracheostomy

- **Case 5:**
  - Car accident
  - T-Boned at high speed
  - Pale
  - Sweaty
  - Hypotensive (40mmHg)
  - Whited out L Lung on Xray
  - **Diagnosis =**
    - Haemothorax
    - Probably also has a pneumothorax but not visible on xray
  - **Treatment =**
    - Emergency chest drain with Intercostal Catheter (ICC)

- **Case 6:**
  - Barking cough
  - Inspiratory stridor
  - Moderate indrawing
  - Very dyspnoeic
  - Agitated & crying
  - **Diagnosis =**
    - Croup (Barking cough & stridor)
  - **Assessment should include:**
    - Clinical Assessment should suffice (in ED situation)
    - Measure Sats.
  - **Treatment =**
    - No antibiotics are needed (croup is viral)
    - Nebulised adrenaline & steroids to decrease swelling.

- **Case 7:**
  - Ph 7.3 - Acidosis
  - Co2 66 – Raised → Respiratory
  - O3 150
  - HCO3 28
  - Base excess = -1 → No metabolic compensation
  - **Diagnosis =**
    - Respiratory acidosis with no metabolic compensation

RESPIRATORY Pathology:
ASTHMA

Airway Hypersensitivity & Asthma

Autonomic Effects on Smooth Muscle:

- **Sympathetic: → Bronchodilation**
  - *β-Adrenergic* Receptors (on Smooth Muscle) → Bronchodilation
    - (ie. Ventalin = β-adrenergic *AGONIST*)
- **Parasympathetic: → Bronchoconstriction**
  - *M_3-Muscarinic Cholinergic* Receptors (on Smooth Muscle) → Bronchoconstriction
    - (Ie. Ipratropium Bromide = Muscarinic *ANTAGONIST*)

Immune-System Effects on Smooth Muscle:

- **Inflammatory Chemicals Can → Bronchoconstriction**
  - (Leukotrienes, Histamines, etc.)
- **Inhaled Irritants Can Directly → Bronchoconstriction**
  - (Dust, haydust, sawdust, perfume, smoke, etc.)

ASTHMA:

What is Asthma?:

- Ie. A chronic ***Inflammatory Disorder*** of the Airways → Episodic, Reversible Constriction.

Aetiology:

- **Types:**
  - **1. Atopic** (Allergic) Asthma (***Type 1 Hypersensitivity Reaction - IgE***.)
  - **2. Non-Atopic** Asthma (Viral-Induced/Drug-Induced (Eg. Aspirin)/Occupational)
- **Environmental Triggers – (**Dust/Pollen/Dander/Mould/Smoke/Pollution/Perfume/Cold Air)
- **Genetic – (**FamHx is Common**)**

Pathophysiology:

- ***Type 1 Hypersensitivity Reaction***:
  - **Rapid Immune Reaction to a Previously-Sensitised Antigen →Mast-Cell/Basophil *Degranulation* → Release Inflammatory Mediators →**
    - **Initial (Early) Phase:**
      - Vasodilation & ↑Permeability (***Bronchial Oedema***)
      - Smooth Muscle Spasm (***Bronchoconstriction***)
      - Epithelial Damage → ↓Mucociliary Function → ***Mucus Accumulation***.
    - **Late Phase:**
      - Immune-Mediated Epithelial Damage
      - ↓Mucociliary Function → Accumulation of Mucus

Clinical Features:

- **Asymptomatic between 'Attacks'** – (But may have Allergic Rhinitis, Hives or Eczema)
- **'Attacks' of Severe Dyspnoea & Wheezing -** (Often Triggered by Allergen (Pollens/Dust/Animal Dander))

Complications:

- ***"Status Asthmaticus"*:** Acute Asthma Unresponsive to Bronchodilators/Corticosteroids. (Can be Fatal)

Diagnosis:

- **Clinical Features:**
  - Dyspnoea, Wheeze, Cough
  - Chest Tightness
  - Tachypnoea, Hyperinflation, ↑Resp. Effort,
- **Spirometry:**
  - **↓FEV_1** (Forced Expiratory Volume in 1 sec) – Due to being an Obstructive condition.
  - **↓PEFR** (Peak Expiratory Flow Rate) – Due to ↑Frictional Resistance
  - **↑RV** (Residual Volume) – Due to Gas Trapping → Hyperinflation of Lungs.
  - **↓Arterial P_{O2}**
  - **Response to Bronchodilators:**
    - Asthma ***RESPONDS*** to Bronchodilators; COPD's ***DO NOT*** .
    - *This is a useful Diagnostic Tool for Determining Chronic & Variable Obstructive Conditions.*

Management:

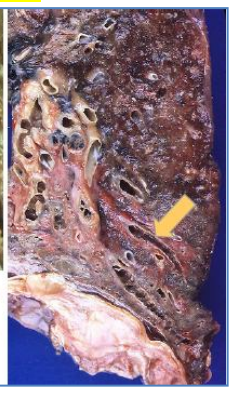
- **Prevention:**
  - **Mild Asthma:** Inhaled Corticosteroids (*Budesonide* or *Fluticasone*)
    Or Inhaled Antimuscarinic (*Ipratropium Bromide*) – If ICS-Intolerant.
  - **Moderate Asthma:** LABA + Inhaled Corticosteroid Combinations
    - Symbicort [*Budesonide* + *Eformoterol*]
    - or Seretide [*Fluticasone* + *Salmeterol*]
  - **Severe Asthma:** Oral Leukotreine Inhibitors (Singulair [*Montelukast*])
- **Acute Attack:**
  - **First Aid (Where *Salbutamol* is the only Rx):**
    - **"4x4x4 Rule" –** 4xPuffs, 4xBreaths/Puff, Wait 4 Mins....Then Repeat if Necessary.
  - **Paediatric:**
    - (Brief History & Examination)
    - O2 if Necessary – (Distressed or SpO2<92%)
    - **1.** Ventolin(***Salbutamol***) Via Spacer <6puffs (<6yo) or <12puffs (>6yo) q20mins in 1st Hour;
    - **2.** (If SEVERE)+/- ***Ipratropium Bromide*** 2puffs (<6yo) or 4puffs (>6yo) q20mins in 1st hr
      - (NB: Spacer should only be loaded with 1x puff/drug at a time)
      - (NB: If no improvement after 1st Hour → Call Ambulance → ED)
    - **3.** (1° HC Setting) add Systemic PO-***Prednisolone*** – (Continue OD for 3-5days);
    - **4.** (If SEVERE & *Still* no improvement, add IV-***Magnesium Sulfate***)
    - **5.** (If *STILL SEVERE* → ICU Admission → IV-***Aminophylline***)
  - **Adult:**
    - (Brief History & Examination)
    - O2 if Necessary – (Distressed or SpO2<92%)
    - **1.** Ventolin(***Salbutamol***) Via Spacer <6puffs (<6yo) or <12puffs (>6yo) q20mins in 1st Hour;
    - **2.** (If SEVERE)+/- ***Ipratropium Bromide*** 2puffs (<6yo) or 4puffs (>6yo) q20mins in 1st hr
      - (NB: Spacer should only be loaded with 1x puff/drug at a time)
      - (NB: If no improvement after 1st Hour → Call Ambulance → ED)
    - **3.** (1° HC Setting) add Systemic PO-***Prednisolone*** – (Continue OD for 7-10days);
    - **4.** (If SEVERE & *Still* no improvement, add IV-***Aminophylline***)

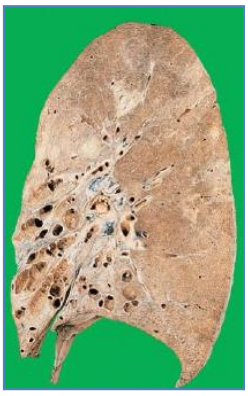
Example of Asthma Management Plan:	
Prophylaxis:	Singulair (Montelukast Sodium), 1x 4mg Tablet, Every Night
Mild Asthma Symptoms: (Mild wheeze, tight chest, shortness of breath)	Ventolin (Salbutamol), 2x Puffs (via spacer if available), Repeat 3-4x daily as necessary.
Moderate Asthma Symptoms: (Moderate wheeze, tight chest, shortness of breath)	Ventolin (Salbutamol), up to 6x Puffs (via spacer if available), Repeat 3-4x daily as necessary. + Prednisolone, 1x 20mg dose (4mLs of 5mg/ml liquid), Immediately & then every morning for at least the next 3 days.
Severe Asthma Symptoms: (Severe wheeze, tight chest, shortness of breath. Eg if...: - Requiring Ventolin >3hrly - No relief from Ventolin - Persistent wheeze >24hrs - Or severe attack)	Ventolin (Salbutamol), up to 6 Puffs (via spacer if available), Repeat dose every 15-30mins if not improving. **Call an ambulance if worried or not improving.** (Continue to give Ventolin as above while waiting for ambulance)

RESPIRATORY Pathology:
BRONCHIECTASIS

BRONCHIECTASIS:

- **= Localized, Permanent Dilation of part of the Bronchial Tree due to Destruction of Muscle & Elastic Tissue.**
- **Aetiology:**
  - **A Result of Chronic or Severe Necrotizing Lung Infections**
  - **Often seen in:**
    - Cystic Fibrosis
    - Post-infectious Conditions
    - Bronchial Obstruction (Eg tumour/foreign bodies)
    - HIV
- **Pathogenesis:**
  - **Chronic *AND/OR* Severe *Bacterial* Lung Infections →**
    - →Bronchial Inflammation, (Often with Necrosis)
    - →Damage to Airway Walls (Destruction of Supporting Smooth Muscle & Elastic Tissues)
    - →Fibrosis & Eventually Dilation of Airways.
      - → Irregular, Permanently Dilated Bronchus filled with Pus.
- **Morphology:**
  - **Macro:**
    - **Usually in lower lobes**
    - **Permanent Dilatation of Bronchi** (Often 4x Normal)(*Extending to the Pleura*)
      - CXR – Bronchial Markings are Visible more than 1/3 the way across a lung x-ray
- **Clinical Features:**
  - **Symptoms:**
    - Cough
    - Copious Purulent Sputum (Green/Yellow), mixed infections
    - Fever
  - **Complications:**
    - Pneumonias (Staph/Strep/Enterococci/Haemophilus/Pseudomonas)
    - Empyema
    - Septicaemia
    - Meningitis
- **Investigations:**
  - **CXR – (**Bronchial Markings out towards Periphery**)**
  - **FBC – (**If ?Current Infection – Typically *Pseudomonas***)**
- **Management:**
  - **Physiotherapy – (**Postural Drainage & Cupping**)**
  - **If Sx of Infection – Anti-Pseudomonal Antibiotics (*Tobramycin*)**





RESPIRATORY Pathology:
BRONCHIOLITIS

BRONCHIOLITIS:

- **Aetiology:**
  - **Respiratory Syncytial Virus (RSV)** (>50%)
  - parainfluenza, influenza, rhinovirus, adenovirus, rarely M. *pneumoniae*
- **Clinical Presentation**
  - Common, affects 50% of children in first 2 years of life
  - **Initial URTI with cough and fever → Respiratory Distress**
    - Wheezing, Tachypnea, Tachycardia
    - Intercostal Recessions, Tracheal Tug, Supraclavicular Recessions, Rib Flaring
  - **+ Feeding difficulties, irritability**
- **Investigations**
  - **CXR** (Air trapping, peribronchial thickening, atelectasis, increased linear markings)
  - **NPA for PCR**
  - **FBC (**Lymphocytosis**)**
- **Treatment**
  - **Fluid** Rehydration
  - **Paracetamol** (fever)
  - **Humidified O2**
  - Bronchodilator (Ventolin [***Salbutamol***])
  - **If Severe → Intubation and Ventilation**
  - **Indications For Hospitalization**
    - **Hypoxia**: SpO2 <92%
    - **Resting Tachypnea** >160/minute
    - **Respiratory Distress even after *Salbutamol***
    - **<6 months old**
    - **Feeding Problems**

RESPIRATORY Pathology:
BRONCHITIS (ACUTE)

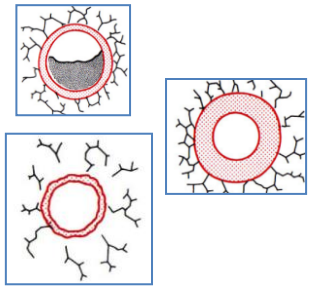
BRONCHITIS (ACUTE)

- **Definition**
  - Acute Infection Of The Tracheobronchial Tree → Inflammation With Resultant Bronchial Edema And Mucus Formation
- **Etiology**
  - **80% viral: rhinovirus**, corona virus, adenovirus, influenza, parainfluenza, RSV
  - 20% bacterial: S. *pneumoniae*
- **Pathogenesis:**
  - Acute Infection Of The Tracheobronchial Tree → Inflammation With Resultant Bronchial Edema And Mucus Formation → Airway Obstruction → Cough/Wheeze
- **Clinical Features:**
  - URTI Symptoms
  - Productive Cough (Esp. @ Night)
  - Wheezing
  - (NB: Lower-Lung Examination Normal; Suspect Pneumonia if Crackles)
- **Investigations**
  - **Typically a Clinical Diagnosis**
  - **CXR – (**Rule out Pneumonia/CHF – if cough >3 weeks, abnormal vital signs, localized chest findings**)**
  - **Spirometry + Bronchodilatory – (**Rule out Asthma**)**
- **Differential Diagnosis**
  - **URTI/Asthma/Exac.COPD/Sinusitis/Pneumonia/Bronchiolitis/Pertussis**
  - **Others:** reflux esophagitis, CHF, bronchogenic CA, aspiration syndromes, CF, foreign body
  - **Bacterial? -** Higher Fevers + Excessive Purulent Sputum.
- **Management**
  - **Symptomatic Relief:** Paracetamol, Rest, Fluids (3-4 L/ Day When Febrile), Humidified O2.
  - **Bronchodilators [*Salbutamol*] – (**May ↓Symptoms**)**
  - **Antibiotics [*Doxycycline* / *Erythromycin*] If:** Elderly/Comorbidities/Suspected Pneumonia.

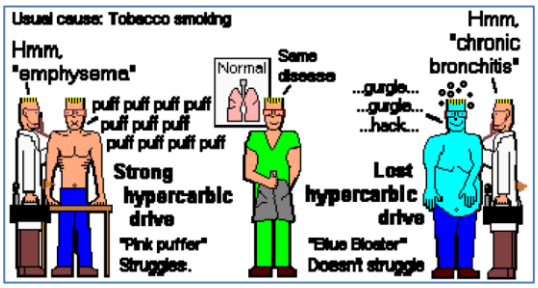
RESPIRATORY Pathology:
COPD

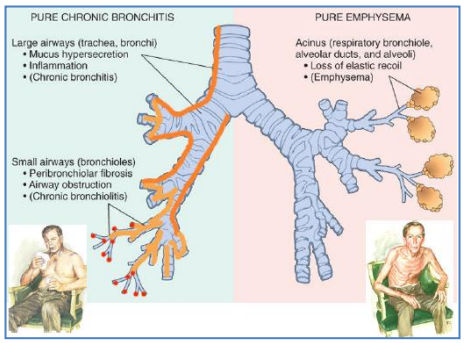
CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD):

- **What Are They?:**
  - Permanent *NARROWING/OBSTRUCTION of the AIRWAY*.
  - Ie**. Increased Resistance to AirFlow.**
  - – Is an 'Umbrella Term' – Usually Refers to **Chronic Bronchitis**, **Emphysema**, or Mixture of BOTH.
- **3 Causes:**



  - **1. Conditions With The Lumen** - (Eg. Excessive Mucous)
  - **2. Conditions Within The Wall of the Airway:**
    - Inflammation & Oedema (Chronic Bronchitis or Asthma)
    - Bronchoconstriction (Asthma)
  - **3. Conditions Outside The Airway:**
    - Destruction of Lung Parenchyma (eg. Emphysema)
    - Localised Compression of Airway
    - Peribronchial Oedema
- **Aetiology:**
  - **#1. Smoking**
  - (Genetic – a1-Antitrypsin Deficiency → Congenital Emphysema)
- **Clinical Features:**
  - **Type A – Pinker 'Puffer' – (*Emphysema*):**
    - Normal Blood Gasses
    - Little/No Cough
    - Breathless
    - Quiet Breath Sounds
    - No Peripheral Oedema
  - **Type B – Blue 'Bloater' (*Chronic Bronchitis*):**
    - Low O_2 + High CO_2 + Cyanosis → Blue (hence name)
    - Chronic Productive Cough
    - Breathless
    - Loud, Abnormal 'Crackling' Breath Sounds ("Crepitations"/"Rales")
    - May Have Peripheral Oedema

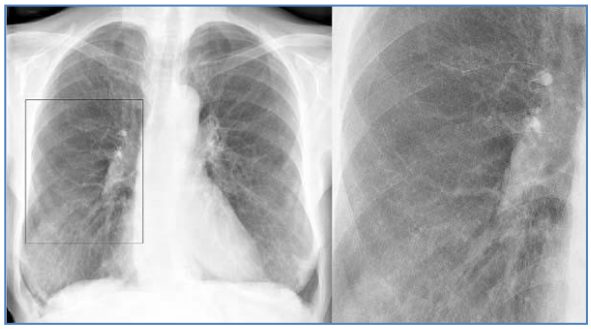


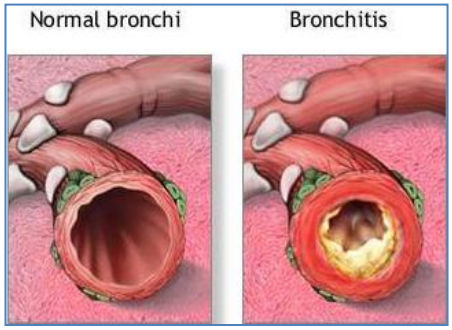


- **Complications of COPD:**
  - **Acute Infective Exacerbations**
  - **Cor Pulmonale – (RV-Failure 2° to Pulmonary HTN):**
  - **Polycythaemia (Due to Hypoxia) → high Hb**
  - **Bronchiectasis**
  - **End Stage Lung Disease (due to extensive lung fibrosis) → Palliative O2 Therapy.**
  - **Lung Cancer (Indirectly – due to smoking)**
- **Investigations:**
  - **↓ Decreased VC**
  - **↓ Decreased FEV1:VC Ratio (FEV1 <80% of Predicted)**
    - Mild – FEV1 60-80% →Cough, Exertional Dyspnoea.
    - Mod – FEV1 40-60% → Above + Wheeze, Sputum.
    - Sev – FEV1 <40% → Above + Right Heart Failure (Corpulmonale).
  - **↓ PEFR**

CHRONIC BRONCHITIS:

- **Aetiology:**
  - **Smoking/Pollution**
- **Pathogenesis:**
  - **Smoking/Pollution → Acute & Chronic Inflammation of Bronchial Mucosa →**
    - → *Chronic, Excessive Mucous Production in Bronchial Tree* → Excessive Sputum
      - Mucous *Plugs* Occlude Small Airways →↑Work of Breathing
- **Morphology:**
  - Acute & Chronic Inflammation of Bronchial Mucosa
  - ↑Mucosal Thickness ("Mucus Gland Hyperplasia") (NB: not seen in terminal bronchioles)
  - Excess Mucous → Plugging
  - Lack of Cilia – Retention of Secretions → Recurrent Secondary Infections.

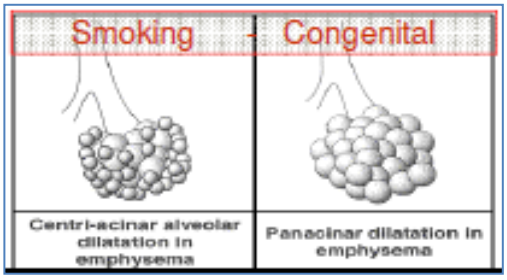




- **Clinical Features:**
  - **"Blue Bloaters"**
    - Productive Cough
    - Marked Cyanosis, Hypoxaemia & Hypercapnea
    - Mild Dyspnoea & Wheezing
    - Obese, Oedema
    - Infections Common – Fever
- **Investigations:**
  - **Diagnostic Criteria = "Persistent Productive Cough for >3mths/year for >2 *Consecutive Years*"**
  - **Spirometry – (**↓FEV1 and FEV1/FVC (<80%); Minimal Change with Bronchodilators**)**
  - **CXR – (**Hyperinflation, Flattened Diaphragms, Bronchial Markings towards Periphery**)**.
  - **ABG – (**↑PCO2, ↓SpO2, ↑HCO3**)**
- **Management:**
  - **Chronic (Symptomatic):**
    - **Bronchodilator:**
      - ***Antimuscarinic [Ipratropium Bromide / Tiotropium]**
      - Or Short Acting B2-Agonist [Albuterol]
      - Or Long Acting B2-Agonist [Eformeterol]
    - **Inhaled Corticosteroids:**
      - Eg. Fluticasone
      - Eg. Budesonide
    - **+/- Oxygen (BUT DO NOT KILL RESPIRATORY DRIVE)**
    - **+ Quit Smoking – (Eg. Nicotine Replacement Therapy)**
    - **+ Pneumovax / Fluvax**
    - **+ Diuretics (If RV-Failure)**
  - **Acute Exacerbation:**
    - **As above…PLUS**
    - **1. *Theophylline***
    - **2. Antibiotics – (Augmentin [*Amoxicillin* + *Clavulanate*] / *Doxycycline* / *Trimethoprim* / *Tobramycin* for Pseudomonas)**
    - **3. +/- Mechanical Ventilation**
- **Complications:**
  - Infective Exacerbations
  - Cor Pulmonale & Heart Failure
  - Lung Cancer

EMPHYSEMA:

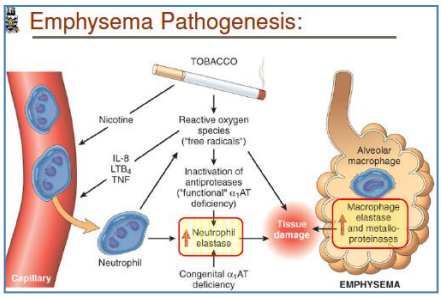
- **Types & Aetiologies:**
  - **** 95% = Centrilobular – SMOKERS**
  - (Panacinar/Panalobular (Congenital - a1-Antitrypsin Deficiency) → Early Age Emphysema)

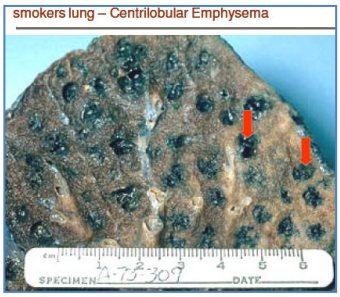


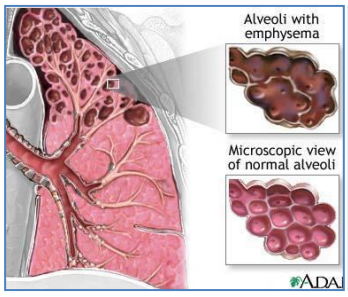
- **Pathogenesis:**
  - **Smoking → O2 Free Radicals → Inflammation (Elastase & Protease) → Direct Alveolar Damage → Loss of "Radial Traction" →Obstruction**
- **Clinical Features:**
  - **"Pink Puffers"**
    - Thin, No Oedema
    - Normal Blood Gasses
    - Little/No Cough
    - Severe Dyspnoea
    - Quiet Breath Sounds
    - No Peripheral Oedema
    - Hyperinflation → Barrel Chest
    - Forward Stooping
  - **Effects on Lung Capacities/Volumes:**
    - ↑TLC (Total Lung Capacity)
    - ↑RV (Residual Volume)
    - ↑FRC(Functional Residual Capacity)

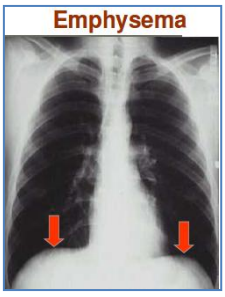
    } Due To Gas-Trapping & Hyperinflation of The Lungs

    - ↓VC (Vital Capacity) - Because They Can't Expel All the Gas in their Lungs
    - ↓FEV_1 (Forced Expiratory Volume in 1 Sec) – Because of Dynamic Airway Compression
- **Diagnosis:**
  - **Clinical +**
  - **Spirometry – (**Low FEV_1, ↑TLC, ↓DCo**)**
  - **CXR – (**Hyperinflated, Flattened Diaphragms, Upper-Zone Bullae, Narrow Mediastinum**)**
- **Management:**
  - **Bronchodilator:**
    - ***Antimuscarinic [Ipratropium Bromide / Tiotropium]**
  - **Inhaled Corticosteroids:**
    - Eg. Fluticasone
    - Eg. Budesonide
  - **+/- Oxygen (BUT DO NOT KILL RESPIRATORY DRIVE)**
  - **+ Quit Smoking – (Eg. Nicotine Replacement Therapy)**
  - **+ Pneumovax / Fluvax**
  - **+ Diuretics (If RV-Failure)**









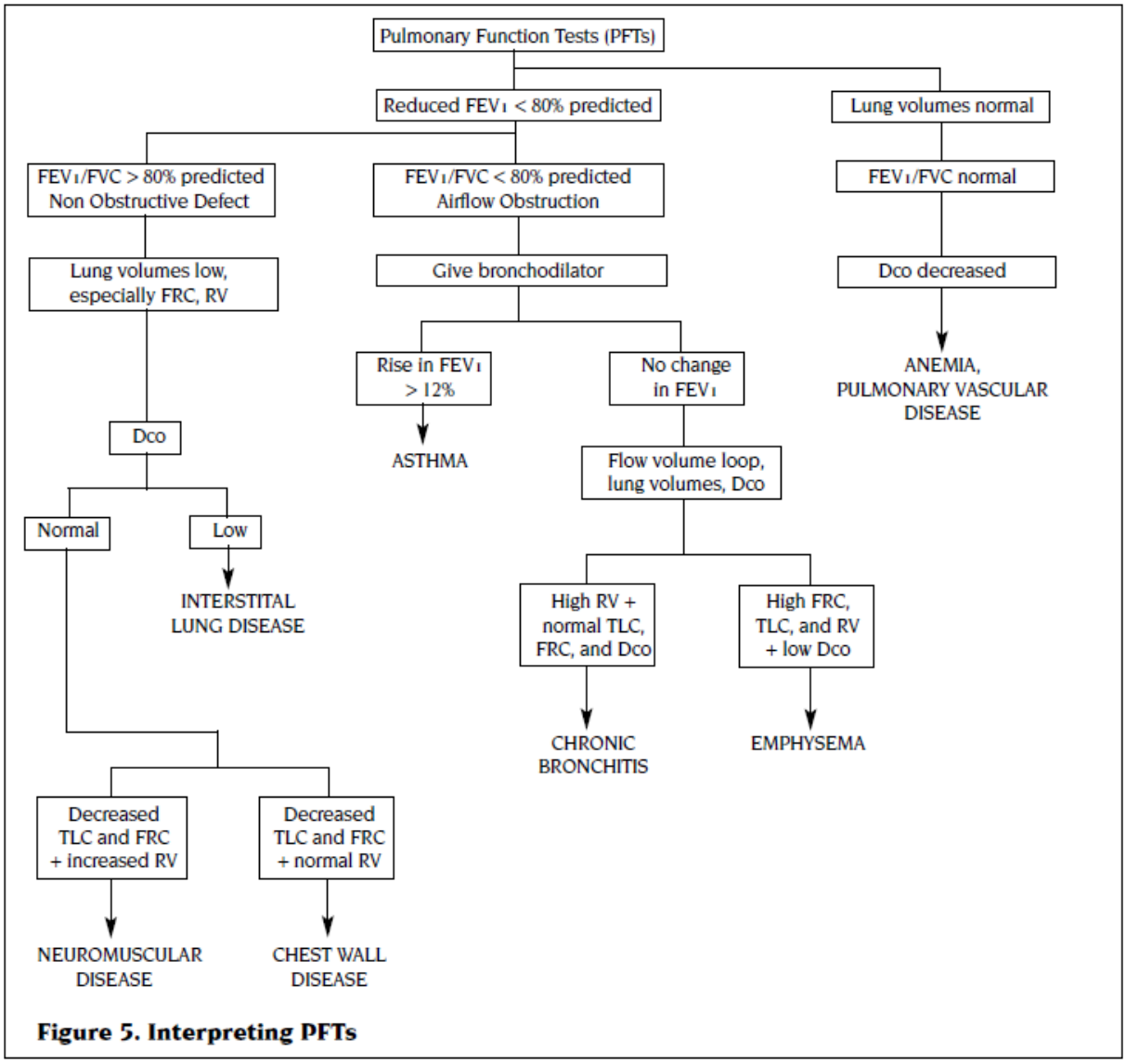


Figure 5. Interpreting PFTs

❑ normal values for FEV_1 are approximately +/– 20% of the predicted values (for age, sex and height); race may affect predicted values

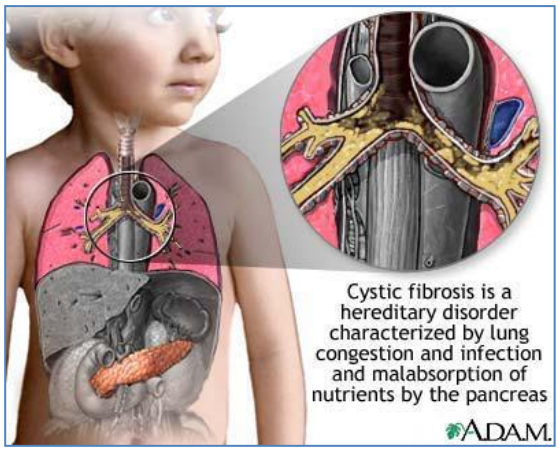
Clinical Pearl

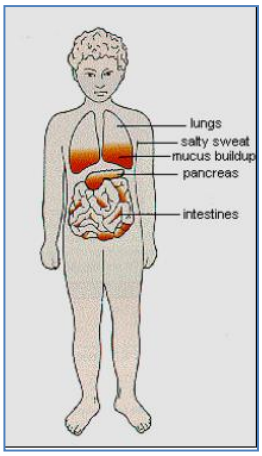
❑ **Dco decreases with: 1) decreased surface area, 2) decreased hemoglobin, 3) interstitial lung disease, and 4) pulmonary vascular disease.**

RESPIRATORY Pathology:
CYSTIC FIBROSIS

CYSTIC FIBROSIS (CF):

- **Aetiology:**
  - **Simple Autosomal Recessive CFTR Gene Mutation (Chromosome 7)**
    - ≈1/25 people are carriers.
- **Pathogenesis:**
  - **CFTR** – Encodes for Active-Chloride Channels (Which Normally Regulates [Salt] in Secretions)
  - → Thick, Salty Exocrine Secretions → Mostly Affects **Lungs, Pancreas, Intestines & Skin.**
- **Clinical Features:**
  - **Lungs:**
    - Thicker Mucus & ↓Clearance → **Frequent Lung Infections**
  - **Pancreas:**
    - Obstructed Pancreatic Duct → Chronic Subclinical Pancreatitis → **Pancreatic Failure**
  - **Intestines:**
    - Poor Digestion & Malabsorption → **Malnutrition**
  - **Reproductive Ducts:**
    - Obstructed Vas-Deferens → Infertility
  - **Sweat Glands:**
    - Salty Sweat → **Hyponatraemia** if not replaced.





- Crepitations (Crackling) & Rhonchi (Rattling/Whistling) – Heard through stethoscope

- **Investigation:**
  - **Spirometry – (Obstructive Pattern -** ↓FEV_1**)**
  - **CXR – (**Gas Trapping & Hyperinflated**)**
  - **Genetic Testing – (Definitive)**
- **Management:**
  - **Enzyme Replacement – (“*Creon Forte*”)**
  - **Salt Replacement – (Salt Tablets)**
  - **Fat-Sol. Vitamins – (ADEK)**
  - **Chest Physio – (**Percussion, Postural Drainage**)**
  - **Mucolytics -** (Eg. DNAse → Destroys Extracellular DNA → ↓Mucous Viscosity)
  - **Antibiotics for Recurrent Infections – (*Tobramycin*)**
- **Prognosis:**
  - **40yr Life Expectancy**

RESPIRATORY Pathology:
HYPOXIA & HYPERCAPNIA

Common Outcomes of Respiratory Emergencies:

- **HYPOXIA:**
  - **Types:**
    - **Hypoxic Hypoxia:**
      - Most common type.
      - Result of Insufficient oxygen available to the lungs (Eg. Obstruction/Drowning/Altitude)
    - **Stagnant Hypoxia:**
      - Not enough Cardiac Output → ↓Tissue Perfusion
    - **Anaemic Hypoxia:**
      - Not enough Haemoglobin → ↓O_2-Carrying Capacity of Blood.
    - **Histotoxic Hypoxia:**
      - Toxin which prevents Oxidative Metabolism @ the Cellular Level
      - Eg. Cyanide/Oligomycin
  - **Effects:**
    - Reduced work Capacity of Muscles
    - Depressed Mental Capacity
  - **Treatment:**
    - Supplemental O_2
- **HYPERCAPNIA:**
  - **= Excess CO_2:**
    - Typically caused by Hypoventilation
    - (Normal pCO2 Range = 35 - 45mmHg)
  - **Effects:**
    - If pCO2 > 60mmHg → Severe Dyspnoea
    - If pCO2 > 80mmHg → Lethargy & Coma
    - If pCO2 > 120mmHg → Anaesthesia, Respiratory Depression & Death
  - **NB:**
    - CO2 Diffuses 20x faster than O_2
    - CO2 is a *More Potent* Respiratory Stimulus than O_2
    - Blood capacity for CO2 is 3x More than O_2
  - **Treatment:**
    - Encourage Hyperventilation
    - Assisted Breathing (if Unconscious)
    - NB: Supplemental O_2 can → Suppress Central Control of Breathing →Respiratory Arrest.

RESPIRATORY Pathology:
INFLUENZA

SEASONAL FLU (INFLUENZA A & B):

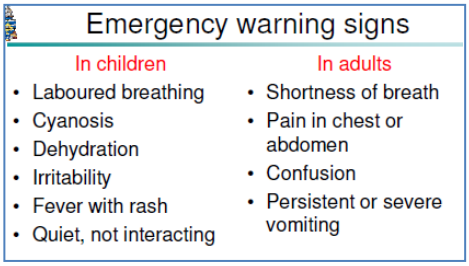
- **Aetiology:**
  - **Influenza Virus A & B**
- **Pathogenesis:**
  - **Transmision:** airborne spread. droplet
  - **Incubation Period:** 1-4 days
  - **Contagious for:** 1day *Before Syx Onset*, and the next 7days.
  - Viral-Induced Epithelial Dysfunction & Destruction
- **Clinical Features:**
  - **Symptoms:** Chills, Fatigue, Cough, Myalgias, Arthralgias, Headache
  - **Signs:** High Fever (<42C); But Chest Clear (Unless 2^{o} Bacterial Pneumonia)
  - **Complications:** 2^{o} Bacterial Pneumonia, Otitis Media, Sinusitis
- **Diagnosis:**
  - **Clinical Diagnosis (Signs & Symptoms)**
  - **+/- Nasopharyngeal Swabs**
  - **+/- Serology**
  - **NB: CXR is usually *Normal*.**
- **Treatment and Prevention**
  - **Primarily Supportive Treatment:**
    - Bed Rest, Fluid, Paracetamol/Analgesics, Antitussives, Decongestants
  - **+/- Antivirals (Effective within 48 hours of onset):**
    - *Oseltamivir* (Tamiflu TM) / *Zanamivir* (Relenza TM) → **Reduce <24hrs of Symptoms**
  - **Vaccine:**
    - **FluVax** is recommended ***Annually*** for ***Everyone***
    - (NB: Vaccine is reformulated each year to include current serotypes)

BIRD FLU (H5N1):

- **Aetiology:**
  - Influenza H5N1
- **Pathogenesis:**
  - **Transmission** – Aerosol/Direct Contact
  - **Incubation Period Generally 2-8 Days**
  - **Infection with Influenza H5N1** → Viral Replication → Virus-induced Epithelial Dysfunction
  - **Mortality Rate** ≈63%
- **Clinical Features:**
  - **Symptoms:** High Fever (>38"C), Headache, Myalgias, Cough (± Sputum), Dyspnoea + Others
  - **Pneumonia:** Consolidation, Tachypnoea, Tachycardia
  - **Often Progresses To ARDS** → Multi-Organ Failure → Death
- **Investigations:**
  - **NPA → PCR**
  - **CXR - (**Infiltrates +/- Pleural Effusions**)**
- **Treatment**
  - **ICU - (**Ventilation, Fluids**)**
  - **Antivirals – (***Oseltamivir* (Tamiflu TM) / *Zanamivir* (Relenza TM)**)**
- **Prevention**
  - No Vaccine
  - Hygiene Precautions
  - Post-?Exposure-Prophylaxis – (*Oseltamivir* / *Zanamivir*)
  - **Notify Public Health**
  - **Contact Tracing and Quarantine**

SWINE FLU (H1N1):

- **Epidemiology**
  - HUMAN to HUMAN - NOT by pigs; documented mass pig slaughtering was unnecessary
  - Incubation Period 24--48 Hours
- **Aetiology:**
  - H1N1 – (A Novel strain - genes from 5 different flu viruses)
- **Pathogenesis:**
  - Droplet Transmission – Human to Human.
  - Respiratory Tract Infection
- **Clinical Features:**
  - **Low Mortality Rate** - 2 deaths in first 600 cases in the US
  - **Infects The Young** (<5yrs) **And Old** (>65yrs)
  - **Transmission:** Aerosol/Contact (Human:Human)
  - **Symptoms:** Fever, Cough, Sore throat, N/V/Dia (25%), Myalgia/Arthralgia, Headache

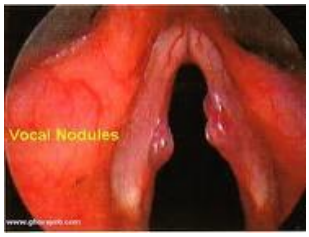


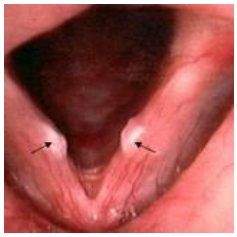
- **Diagnosis:**
  - **Clinical Suspicion**
  - **PCR – (**Nasal/Nasopharyngeal/Oropharyngeal**)**
  - **Notify Public Health**
  - **Contact Tracing and Quarantine**
- **Treatment**
  - **Antivirals – (***Oseltamivir* (Tamiflu TM) / *Zanamivir* (Relenza TM)**)**
  - **+Supportive.**

RESPIRATORY Pathology:
LARYNGEAL TUMOURS

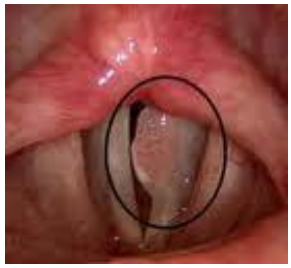
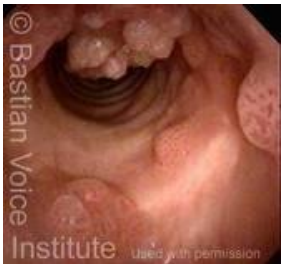
Benign laryngeal Tumours:

- **VOCAL CORD NODULES:**
  - **Aetiology:**
    - Chronic Irritation (Singers/Smokers)
  - **Pathogenesis:**
    - Chronic Irritation → Fibrosis → Nodules
  - **Morphology:**
    - Fibrous
  - **Clinical Features:**
    - May Bleed
    - Non Malignant





- **RECURRENT PAPILLOMATOSIS:**
  - **Aetiology:**
    - HPV Infection in Children (From infected Mothers)
  - **Pathogenesis:**
    - HPV Infection → Causes cell mutations → Dysregulated Cell Proliferation
  - **Morphology:**
    - Warty Lesion on the Vocal Cords. (May extend down the trachea)
  - **Clinical Features:**
    - Children

LARYNGEAL CARCINOMA (SCC) (MALIGNANT):

- **Aetiology:**
  - Smokers, Alcohol & Radiation
  - 7:1 - M:F
- **Pathogenesis:**
  - Squamous Cell Carcinoma
- **Morphology:**
  - Invasive SCC
- **Clinical Features:**
  - Persistent Hoarseness of Voice
  - Dysphagia
  - Sore Throat
- **Investigations:**
  - Head CT (Staging)
- **Management:**
  - Excisional Biopsy (Grading)
- **Prognosis:**
  - 30% Mortality (due to Metastasis)

RESPIRATORY Pathology:
LUNG CANCER

Lung Tumours:

- **Classification of Malignant Lung Tumours:**
  - ****Bronchogenic Carcinomas (95% of Lung Cancers)** – From the Bronchi

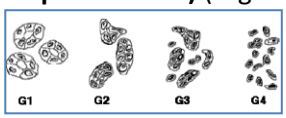
	Risk Factors?	Cent/Periph?	Aggressive?	Treatment
Small Cell Ca. (SCC) 20%	Smoking Male	Central →Spreads	Highly Aggressive, Poorly Demarcated	Chemotherapy (NOT Surgery)
Non-Small Cell Ca (NSCC) 80%				
- **Squamous Cell Carcinoma**	Smoking Male	Central Local	Mildly Aggressive, Well Demarcated	Surgery (NOT Chemo)
- **Adenocarcinoma**	**Female, Non-Smokers**	Peripheral	Mildly Aggressive, Well Demarcated	Surgery (NOT Chemo)
- **Large Cell Anaplastic Ca.**	Male	Central Local	Mildly Aggressive, Well Demarcated	Surgery (NOT Chemo)

  - **(Metastasis from other organs)** → Cannon-Ball appearance on X-Ray
  - **Mesothelioma –** Asbestosis

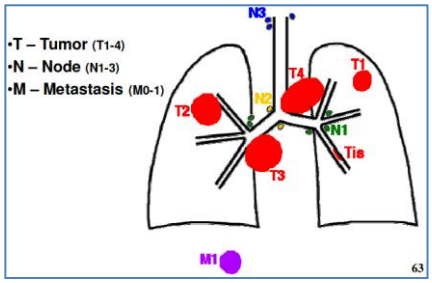
BRONCHOGENIC LUNG CANCERS:

- **Aetiologies:**
  - ***STEPWISE ACCUMULATION OF GENETIC MUTATIONS DUE TO ENVIRONMENTAL INSULTS*:**
    - ***Smoking:** 90% Are Due to Smoking. (20x Risk if >40/day)
    - **Occupational Exposure:** Asbestos / Coal Dust / Smoke
    - **Radiation Exposure:** Nuclear scientists / Atomic Bomb Survivors
- **Pathogenesis:**
  - **Carcinogens→ Mutations (Oncogene Activation→ Promotion → Pleomorphism)→ Cancer**
    - (Normal → Metaplasia → Dysplasia → **Pleiomorphism → Neoplasia →**Invasion)
- **Clinical Features of Bronchogenic Carcinomas:**
  - **Symptoms:**
    - **(**NB: Often *Asymptomatic* until Advanced Disease)**
    - **Most Common *Presenting* Symptoms:**
      - ***Dry Cough + Dyspnoea***
      - ***Haemoptysis***
      - ***Chest Pain***
      - **Weight Loss**
    - **Other Symptoms:**
      - **Airway Obstruction →**
        - → ***Pneumonia*** in the obstructed lobe only
        - → ***Atelectasis*** (Collapse of Lung) - (→ Tracheal + Mediastinal Deviation)
        - →***Bronchiectasis*** (Overstretched Bronchial Tubes)
        - → ***Abscess***
      - **Tumour Invasion Of:**
        - **Pleura →*Pleural Effusion***
        - **Pericardium → *Pericarditis/Pericardial Effusion* → *Tamponade***
        - **Laryngeal Nerve → *Hoarseness***
        - **Phrenic Nerve → *Diaphragm Paralysis***
        - **Oesophagus →*Dysphagia***
        - **Sympathetic Ganglia → *Horner's Syndrome***
        - **SVC → *SVC Syndrome (Permberton's Sign)***
        - **Alveoli/Pulmonary Vessels →*Haemoptysis***
        - **Bone → *Bone Pain/Path-Fractures***
        - **Brain → *Epilepsy/Focal Neurology***

- **Complications:**
  - **Paraneoplastic Syndromes – Typically in *SMALL CELL CARCINOMAS*:**
    - **Hypertrophic Pulmonary Osteo Arthropathy (HPOA) → ↑PTH -like Hormone:**
      - → Wrist Tenderness (Osteoarthropathy) + Finger Clubbing + Hypercalcaemia
    - **Carcinoid Syndrome → Carcinoid Tumours Secrete ↑Serotonin:**
      - → Hot Flushes + Diarrhoea + Abdo Cramps
    - **↑ADH (SIADH – Syndrome of Inappropriate Anti-Diuretic Hormone Secretion):**
      - → Hyponatraemia
    - **Cushings Syndrome → ↑ACTH (Adreno Cortico-Tropic Hormone) → ↑Cortisol:**
      - → "Moon Facies" + Rapid Weight Gain + Hypertension + Insomnia + Impotence
  - **Pancoast Tumours (Apical Lung Tumours):**
    - **Horner's Syndrome:**
      - Sympathetic Chain Compression → Symptoms mimic Loss of Sympathetic NS.
      - **(Remember *Horny Pamel*a):**
        - **P** **Ptosis** (Unilateral) (Droopy Eyelid)
        - **A** **Anhydrosis** (Unilateral) (Loss of sweating)
        - **M** **Miosis** (Unilateral) (Pupillary Constriction)
        - **E** **Enophthalmos** (Unilateral) (Recession of Eyeball)
        - **L** **Laryngeal Nerve Palsy** → Hoarseness
    - **Pancoast Syndrome (Brachial Plexus Compression):**
      - → Shoulder Pain
      - → Wasting of Intrinsic Hand Muscles
      - → Paresthesia
      - → Motor Disturbances in Hands
    - **SVC Syndrome/Pemberton's Sign (SVC Obstruction):**
      - **Pemberton's Sign:** Facial flushing & ↑JVP If arms are raised above Pt's head
- **Investigations:**
  - **Clinical:** History/Exam
  - **Imaging:** CXR/CT/PET/Bone Scan
  - **Cytology:** Sputum/Bronchial Lavage
  - **Biopsy:** Needle Aspirate/Excision
  - **Tumour Markers** (Monitoring only)
- **Grading Vs Staging:**
  - **Grading = Microscopic (Microscopic Features)** (Higher = More Aggressive)



  - **Staging = Clinical (Progression – TNM)**
    - **T =** Tumour Size
    - **N =** lymph node involvement – Primary/Secondary/Tertiary
    - **M =** Metastasis



- **Prognosis:**
  - **Poor - 5yr average survival – (Depends on the Type, Grade & Stage of Cancer)**
- **Treatment:**
  - **Surgery – (**Usually Lobectomy, Unilateral Pneumonectomy**).**
  - **Chemotherapy – (**Not curative *on its own*; but often a good Adjuvant to surgery or for Palliative**).**
  - **Radiation – (**Can cure NSCLC, although not first line**)** – Also Effective in Palliative Care

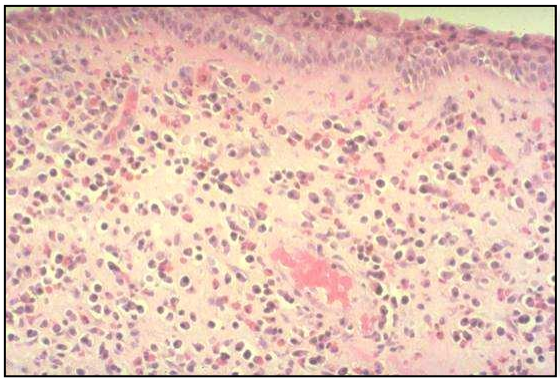
MESOTHELIOMA:

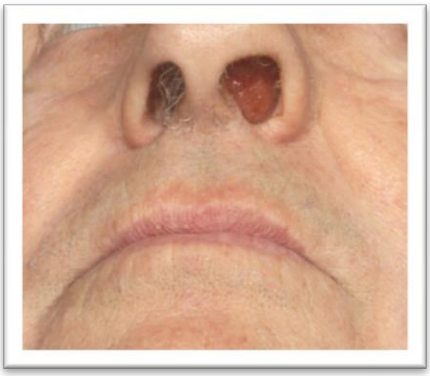
- **Aetiology:**
  - ***Asbestosis – Risk Factor**
- **Pathogenesis:**
  - **Malignant Neoplasm of the Pleura** (No change in lung tissue)
  - See General Carcinogenesis
- **Morphology:**
  - **Poorly Demarcated**
  - **Spreads *Around the Pleura* → Encases the Lungs**
- **Clinical Features:**
  - Rare tumour
  - Looks like thickening of the pleural surface on CT
  - → **Recurring Pleural Effusions, Chest Pain, Dyspnoea
  - →Metastasis
  - **VERY Poor Prognosis (50% 1yr Mortality)**

RESPIRATORY Pathology:
NASOPHARYNGEAL TUMOURS

NASAL POLYPS (Inflammatory):

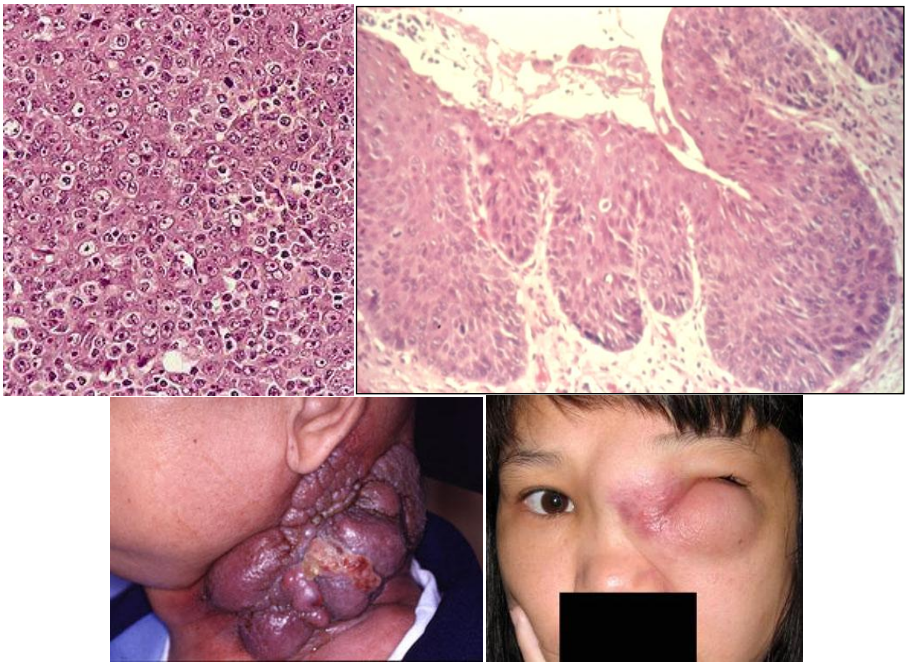
- **Aetiology:**
  - Chronic/Recurrent URTI
  - Allergy, Hypersensitivity
- **Pathogenesis:**
  - Chronic Mucosal Inflammation + Oedema → Inflammatory Hyperplasia → Polyp
  - **NB: 100% Benign: NO Malignant Potential!**
- **Clinical Features:**
  - Mobile, Non-Tender Polypoid Masses
  - **Symptoms:**
    - Nasal Block
    - Sinusitis
    - Anosmia (Loss Of Smell)
    - Secondary Infection → Headache
- **Investigations:**
  - Nil
- **Management:**
  - Nasal Corticosteroids (Nasonex)





Nasopharyngeal Carcinoma:

- (Most common cancer of the nasopharynx)
- **Aetiology:**
  - Risk Factors:
    - EBV
    - Chinese/African
    - Male
- **Pathogenesis:**
  - A Malignant Neoplasm, Arising From The Mucosal Epithelium Of The Nasopharynx
- **Morphology:**
  - Dedifferentiated Carcinoma (Often Keratinizing Squamous Cells)
  - Many Reactive Lymphocytes
  - Locally Invasive
- **Clinical Features:**
  - **Signs/Symptoms:**
    - Cervical lymphadenopathy
    - trismus (inability to normally open the mouth)
    - Pain
    - otitis media
    - nasal regurgitation due to paresis of the soft palate
    - hearing loss
    - cranial nerve palsies
    - nasal obstruction or bleeding
  - **Metastatic spread** → may result in bone pain or organ dysfunction



RESPIRATORY Pathology:
NECK MASSES

NECK MASSES

- **Approach to a Neck Mass**
  - Ensure that the neck mass is not a normal neck structure (hyoid, transverse process of C1 vertebra)

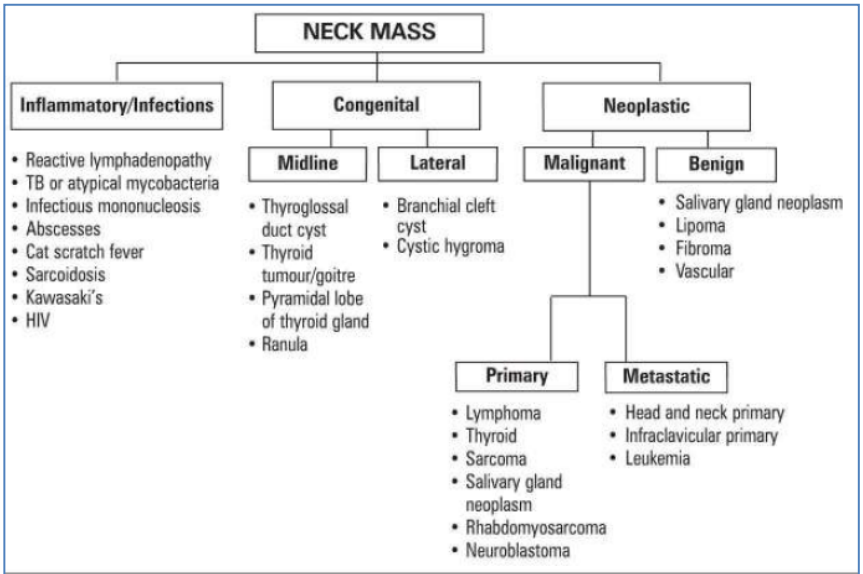
Table 15. Acquired Causes of Neck Lumps According to Age

Age (yrs)	Possible Causes of Neck Lump
<20	• Congenital: lateral (branchial cleft cyst, laryngocele, cystic hygroma), midline (thyroglossal duct cyst) • Inflammatory neck nodes (tonsillitis, infectious mononucleosis, Kawasaki's) • Lymphoma
20-40	• HIV • Salivary gland (calculi, infection, tumour) • Thyroid (goitre, infection, tumour) • Granulomatous disease (TB, sarcoidosis)
>40	• Primary or secondary malignant disease

- **Evaluation**
  - **Investigations**
    - **History And Physical (Including Nasopharynx And Larynx)**
    - **Laboratory Investigations**
      - WBC - infection vs. Lymphoma?
      - Mantoux – TB?
      - TFTs and scan – Hypothyroid?
    - **Imaging**
      - neck XR
      - CT scan
      - angiography - vascularity and blood supply to mass
      - radiologic exam of stomach, bowel and sinuses
    - **Biopsy - For Histology**
      - fine needle aspiration (FNA) - least invasive
      - open biopsy - for lymphoma
    - **Identification Of Primary Tumour**
      - Panendoscopy: Nasopharyngoscopy, Laryngoscopy, Esophagoscopy, Bronchoscopy With Washings, And Biopsy Of Suspicious Lesions
      - biopsy of normal tissue of nasopharynx, tonsils, base of tongue, and hypopharynx
      - **Primary identified 95% of time -** Stage and Treat
      - **Primary occult 5% of time** - Excisional Nodal Biopsy for Histology + Radiotherapy and/or neck dissection (squamous cell carcinoma)

Inflammatory vs. Neoplastic Neck Masses

	Inflammatory	Neoplastic
History		
Painful	Y	N
H&N infection	Y	N
Fever	Y	N
Weight loss	N	Y
CA risk factors	N	Y
Age	Younger	Older
Physical		
Tender	Y	N
Rubbery	Y	Occ.
Rock hard	N	Y
Mobile	Y	± fixed
Size	<2 cm	>2 cm

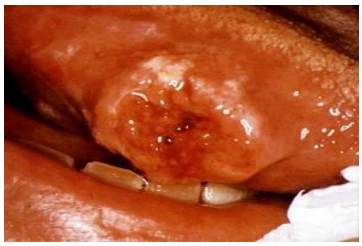


Differential Diagnosis of a Neck Mass

RESPIRATORY Pathology:
ORAL TUMOURS

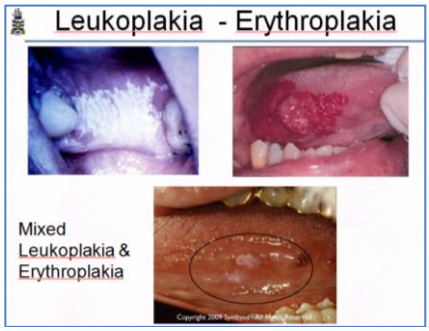
ORAL SQUAMOUS CELL CARCINOMA:

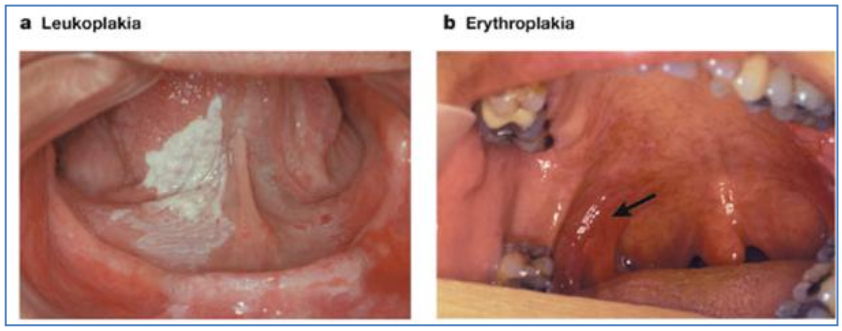
- **Aetiology:**
  - Tobacco, Alcohol, HPV
- **Pathogenesis:**
  - Carcinogenesis of the Squamous Oral Mucosal Epithelium.
- **Clinical Features:**
  - Start as white-gray plaques → Nodular Masses or Necrotic Ulcers
  - **Common Sites:**
    - Border of Lower Lip
    - Floor of mouth
    - Lateral tongue
- **Investigations:**
  - Head CT
- **Management:**
  - Excisional Biopsy
  - +/- Sentinal Node Resection
- **Prognosis:**
  - (NB: 50% of oral SCC's have nodal involvement at diagnosis)
  - 30% 5yr survival rate.



Oral SCC Precursor Lesions = LEUKOPLAKIA/ERYTHROPLAKIA:

- **Aetiology:**
  - Associated with Tobacco
- **Pathogenesis:**
  - Hyperkeratosis & Parakeratosis
- **Morphology:**
  - Well-defined, white or red plaque (Due to Hyperkeratois)
- **Clinical Features:**
  - 5-15% Transform to Cancer.

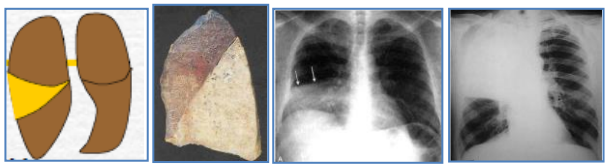




RESPIRATORY Pathology:
PNEUMONIA

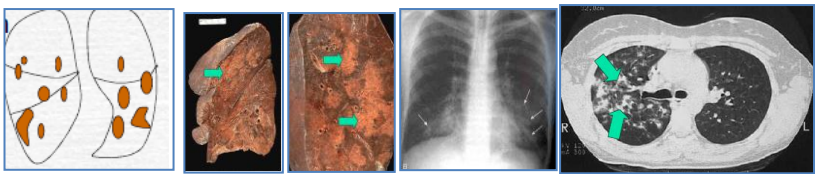
PNEUMONIAS ("Infections of the Lung"):

- **Aetiology:**
  - **Bacterial:**
    - **Community Acquired:**
      - **Usually Gram-Positive – (**Strep pneumonia [90%]**)**
      - **Occasionally Gram-Negative – (**H.Influenzae**)**
    - **Hospital Acquired (Nosocomial - >48hrs POST Admission):**
      - **Usually Gram-Negative – (**Pseudomonas.aeruginosa**,** E.coli, Klebsiella**)**
    - **Atypical/Interstitial Pneumonia ("Walking Pneumonia"):**
      - **Intracellular Bacteria – (**Mycoplasma, Chlamydia, Legionella, Coxiella Burnetii**)**
    - **In Immunocompromised:**
      - Cytomegalovirus
      - Pneumocystis jirovecii
      - Fungal (Candida/Aspergillus)
- **Clinical Features:**
  - **General *Pneumonia Triad (WHO)*:**
    - **Fever**
    - **Tachycardia**
    - **Tachypnoea (+/- Breathlessness)**
- **Types - Based on Morphology:**
  - ***Lobar-Pneumonia (Well Defined; One Lobe):***
    - **Aetiology:**
      - Typically ***Strep Pneumoniae*** (Gram Positive Diplococci)
      - (Or *Klebsiella* in Aged)
    - **Pathogenesis:**
      - Whole Lobe Involvement
      - Exudate *Within Alveolar Spaces* → Alveolar Consolidation
    - **Morphology:**
      - Follows Anatomical Boundaries (Physically & on CXR)
      - Entire Lobe Consolidation/Opacity on CXR



    - **Clinical Features:**
      - **Symptoms:**
        - Abrupt onset High Fever + Chills
        - Productive Cough (Occasionally Rusty Sputum &/or Haemoptysis)
        - Pleuritic Chest pain + Pleural Rub.
      - **Signs:**
        - Usually Unilateral
        - Exudation – Entire Lobe Consolidation
        - Cardinal Pneumonia Signs –(Fever, Tachycardia, Tachypnoea)

- ***Broncho-Pneumonia (Patchy; Multiple Lobes):***
  - **Aetiology:**
    - **Secondary to Debilitating Diseases, Extremes of Age, or Post-Surgery:**
      - **Gram Pos - Strep Pneumoniae, Staph Aureus**
      - **Or Gram Neg - H. Influenzae**
  - **Pathogenesis:**
    - Patchy Areas of Acute Suppurative Inflammation → Patchy Consolidation
    - Basal Lower Lobes Common (Due to gravity – bacteria settle in the lower lungs)
  - **Morphology:**
    - Doesn't follow anatomical boundaries – Often *Multi-Lobar & Bilateral*.
    - Usually Bilateral Patchy Consolidation →Scattered Opacities on CXR



  - **Clinical Features:**
    - **Symptoms:**
      - Abrupt onset High Fever + Chills
      - Productive Cough (Occasionally Rusty Sputum &/or Haemoptysis)
      - Pleuritic Chest pain + Pleural Rub.
    - **Signs:**
      - Usually Bilateral
      - Patchy Consolidation – Usually Bilateral
      - Cardinal Pneumonia Signs –(Fever, Tachycardia, Tachypnoea)

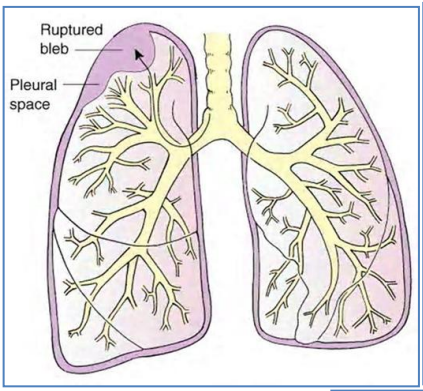
- ***Atypical, Interstitial Pneumonia ("Walking Pneumonia"):***
  - **Aetiology:**
    - **Typically Intracellular Bacteria:**
      - Mycoplasma, Chlamydia pneumonia, Legionella, Q-Fever (Coxiella burnetii)
    - **Or Viral:**
      - Influenza A/B, RSV – Respiratory Syncytial Virus, Corona Virus (SARS)
  - **Pathogenesis:**
    - Interstitial Inflammation (NOT within the Alveolar *Spaces*)
    - NB: 2^{o} Bacterial Pneumonia (Typically Strep/Staph) may follow.
  - **Morphology:**
    - Inflammation localised to Alveolar Wall/Septa (Interstitium); NO Alveolar Exudate
    - Typically Bilateral.
  - **Clinical Features:**
    - **Symptoms:**
      - Initial URTI → SLOW Onset (Days-Weeks)
      - Symptoms more *General* & *'Flu-like'*.
      - Few Localizing Symptoms:
        - Often NO Cough
        - Wheezing (Not seen in other pneumonias)
    - **Signs:**
      - No *Physical Signs* of Consolidation
      - *Unresponsive* to Common Antibiotics

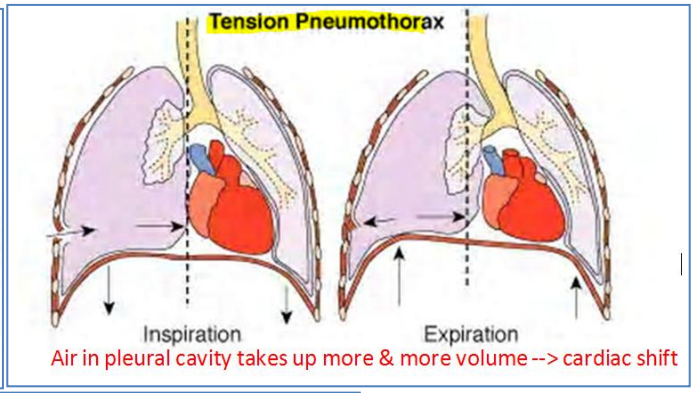
- **Investigations For Pneumonia:**
  - **CXR – (**Consolidation Lobar/Broncho/Interstitial**)**
  - **Sputum MCS – (**Sputum / NPA – Nasopharyngeal Aspirate / BAL – Bronchio-Alveolar Lavage**)**
  - **Blood Culture if ?Septic**
  - **Serological Testing – (If ?Atypical Pneumonias)**
- **Management:**
  - **?Admit to ICU? – *CURB-65* – (Score >3 → ICU):**
    - **Confusion**
    - **Uraemia**
    - **Resp Rate >30**
    - **BP <90/60**
    - **>65yo**
  - **Antibiotics:**
    - **Empirical:**
      - **?G-Pos: *Amoxicillin* / *Benz-Penicillin-V* / *Doxycycline* / *Clarythromycin***
      - **?G-Neg: *Gentamicin* / *Ceftriaxone***
      - **Severe: + *Meropenem* / *Imipenem***
    - **But Ultimately Dictated by MCS.**
  - **Fluids**
  - **O2 if Sats <92%**
  - **+/- Ventilation**
- **Possible Complications of Pneumonia:**
  - **ARDS – Acute Respiratory Distress Syndrome:**
    - Severely Impaired Gas Exchange → Hypoxia & Confusion.
    - **Rx. Mechanical Ventilation and ICU.**
  - **Lung Abscesses**
  - **Pleuritis/Pleural Effusion/Empyema**
    - Inflammation of the pleura (Strep Pneumoniae)
    - Blood Rich Exudate/Pus in Pleural Space
    - **Rx. Drainage + MCS → IV Antibiotics**
  - **Septicemia, Meningitis**
  - **Fibrosis, Scarring, Adhesions**
  - **Rarely Adenocarcinoma**

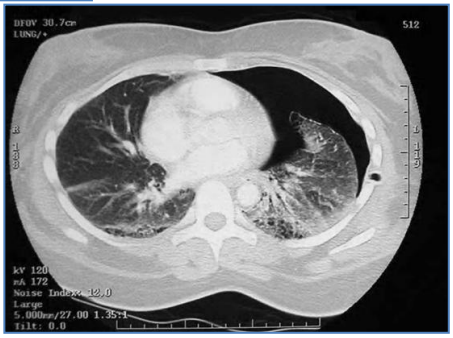
RESPIRATORY Pathology:
PENUMOTHORAX

PNEUMOTHORAX:

- **Aetiology:**
  - Penetrating Chest Trauma
  - Bullous Emphysema
  - Lung Cancer
- **Pathogenesis:**
  - Where Air/Fluid Enters The Pleural Space → Disrupts –ve Intrapleural Pressure → Lung Collapses
  - **Spontaneous Pneumothorax – (Eg. Bullous Emphysema)**:
    - Rupture of small "Blebs" on Surface of Lung → Air enters Pleural Space From *Within*.
  - **Tension Pneumothorax – (Penetrating Injury):**
    - Penetrating Injury → Air Enters Pleural Space → Forms *Valve* (Air Enters But Can't Escape).
      - Compresses Major Vessels
      - Impedes Venous Return
      - Causes Respiratory Distress
      - Causes Tachycardia
      - Causes Tracheal Deviation
- **Clinical Features – (*Of Tension Pneumothorax*):**
  - **Symptoms:**
    - Pleuritic Chest Pain
    - Dyspnoea
  - **Signs:**
    - Tracheal Deviation
    - Respiratory Distress
    - Tachycardia
- **Investigations:**
  - **CXR – (**Air in Pleural Cavity, Displaced Mediastinum, Lung Markings Absent in Periphery**)**
  - **CT – (**If ?Rib# / ?Cancer / ?Haemothorax**)**
- **Management:**
  - **Pleural Tap w. One-Way Valve**
  - **Correct Underlying Cause**
  - **O2 Supps.**
  - **Chest Physio – (**To Reinflate Lung & Prevent 2^{o} Pneumonia**)**







RESPIRATORY Pathology:
Q-FEVER

Q-FEVER

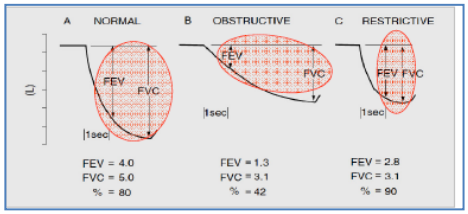
- **Aetiology:**
  - *Coxiella Burnetii* - (found in cattle, sheep, goats and other domestic mammals, (cats and dogs))
- **Transmission:**
  - Inhalation of Endospores / Contact with Unpasteurised Milk, Urine, Faeces of infected animals.
- **Pathogenesis:**
  - **2-3wk Incubation**
  - **Two-Stage Disease:**
    - **Acute** Stage (Headaches, chills, and respiratory symptoms)
    - **Chronic** Stage (Asymptomatic, Insidious)
- **Clinical Features:**
  - ***Acute* Symptoms:**
    - **Flu-Like Symptoms:** Abrupt Onset Fever, Chills, Sweats & Malaise
    - **Respiratory** - Dry Cough, Pleuritic Pain
    - **GI Symptoms** - Nausea, Vomiting And Diarrhea.
    - **Neuro:** +/- Severe Headache & Confusion
    - **MSK:** +/- Myalgia & Arthralgia
- **Diagnosis:**
  - **Serology**
  - **PCR**
  - **TOEcho** – (If Suspected Endocarditis)
  - **LFT – (**↑ALT & AST**)**
- **Treatment:**
  - **Antibiotics – *Doxycycline***
- **Complications:**
  - Progression to **Atypical Pneumonia** → life threatening **ARDS**
  - Rarely **Granulomatous Hepatitis** which can → hepatomegaly and RUQ pain.
  - Chronic form of Q fever → **Endocarditis**
- **Prevention:**
  - **Q-Vax** (Whole-cell, killed vaccine via intradermal injection)
  - (NB: Skin and blood tests should be done first to identify preexisting immunity; vaccinating subjects who already have an immunity can result in a severe local reaction.)

RESPIRATORY Pathology:
RESTRICTIVE (INTERSTITIAL) LUNG DISEASES

Restrictive (Interstitial) Pulmonary Diseases:

- Loss of Lung/Chest-wall Compliance → Restricted Lung Expansion
- **Pathogenesis:**
  - Chronic Interstitial Inflammation → Fibrosis/Thickening/Stiffening of *Lung Parenchyma*
- **Clinical Manifestations:**
  - Normal PEF
  - Normal FEV1/FVC (>80%)
  - ↓TLC (Total Lung Capacity)
  - ↓VC (Vital Capacity)
  - ↓IC (Inspiratory Capacity)

} Due to ↑Resistance to *Lung Expansion*



IDIOPATHIC PULMONARY FIBROSIS (IPF):

- **Aetiology:**
  - Unknown (*Idiopathic*)
- **Pathogenesis:**
  - Abnormal & Excessive Fibrosis of Pulmonary Interstitium (Mainly Alveolar Walls)
- **Morphology:**
  - Severe Interstitial Fibrosis & Scarring
- **Clinical Features:**
  - Typically in >50yo's
  - Gradual Onset of Symptoms
  - **Symptoms:** Progressive Dyspnoea, Dry Cough, Hypoxia/Cyanosis
  - **Signs:** Clubbing, Velcro-like Inspiratory Crackles
  - **Very poor prognosis (3 yrs)**
- **Investigation:**
  - **Spirometry – (**Restrictive Pattern**)**.
- **Management:**
  - No Known Treatment

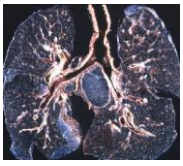
SARCOIDOSIS:

- **Aetiology:**
  - Idiopathic Immune
- **Pathogenesis:**
  - Infiltrating Non-Caseating Granulomas → Nodules in Multiple Organs
- **Morphology:**
  - Multiple Fine Nodules in Multiple Organs (**Lungs, Heart, CNS, Lymph Nodes...)
  - Pulmonary Fibrosis
- **Clinical Features:**
  - **Lung Manifestations – (**Dyspnoea, Restrictive Lung Disease**)**
  - **Other Organs – (**Lymphadenopathy, Erythema Nodosum, Kidney, Occular, CNS Damage**)**
- **Investigations:**
  - **CT**
  - **Guided Biopsy**
- **Management:**
  - **Corticosteroids**
- **Prognosis:**
  - 50% Spontaneous Resolution within 1-3yrs
  - Significantly Increased risk of Lung Cancer

Pneumoconioses:

- ***ASBESTOSIS*:**
  - **Aetiology:**
    - Inhalation of Asbestos Micro-Fibres
  - **Pathogenesis:**
    - Asbestos Micro-Fibres in Alveoli → Macrophage Activation → Inflammamation → Fibrosis
      - → ↓Elasticity & ↓Gas Diffusion
    - **+ → Mesothelioma**
  - **Morphology:**
    - Typically in the Lower Lobes
    - **Marked Interstitial (Parenchymal) Fibrosis/Scarring**
  - **Clinical Features:**
    - **Symptoms:**
      - Long Latent Period (Several Decades after Exposure)
      - ****Severe Dyspnoea**
      - ****Productive Cough**
    - **Signs:**
      - Inspiratory Crackles
  - **Investigations:**
    - **Spirometry – (**Restrictive Pattern, ↓VC, ↓TLC**)**
    - **CT – (?Mesotheioma)**
    - **Lung Biopsy – (**Ferruginous Bodies**)**
  - **Treatment:**
    - None
    - Supportive Rx
    - Surgery (Pleurectomy if Mesothelioma)
  - **Complications:**
    - Mesothelioma
    - Pleural Effusions
    - Corpulmonale
    - Respiratory Failure

- **ANTHRACOSIS *("Coal Miner's Lung")*:**
  - **Aetiology:**
    - Long Term Inhalation of Carbon Dust (Coal Dust)
  - **Pathogenesis:**
    - Coal Dust → Macrophage Phagocytosis & Activation → Inflammation → Fibrosis
  - **Clinical Features:**
    - Initially Benign
    - Dyspnoea, Chronic Cough
    - Lung function *reasonably* preserved.

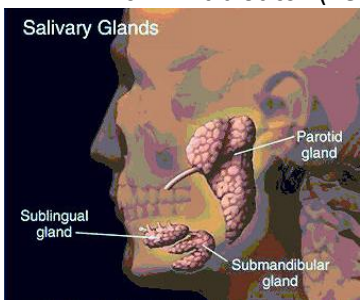


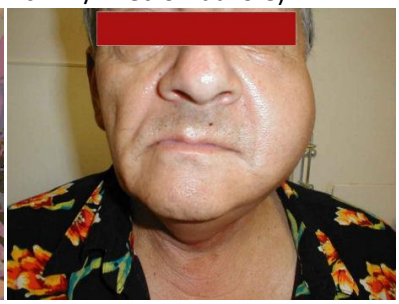
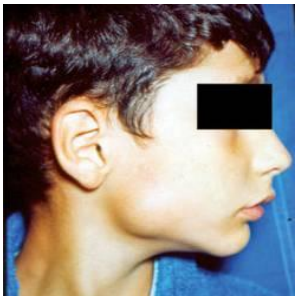
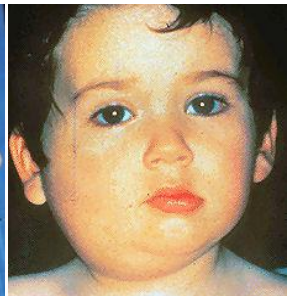
- ***SILICOSIS*:**
  - **Aetiology:**
    - Inhalation of Sand & Stone Dust (Silicone)
  - **Pathogenesis:**
    - Silicone Dust in Alveolar Walls → Macrophages Ingest Particles → Inflammation + Fibrosis
  - **Clinical Features:**
    - Initially Asymptomatic
    - Dyspnoea, Cough, Cyanosis
  - **Investigations:**
    - **Spirometry – (**Restrictive Pattern, ↓VC, ↓TLC**)**

RESPIRATORY Pathology:
SALIVARY GLAND – INFECTION

Sialadenitis (*Parotitis*):

- **Definition:**
  - Acute Inflammation of the salivary glands
  - (**Parotid** Most Common)
- **Aetiology:**
  - Dehydration/Dry Mouth (Xerostomia) - (Common in Post-Op Patients)
    - →Infective – Bacterial (Staph. Aureus), or Viral (Mumps)
- **Pathogenesis:**
  - Dry Mouth (Xerostomia) → Drying of Salivary Secretions in the glands → Infection (Bacterial/Viral)
    - (→ Duct obstruction → Recurrent Sialadenitis)
- **Morphology:**
  - Grossly Enlarged Parotid Gland.
- **Clinical Features:**
  - **Symptoms:**
    - Fever
    - Dry Mouth
    - Abnormal/Foul Tastes
    - ↓Ability to Open Mouth
    - Mouth or Facial Pain, (esp. when eating)
    - Redness over the side of the face or the upper neck
    - Swelling of the face
  - **Complications:**
    - Sialolithiasis (Salivary Gland Calculi) or Fibrosis → Duct Obstruction
- **Management:**
  - Antibiotics –(Penicillin / Metronidazole)



RESPIRATORY Pathology:
SALIVARY GLAND – STONES

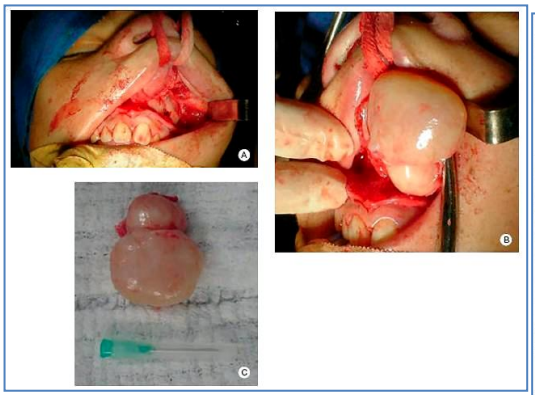
Sialolithiasis (Salivary Gland Calculi):

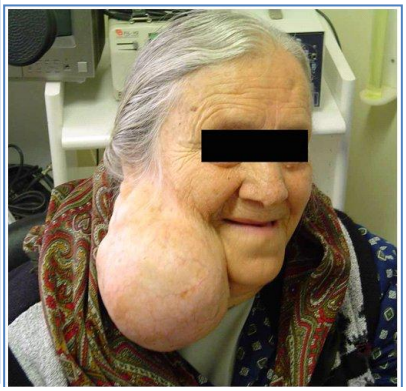
- **Definition**
  - Ductal Stone (mainly hydroxyapatite) in Salivary Gland → Chronic Sialadenitis
  - **80% in submandibular gland**, <20% in parotid gland, -1% in sublingual gland
- **Risk Factors**
  - Anything causing Drymouth (e.g. Dehydration, Diabetes, EtOH, Anticholinergics)
- **Clinical Features**
  - Painful, Tender Gland.
  - Swelling following Meals
  - Palpation of gland reveals Calculi
- **Investigations**
  - Sialogram
  - CT
- **Treatment**
  - May Resolve Spontaneously
  - Encourage Salivation To Clear Calculus
  - Dilation And Excision Through Floor Of Mouth
  - If Calculus Is in the Gland (not the duct) the Gland Must Be Excised

RESPIRATORY Pathology:
SALIVERY GLAND – TUMOURS

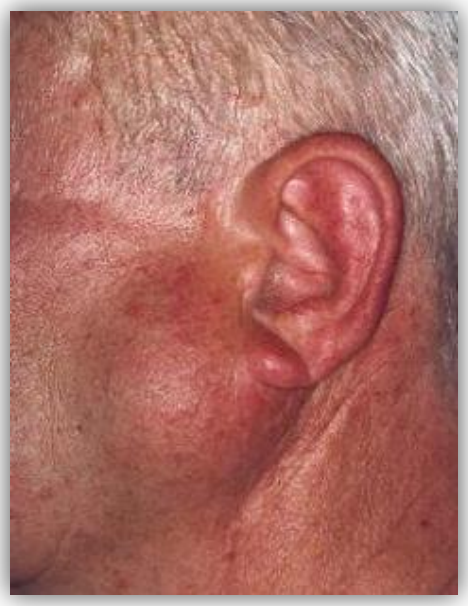
Salivary Gland Tumours

- **Pleomorphic Adenoma (80% in Parotid Gland)(80% of all Salivary Gland Tumours):**
  - **Definition:**
    - Benign Neoplastic Tumor Of The Salivary Glands
  - **Aetiology:**
    - Unknown – But Strong Association with Cigarette Smoking
  - **Pathogenesis:**
    - Slow-Growing
    - Benign
  - **Morphology:**
    - **Macro:**
      - Enlarged Parotid Gland
      - Firm, Mobile, Nodule/s.
    - **Micro:**
      - Architectural Pleomorphism (variable appearance) seen by light microscopy
        - Cysts lined by *Squamous Epithelium*
        - Anastomosing Trabeculae
        - Myxoid Areas (Mucoid/Mucous like)
        - Chondroid Areas (Cartilage)
      - Adenoma = Ductal Origin
        - Glands
      - Tumor is Not Enveloped, but is surrounded by a *Fibrous Pseudocapsule*.
  - **Clinical Features:**
    - Adults
    - Benign (But may transform to malignant "**Carcinoma Ex-Pleomorphic Adenoma**")
    - Enlarged Parotid Gland
    - Painless & Slow-Growing, Firm Single Nodular Mass.
    - Asymptomatic
  - **Investigations:**
    - fine needle aspiration biopsy
    - CT or MRI to determine extent of tumour
  - **Treatment:**
    - Excision = Gold Standard for ALL Salivary Gland Tumours (Benign *OR* Malignant)





- **Warthin's Tumour (AKA: "Papillary Cystadenoma Lymphomatosum")(10% of all Salivary Gland Tumours):**
  - **Aetiology:**
    - Unknown – But Strong Association with Cigarette Smoking
  - **Pathogenesis:**
    - Benign
  - **Morphology:**
    - Macro:
      - 80% in Parotid Gland
      - Parotid Swelling (Typically @ the tail near the angle of the Mandible)
    - Micro:
      - Epithelium-lined Lymphoid Tissue
      - Cystic Spaces surrounded by a 2-layered Epithelium with Central Pyknotic Nuclei.
      - Epithelium has Lymphoid Stroma with Germinal Center Formation.
  - **Clinical Features:**
    - Male; Old Age (60-70yrs).
    - Painless, Slow-Growing Parotid Gland (Typically @ the tail near the angle of the Mandible)
    - Benign (But risk of malignant transformation)
  - **Investigations:**
    - fine needle aspiration biopsy
    - CT or MRI to determine extent of tumour
  - **Treatment:**
    - Excision = Gold Standard for ALL Salivary Gland Tumours (Benign *OR* Malignant)



RESPIRATORY Pathology:
SARS

SARS – SEVERE ACUTE RESPIRATORY SYNDROME:

- **Definition**
  - Rapidly progressing viral pneumonia caused by the SARS-associated coronavirus (SARS-CoV)
- **Aetiology:**
  - **SARS-Associated Coronavirus**
  - Incubation: 2-7 days
- **Pathophysiology**
  - Droplet Transmission – Human to Human.
  - Respiratory Tract Infection with SARS-Associated Coronavirus
  - → Atypical Pneumonia +/- Respiratory Distress Syndrome
- **Clinical Features**
  - **Difficult To Differentiate SARS from other Community-Acquired Pneumonias Because:**
    - ***Initial* Symptoms Are Not Specific:**
      - Fever, Chills, Malaise,
      - Headache, Myalgia,
      - Cough, Sore Throat, Productive Cough
    - ***However,* 2/3 Of Patients Deteriorate with:**
      - Persistent Fever,
      - ↑SOB & Desaturation
    - **20% Require ICU Admission and Mechanical Ventilation**
- **Complications**
  - Respiratory failure
  - Liver failure
  - Heart failure
- **Diagnosis:**
  - **Clinical Suspicion – Symptoms, Hx of Travel, Hx of Contact**
- **Investigations:**
  - **CXR** – Features of Atypical Pneumonia
  - **Lab** – Neutrophilia, Lymphopenia, ↑CRP, & ↑LDH
  - **RT-PCR** – from Blood/Sputum/NPA/Swabs.
  - **Serology** – (antibody detection via ELISA)
- **Treatment**
  - **Notify public health**
  - **Quarantine** (negative-pressure room, N95 Mask, gown, gloves, eye protection)
  - **Antivirals** – (*Ribavirin*)
  - **Steroids** - (To prevent immune mediated lung damage)

Respiratory Diseases

Host defences

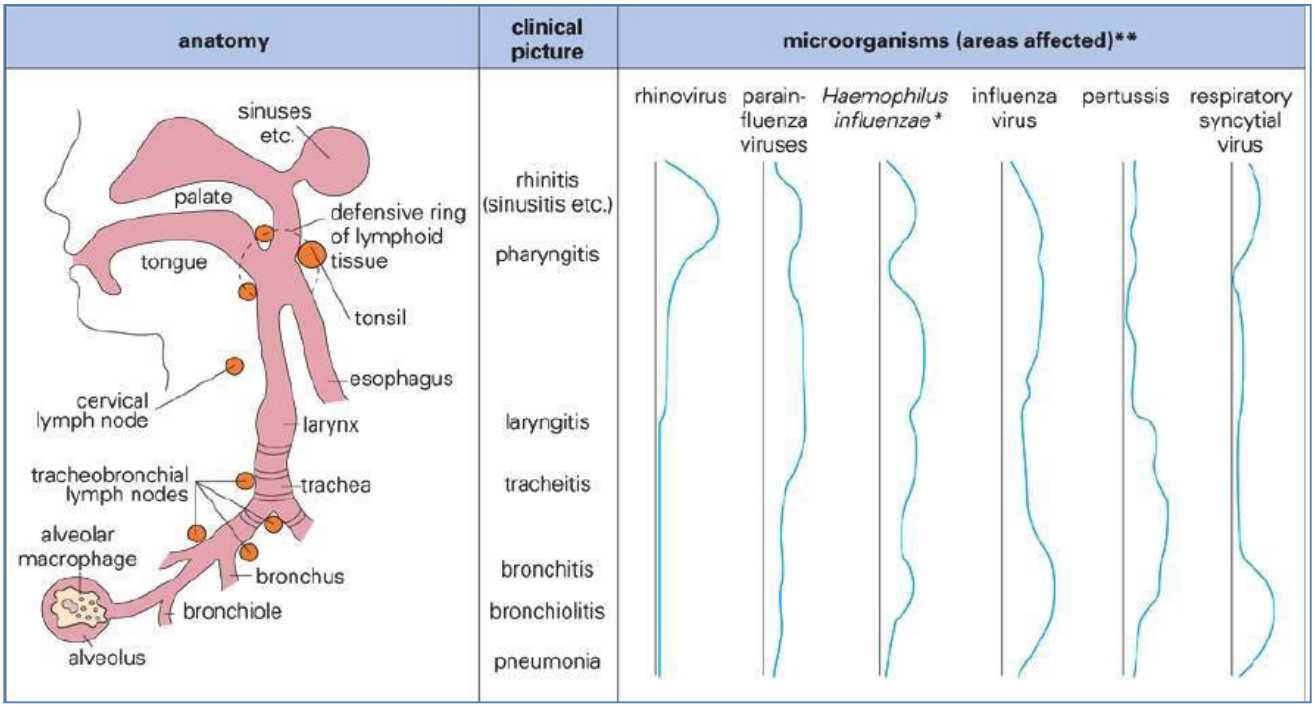
- **Lower Resp. Tract is Sterile - maintained by host defences**
  - immunological & anatomical
- **Physical Barriers to Infection:**
  - Nasal hairs
  - Cilia
  - Cough & sneeze reflexes
  - Bronchial mucous + Mucociliary Mechanism → Swallowed
- **Immunological Barriers to Infection:**
  - Tonsils / lymph nodes
  - Antibody (sIgA)
  - Alveolar macrophages
- **Normal flora of URT:**
  - Compete with The Pathogens
- **NB: Respiratory Infections may Remain Localised, or Spread through the Body.**

Predisposing Factors to Respiratory Infections:

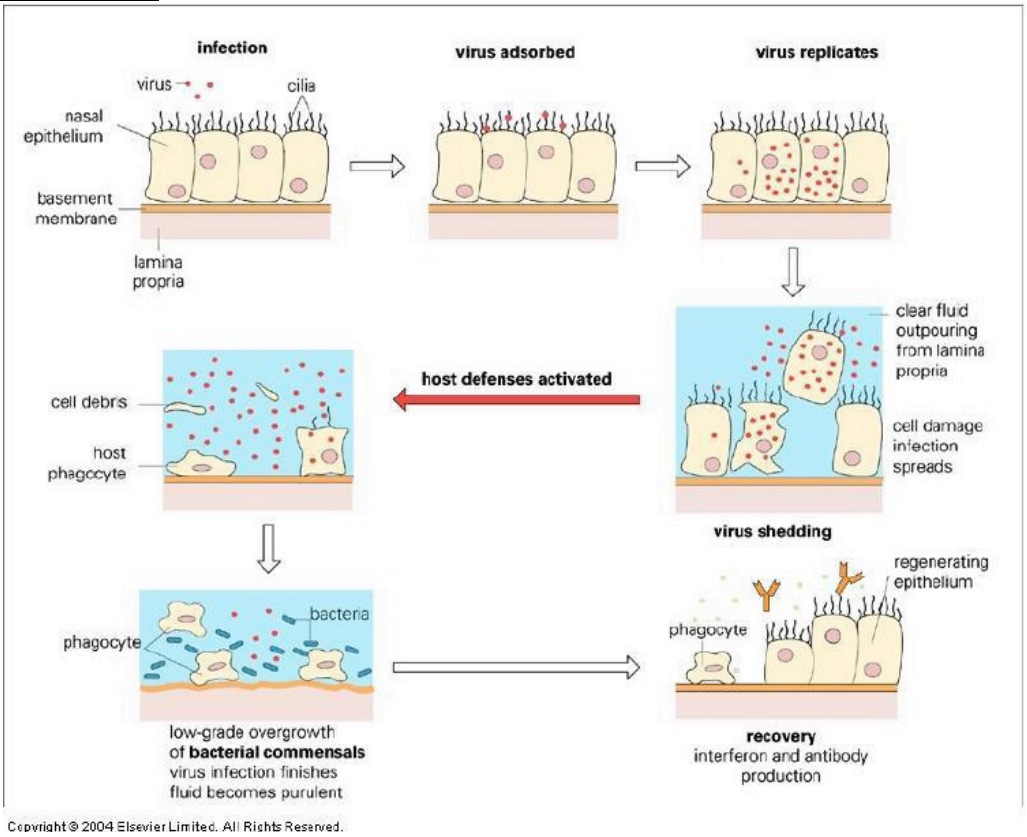
- Young age
- Old age
- Smoking
- COPD
- Poverty
- Alcoholism
- Immunosuppression
- Cancer
- **Reservoirs of infection:**
  - Other infected people
  - URT → LRT

Location of different RTI's & Which Organisms are Responsible:

- NB: Upper Resp Tract favours organisms which grow in lower temperatures



Pathogenesis of Viral RTIs:



Viruses Causing Common Colds – (Typically Rhinoviruses):

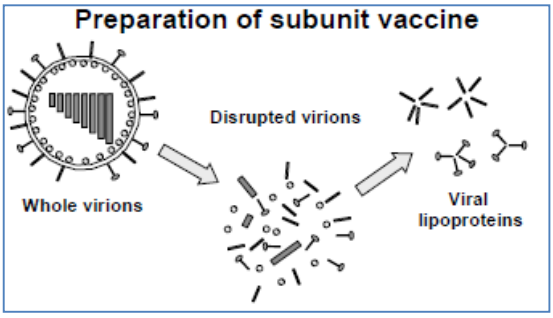
- **#1 Rhinoviruses:**
  - Typically restricted to URT
  - **Many Serotypes:**
    - Endemic throughout the year
    - No Cross-Protection between Serotypes
    - → **Possibility of Repeated Infections**
  - Short Incubation Period (2-3 days) with Inflammation, Oedema and Copious Exudate
  - Resolution due to Immune System. (Self Limiting)
- **Adenovirus:**
  - Most infections occur in early-life <5yrs
  - Rarely causes disease
  - Symptoms = Nasal Congestion, Cough, Pharyngitis (Sore Throat)
- **Coronaviruses:**
  - Can infect URT & LRT
  - Replication is confined to the Epithelial Layer
  - Infection is usually Mild
  - (Including SARS)
- **Coxsackie Virus A**
- **Orthomyxoviruses: Influenza Viruses** (may also cause LRTI)
- **Paramyxoviruses:**
  - **Parainfluenza Viruses (1-4)**
  - **Respiratory Syncytial Virus**

***Paramyxoviruses (2 Subfamilies)*:**

- **Subfamily: *Paramyxovirinae***
  - ***Respirovirus (Human Parainfluenza Virus)*:**
    - Causes 30% of all RTIs
    - Causes 50% of RTIs in Preschool Children
    - Can be Asymptomatic
    - Transmission is by Respiratory Secretions (Eg. Toys in Childcare Centres)
    - →Major Manifestations =
      - Necrotising Bronchiolitis
      - Respiratory Syncytia
    - Diagnosis: Viral Isolation or *RT-PCR*.
  - ***Morbillivirus (Measles Virus)*:**
    - Developed Countries: High Herd Immunity → Low Prevalence
      - Attenuated Vaccine in the MMR Vaccine (Admin at least 3x in Childhood)
    - Developing Countries: Low Herd Immunity → Higher Pervalence
    - Relatively High Death-Rates in Non-Immune.
    - Transmission is by Respiratory Secretions
    - → Major Manifestations =
      - URTI
      - Fever
      - Maculopapular Erythematous Rash.
    - Complications:
      - Generalised Infection (Eye, Ear & Intestines)
      - CNS Infection → Serious
      - Post Infection Encephalitis
      - Subacute Sclerosing Panecephalitis (rare but fatal)
  - ***Rubulavirus (Mumps Virus)*:**
    - Attenuated Vaccine in the MMR Vaccine (Admin at least 3x in Childhood)
    - Often Asymptomatic
    - Usually Self-Limiting
    - Entry via Respiratory Tract → Can Spread to Distant Lymph Nodes → Viraemia → Spread to Other Organs (Particularly Parotid Salivary Glands)
    - → Major Manifestations:
      - Fever & Malaise
      - Painful Enlargement of Parotid Salivary Glands → Parotitis
- **Subfamily: *Pneumovirinae***
  - ***Pneumovirus (Respiratory Syncytial Virus)*:**
    - Highly Contagious
    - Transmission is by Respiratory Secretions (Eg. Toys in Childcare Centres)
    - → Major Manifestations:
      - Initial Cold-Like Symptoms
      - *Necrotizing Bronchiolitis
      - (+/- Pneumonitis)
      - Respiratory Syncytia – (Because viruses enter via fusion proteins → Which join cells together)
      - Within 24hrs - Severe Illness, Cyanosis & Distress
    - Significant Mortality
    - Reinfection later in life is frequent.
    - Diagnosis: Viral Isolation or *RT-PCR*.
  - ***Metapneumovirus (Metapneumovirus)***
    - Recently been recognised in Humans
      - Originally a Primate Virus, not an Avian Virus.
    - Similar Disease to that produced by RSV
    - Endemic in Holland

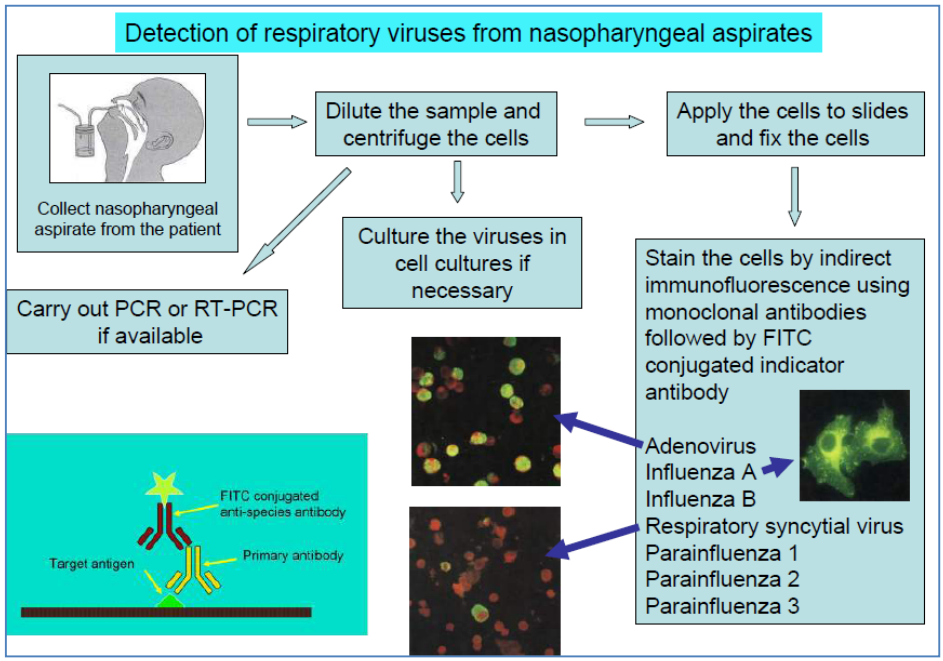
Orthomyxoviruses: Influenza Viruses:

- **Influenza = The last uncontrolled plague**
- **Three Species:**
  - A, B and C
    - (A Is Most Common & Most Important)
  - Distinguished on the basis of their matrix (M) and nucleoprotein (N) antigens.
- **Strains:**
  - Designated by their Haemagglutinin (HA) and Neuraminidase (NM) antigens eg H3N2.
  - New strains are constantly mutating over time – **Antigenic Shift & Antigenic Drift**
- **Prevalence:**
  - Up to 20% of the population may be infected in any one year
  - Majority of Deaths are Infants and Elderly
  - ≈ 1,000 deaths/year in Australia
- **Pathogenesis:**
  - **Short Incubation Period (2-3 days)**
  - **Abrupt Onset of Symptoms:**
    - Shivering/Fever (39C)
    - Malaise
    - Headache
    - Aching in the limbs and back
    - Sometimes Pneumonia
  - **Few Complications:**
    - Mainly Secondary Bacterial Infections
- **Vaccination:**
  - Indication = Anyone over 6mths who wants to ↓Risk of Catching Influenza.
  - Especially those over 50yrs



Diagnosis of Respiratory Viruses from Nasopharyngeal Aspirates:

- **NPAs are the Specimen of Choice for Viral Respiratory Infections:**
  - Large Sample Size
  - Includes Intact Cells
- **How you would determine the length of tube required for the successful collection of the specimen?**
  - Measure the distance between the nose and the ear (that is the distance)
- **Why is the timing of collection of specimens for viral detection important?**
  - You have to take the sample when the viruses are shedding.
- **Principles of each of the following methods of viral detection:**
  - **Immunoflourescence:**
    - Antigen Detection with fluorescently labelled antibodies → Flouresce under the microscope.
  - **Viral culture:**
    - Growth of Viruses in Culture in order to have enough organisms for specific testing.
  - **PCR and RT-PCR:**
    - Antigen Detection
    - (However, you can only do PCR when you know what you're looking for)

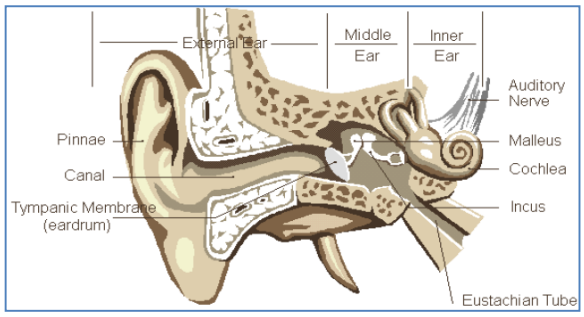


Bacterial Respiratory Tract Infections

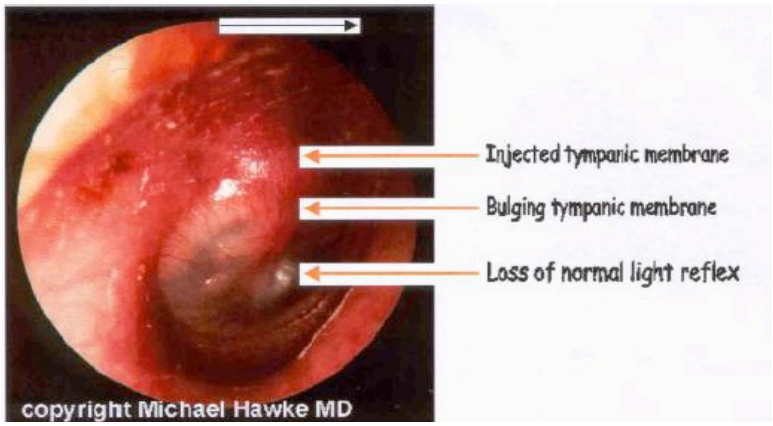
Respiratory Infection And Acute Otitis Media:

- **Generally, Otitis Media is not Viral, However:**
  - Respiratory Syncytial Virus Can →Secondary Acute Bacterial Otitis Media (AOM)
  - Rhinoviruses Do NOT

- **Acute Bacterial Otitis Media:**
  - Clinical features variable
  - Infants: fever, vomiting, diarrhoea, irritability
  - Older children: severe ear pain
  - **Aetiology**:
    - ***Streptococcus pneumonia*** *(Gram Positive)(Has a Capsule – a Virulence Factor)*
    - ***Haemophilus influenzae***
    - *Micrococcus Catarrhalis*



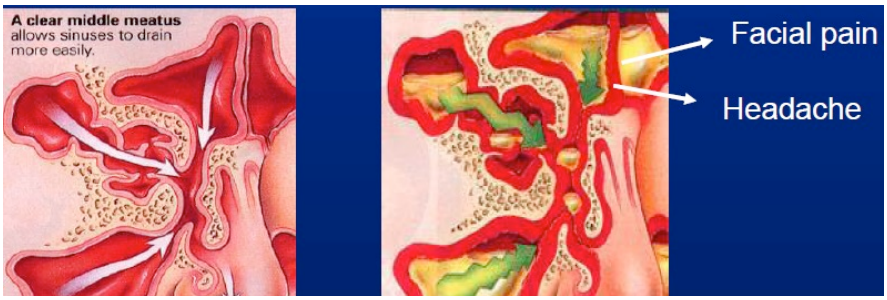
- **Epidemiology:**
  - Common infection of young infants/children (Due to a very narrow Eustachian tube)
  - Highest rates in 6-18mths
- **Pathogenesis:**
  - Virus disrupts normal structure via inflammation/exudates/swelling
  - Depends on infection/mehanical disturbance
  - Usually preceded by viral URTI
  - Blockage of eustachian tube
    - negative pressure (Inside the Middle Ear)
    - →sucks in nasopharyngeal commensals



- **Chronic Suppurative Otitis Media:**
  - (Chronic middle ear discharge through a perforated ear drum)
  - **Organism:**
    - *Pseudomonas Aeruginosa*
  - **Complications:**
    - Mastoiditis, Meningitis, Brain Abscesses, Death

Acute Sinusitis:

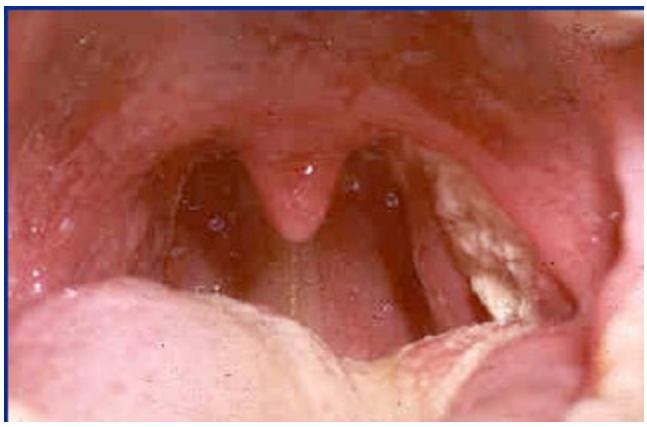
- **Aetiology:**
  - ***Streptococcus pneumoniae***: 40%
  - ***Haemophilus influenzae***: 30%
- **Develops when:**
  - Action of the cilia impaired (Eg. Smoking) and/or sinus ostia narrowed
  - Common (viral) cold: ciliary clearance is reduced and ostia blocked by mucosal swelling
- **Risk factors:**
  - Anatomical abnormalities of nasal septum and turbinates
  - Allergic inflammation
  - Tooth abscessation



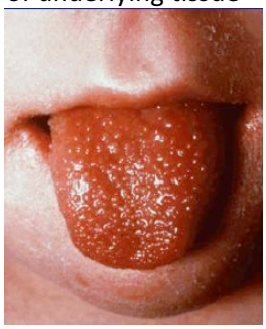
***Streptococcus Pyogenes – PHARYNGITIS & SCARLET FEVER*:**

- Common cause of **Bacterial Pharyngitis**, **& Scarlet Fever**
- Most frequent between 5 and 15 years of age
  - Can occur over and over again – (Due to poor cross protection of immunity to different serotypes)
- Transmission is by droplet
- Asymptomatic carrier rate in the URT is 10 - 30% worldwide
- Invasive disease results from dissemination from skin or throat to other sites
- Can cause manifestations which primarily occur as sequelae to pharyngitis or impetigo

- ***Pharyngitis*:**
  - **Aetiology:**
    - ***Group A β-haemolytic streptococci (Strep Pyogenes)***
    - Variety of other bacteria & viruses
      - Adenovirus, enterovirus, influenza, EBV
    - Interpret microbiology with caution:
    - nasopharyngeal carrier state



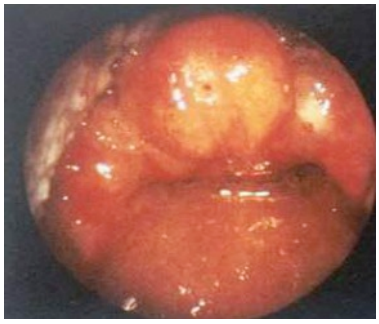
- **Scarlet Fever:**
  - **Organism:**
    - Certain strains of ***Strep pyogenes*** *(Which carry a Bacteriophage* – A virus infecting the bacteria → Produce an Eruthrogenic toxin)
  - **Pathogenesis:**
    - Disease caused by ***Exotoxin*** Released by Strep. Pyogenes.
    - Local effect on tonsils
    - →Abnormalities of tongue
      - Initially covered with white exudate
      - Exudate is shed
      - inflammation of underlying tissue



***Haemophilus influenza – EPIGLOTTITIS & PNEUMONIA*:**

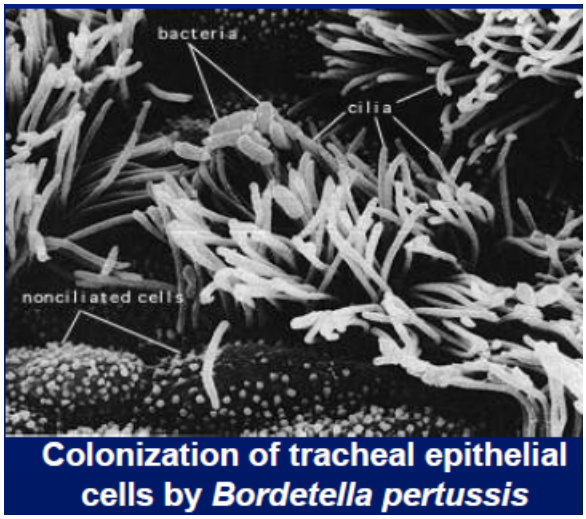
- → **Pneumonia, Epiglottitis.**
- *Haemophilus influenza B* – 95% (prior to Immunisation)
  - Now only 5% are due to HIB
  - However, it has allowed other serotypes of Haemophilis Influenza (C & F) which aren't encapsulated and therefore not as virulent.
- Now serotypes c,f, nonencaspsulated
- Gram neg coccobacillus
- Facultative anaerobe
- Nonencapsulated species colonise URT of humans within
  - first months of life
  - spread locally

- **Epiglotitis**
  - **Clinical Presentation:**
    - High fever, sore throat, pain on swallowing
    - Respiratory distress
    - Inspiratory stridor and hoarseness
  - **Aetiology:**
    - ***Haemophilus influenza*** (Gram Negative)
    - ***Streptococcus pneumoniae***
    - ***Staphylococcus aureus***
  - **Treatment:**
    - Urgent Intubation → Secure the Airway.
    - Antibiotic Treatment



***Pertussis - WHOOPING COUGH*:**

- Severe childhood disease
- Highly communicable (infants <12mths)
- Widespread tracheo-bronchitis
- Despite vaccine (DPT), epidemics still occur
- **Aetiology:**
  - ***Bordetella pertussis***
    - Obligatory human pathogen (You only get it from other people) – Always Pathogenic
  - doesn't survive in animal reservoir or environment
- **Pathogenesis:**
  - **Colonization of tracheal epithelial cells by *Bordetella pertussis***
  - ***Produces Toxins → Disease***
    - ***One toxin destroys Cilia***
    - ***Another toxin prevents formation of new Cilia***
  - **Pertussis toxin**
    - upregulation of cAMP
    - increased secretions → Cough
  - **Dermonecrotic toxin**
    - vasoconstriction, ischaemia
  - **Tracheal cytotoxin**
    - inhibition of cilia movement



RESPIRATORY Pathology:
URTI – CROUP

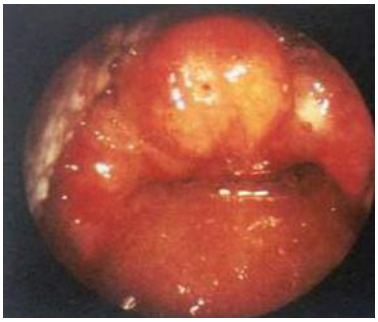
ACUTE LARYNGOTRACHEOBRONCHITIS (CROUP)

- **What is it?**
  - Inflammation Of Tissues In Subglottic Space ± Tracheobronchial Tree
  - + Thick, Viscous, Mucopurulent Exudates Which Compromises Upper Airway →Barking Cough
- **Etiology – Viral:**
  - ***RSV** **or** **Parainfluenzae** (Most Common), II, III, Influenza A And B
- **Pathogenesis:**
  - URTI
  - →Inflammation Of Tissues In Subglottic Space
  - →Thick, Viscous, Mucopurulent Exudates Which Compromises Upper Airway →**Barking Cough**
- **Morphology:**
  - Inflamed Upper Airways + Larynx
- **Clinical Features**
  - Typically Children <5yrs
  - **Signs of Croup - the 3 S's**
    - **1. Stridor**
    - **2. Subglottic swelling**
    - **3. Seal bark cough**
  - **+/- Cyanosis & Respiratory Distress**
- **Treatment**
  - (NB: Viral :. NO Antibiotics)
  - **Oral/IM Corticosteroids (*Dexamethasone* / *Prednisone*)**
  - **Nebulised *Epinephrine***
  - **Humidified O2**
  - +/- Intubation If Severe

RESPIRATORY Pathology:
URTI – EPIGLOTTITIS

Acute Epiglottitis

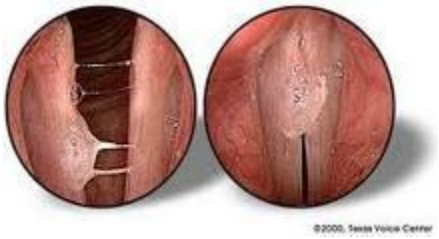
- **Etiology**
  - ***HiB* – (*Haemophilus Influenzae* type B)** (Uncommon due to HiB vaccine)
    - (Gram neg coccobacillus)
- **Clinical Features**
  - Typically Children 1-4yo
  - High Fever & Unwell
  - Sore Throat, Dysphagia, Anorexia
  - **Obstructive Symptoms – *MEDICAL EMERGENCY → INTUBATE*:**
    - **Difficulty Swallowing, DROOLING, cyanotic/pale, inspiratory stridor, slow breathing,**
- **Investigations:**
  - **Preparations For Intubation Or Tracheotomy** Must Be Made Prior To Any Manipulation
  - **Lateral Neck XR** - Cherry-Shaped Epiglottic Swelling ("Thumb Sign") - Only If Stable
  - **WBC (Elevated)**
  - **Blood And Pharyngeal Cultures After Intubation**
- **Treatment**
  - ***Admit to ICU**
  - **Urgent Intubation → Secure Airway**
    - + Humidified O2
  - **Antibiotics – (*Ceftriaxone* + *Clindamycin*)**
  - **Extubate When Afebrile**
  - **Watch For Meningitis**



RESPIRATORY Pathology:
LARYNGITIS

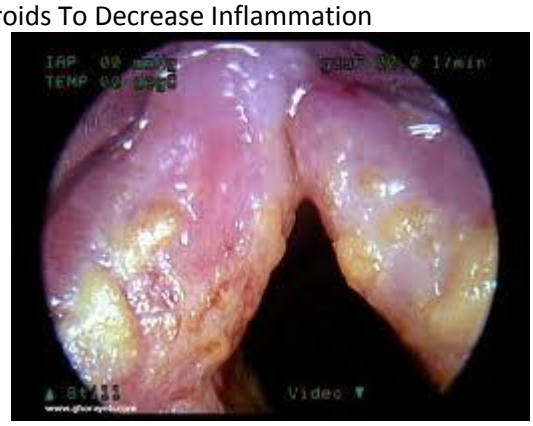
Acute Laryngitis

- **Etiology (NB: Infective aetiologies similar to pharyngitis):**
  - **Viral:** Adenovirus, Influenza
  - **Bacterial:** Group A *Streptococcus*
  - **Acute Voice Strain** → Submucosal Hemorrhage →Vocal Cord Edema →Hoarseness
  - **Toxic Fume Inhalation**
- **Clinical Features**
  - URTI Symptoms, Hoarseness, Aphonia, Cough Attacks, ± Dyspnea
- **Morphology:**
  - True Vocal Cords Erythematous/Edematous With Vascular Injection And Normal Mobility
- **Treatment**
  - Self-Limited, Resolves Within -1 Week
  - Voice Rest
  - Humidification, Hydration
  - Avoid Irritants (E.G. Smoking)
  - Treat With Antibiotics If There Is Evidence Of Coexistent Bacterial Pharyngitis



Chronic Laryngitis

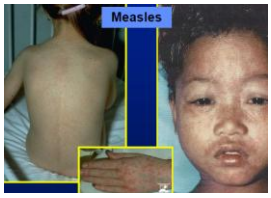
- **Definition**
  - Long Standing Inflammatory Changes In Laryngeal Mucosa
- **Etiology**
  - Repeated Attacks Of Acute Laryngitis
  - Chronic Irritants (Dust, Smoke, Chemical Fumes)
  - Chronic Voice Strain
  - Chronic Sinusitis With Postnasal Drip (PND)
  - Chronic Alcohol Use
  - Esophageal Disorders: eg. GORD, Hiatus Hernia
- **Clinical Features**
  - Chronic Dysphonia – (NB: Rule Out Malignancy)
  - Cough, Globus Sensation, Frequent Throat Clearing 2° To GORD
- **Morphology:**
  - Cords Erythematous, Thickened With Ulceration / Granuloma Formation And Normal Mobility
- **Treatment**
  - Remove Offending Irritants
  - Treat Related Disorders E.G. Antisecretory Therapy For GORD
  - Speech Therapy With Voice Rest
  - ± Antibiotics, ± Steroids To Decrease Inflammation



RESPIRATORY Pathology:
URTI – MEASLES, MUMPS & RUBELLA

MEASLES VIRUS:

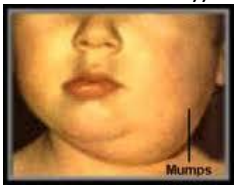
- **Aetiology:**
  - **Measles Virus**
- **Pathogenesis:**
  - **HIGHLY CONTAGIOUS - Aerosol/Contact Transmission**
  - Typically a Respiratory Infection; Also →Produces a Viraemia → Rash
- **Presentation:**
  - **Fever**
  - **URTI** - Cough, Rhinorrhoea, Red Eyes
  - **Rash** - Maculopapular Erythematous (Morbilliform)
  - **"Koplik's Spots"** – Seen on the Inside of the Mouth



- **Diagnosis:**
  - **Clinical Diagnosis** (Genearlised Maculopapular Rash + Fever)
  - **Serology**
  - **PCR**
- **Treatment:**
  - Supportive Mx.
  - ***Vitamin A Supps.***
  - ***+/- Ribavirin*** **(Antiviral)**
  - **Prevented by MMR Vaccine –(NB: Contra'd in Pregnancy)**
- **Complications Include:**
  - Croup, Otitis Media, Gastroenteritis
  - Febrile convulsions
  - **Subacute Sclerosing Panencephalitis (very rare)**
    - (Progressive Encephalitis due to Chronic Measles Infection)
    - No Cure; Fatal

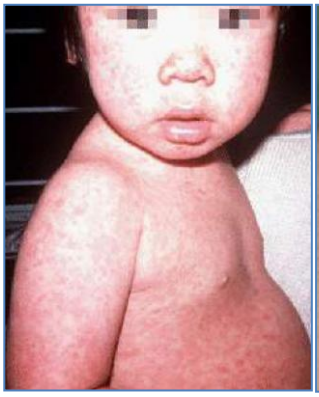
MUMPS VIRUS:

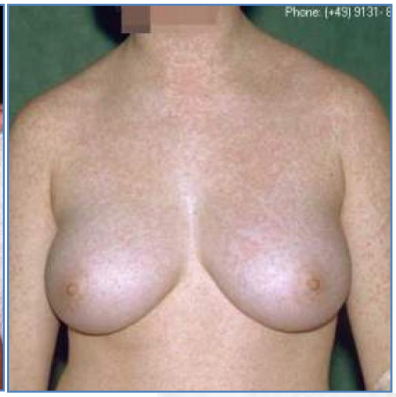
- **Aetiology:**
  - **Mumps Virus**
- **Pathogenesis:**
  - Aerosol Transmission
  - Respiratory Tract Infection → Lymph Nodes & Salivary Glands (+Viraemia)
- **Presentation:**
  - Fever & Malaise
  - Painful Enlargement of Parotid Salivary Glands → Parotitis
- **Diagnosis:**
  - **Serology**
  - **PCR**
- **Treatment:**
  - Usually Self-Limiting
  - (+ MMR Vaccine (Admin at least 3x in Childhood))

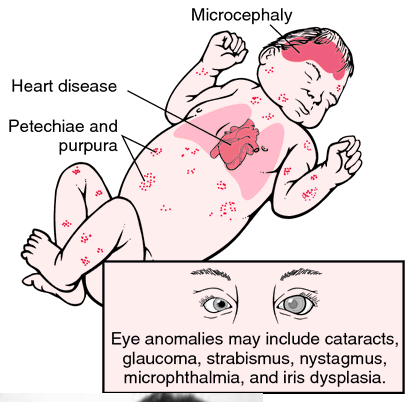


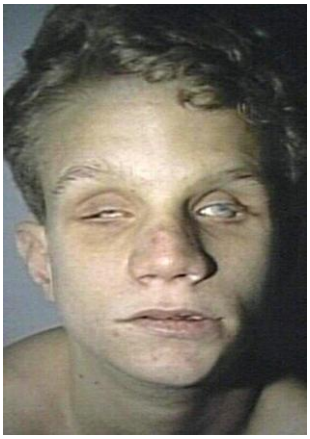
RUBELLA VIRUS (Aka "German Measles):

- **Organism:**
  - Rubella Virus
- **Transmission:**
  - **Aerosol Transmission**
- **Presentation:**
  - Initial Flu-Like Symptoms
  - *** Generalised Rash – (**Red & Itchy**)**
  - Low-grade Fever, Lymphadenopathy, Joint Pains, Headache, Conjunctivitis.
- **Diagnosis:**
  - Clinical Diagnosis
  - Presence of Virus-Specific IgM Antibodies
- **Treatment:**
  - No Specific Treatment
  - Controlled in Australia by vaccination (MMR Vaccine)
  - **Test pregnant women for immunity early.**
- **Prevention:**
  - (NB: Rubella *Itself* is relatively Benign, so why bother Vaccinating?)
  - **MMR Vaccine:**
    - **(Live Attenuated)**
    - **#1 Aim:** Prevent Rubella in Pregnant Women → ↓Congenital Rubella Syndrome.
    - Aimed at *BOTH* Males & Females to ↓Male Transmission to Pregnant Females
- **Prognosis:**
  - **Typically Benign** – (Self-Limiting [1-3 Days])
- **Complications:**
  - Complications may include arthritis, thrombocytopaenia purpura, and encephalitis
  - *****HOWEVER, Maternal Infection in PREGNANCY can be SERIOUS!!**
    - ***CONGENITAL RUBELLA SYNDROME*** **– (If Infected in the 1st 20wks of Pregnancy)**
      - **→Miscarriage**
      - **→ Serious Malformations** – (Cardiac/Cerebral/Blindness/Deafness)









RESPIRATORY Pathology:
URTI – OTITIS

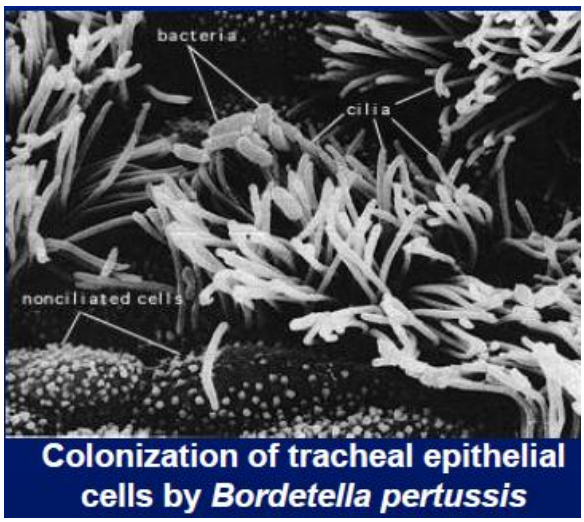
ACUTE OTITIS MEDIA (AOM)

- **Etiology**
  - S. *pneumoniae* - 35% of cases (incidence decreasing due to pneumococcus vaccine)
  - H. *influenzae* - 25% of cases
  - S. *aureus* and S. *pyogenes* (all beta-lactamase producing)
- **Predisposing Factors**
  - Eustachian Tube Dysfunction / Obstruction – (Eg. Down's Syndrome, Tumour, etc)
  - Upper Respiratory Tract Infection (URTI)
  - Allergies / Allergic Rhinitis
  - Chronic Sinusitis
- **Pathogenesis**
  - **Obstruction Of Eustachian Tube** → Middle Ear Stasis → Infection
- **Clinical Features**
  - **Epidemiology**
    - **70% of Children have AOM before 3yo**
    - Typically Children <6yo
  - **Classic Triad:**
    - **Otalgia**
    - **Fever** (especially in younger children)
    - **Hearing Loss**
    - (+ Rarely Tinnitus, Vertigo)
    - (+Otorrhea If Tympanic Membrane Perforated)
  - **Infants / Toddlers**
    - Ear-Tugging
    - Irritable, Poor Sleeping
    - Vomiting And Diarrhea
- **Investigations:**
  - **Otoscopy Of Tympanic Membrane**
    - Hyperemia
    - Bulging TM
    - Loss Of Landmarks: Handle And Short Process Of Malleus Not Visible
  - **Swab MCS if Perforated & Exudative**
  - **Audiometry**
- **Treatment**
  - **Medical:**
    - **Antibiotics –(*Amoxicillin* +/- *Ciprofloxacin* Ear Drops)**
    - **"*Sofradex*" Aural Toilet**
  - **Symptomatic Therapy**
    - *Paracetamol*
    - Nasal Decongestants – (*Phenylephrine / Pseudoeffedrine*)
  - **Surgery – (If Medically Unresponsive)**
    - Tympanotomy
    - Gromits Insertion
    - +/- Tonsilectomy
    - +/- Adenoidectomy
- **Complications of AOM**
  - **CHRONIC (>2wks) SUPPURATIVE OTITIS MEDIA**
    - **Pseudomonas (*Tobramycin*) or MRSA (*Rifampicin*)**
  - **MASTOIDITIS**
  - **CHOLESTEATOMA**
  - **MENINGITIS**
  - **FACIAL NERVE PARALYSIS**
  - **DEAFNESS –(+/- Learning Delays)**

RESPIRATORY Pathology:
URTI - PERTUSSIS (WHOOPING COUGH)

PERTUSSIS - WHOOPING COUGH:

- **Aetiology:**
  - ***Bordetella pertussis –*** (Only a human pathogen)
- **Pathogenesis:**
  - **Infection of Trachea & Bronchi → *Toxins* → Widespread Trachea/Bronchi Inflammation**
- **Clinical Features:**
  - Severe childhood disease
    - → Dyspnoea
    - → Chronic, Severe Coughing Fits
  - Highly Contagious (infants <12mths)
- **Investigations:**
  - **Diagnosed on Clinical Suspicion**
  - (Culture takes <2wks – TOO Long!)
- **Management:**
  - **Empirical Antibiotics – (*Azithromycin* / *Clarithromycin* / *Erythromycin*)**
  - **+ Booster Vaccination (Unvaccinated / Adolescents / Adults)**
  - **+ Vaccinate close contacts (DTP Vaccine)**
  - **+/- Post-Exposure Prophylaxis in Close Contacts (*Azithromycin*)**

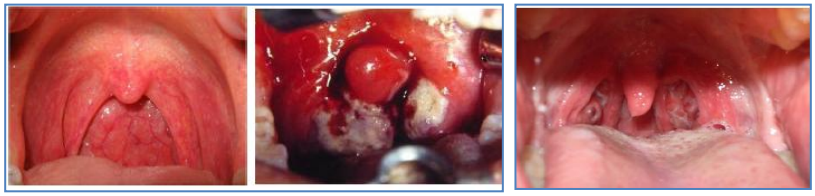


Colonization of tracheal epithelial cells by *Bordetella pertussis*

RESPIRATORY Pathology:
URTI – PHARYNGITISES

Pharyngitis (Sore Throat)

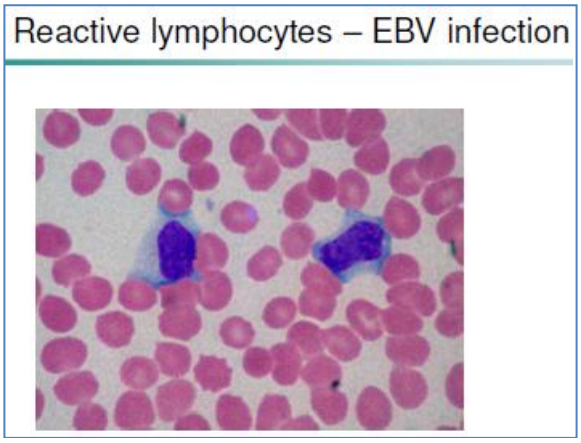
- **Definition**
  - = Inflammation of the Oropharynx (*Without* inflammation of the tonsils)
- **Aetiologies:**
  - **Viral (40-60%) – Most Common:**
    - **Adenovirus**, Coxsackie, HSV, **EBV**, **Influenza** Virus (Orthomyxovirus),
  - **Bacterial**
    - **"Strep. Pyogenes" (GABH-*Streptococcus*) – (*Rh-Heart Disease, PSGN & Scarlet Fever)**
    - *Neisseria gonorrheae, Chlamydia pneumoniae, Mycoplasma pneumoniae,* ***Corynebacterium diphtheria***
- **Morphology:**
  - Red, Inflamed Oropharynx
  - May have white lesions
  - May have pus



- **Clinical Features**
  - Typically a self-limited infection with no significant sequelae
  - **Bacterial - Group A Beta-Hemolytic *Streptococcus***
    - **Absence Of Cough**, Pharyngitis, + Flu-Like Illness
    - **Signs: Fever + Tonsil Exudate + Lymphadenopathy + <15yo + NO Cough**
    - **Complications!!**
      - *Rheumatic Fever*
      - *Glomerulonephritis*
      - *Meningitis*
  - **Viral - Adenovirus**
    - **Cough – (**Due to Rhinorrhea**)**, Pharyngitis, + Flu-Like Illness
  - **Viral - Ebv (Infectious Mononucleosis)**
    - Pharyngitis, Fever, **Lymphadenopathy, Fatigue, Rash**
- **Investigations**
  - **Suspected GABH-Strep:**
    - **Throat Culture = Definitive** (But TOO SLOW in the real world!!)
    - **RDT For Streptococcal Antigen**
    - **ASOT (Anti-Streptolysin-O-Titres)** – (But only shows recent infection).
  - **Suspected EBV (Infectious Mononucleosis):**
    - **Peripheral Blood Smear** – (Reactive Lymphocytes)
    - **"Monospot" Test** (I.E. The Latex Agglutination Assay, Or "Monospot")
    - **EBV Serology**
- **Management**
  - **If ?GABH-Strep:**
    - ****Throat Swab if: Fever + Tonsil Exudate + Lymphadenopathy + <15yo**
    - **Antibiotics!!: *Penicillin-V/G* or *Erythromycin* if Penicillin Allergic**
  - **If ?Viral Pharyngitis:**
    - **Antibiotics NOT indicated**
    - ***Paracetamol*/NSAIDs**
    - **Decongestants (*Phenylephrine*)**
  - **If ? Infectious Mononucleosis (EBV):**
    - **Antibiotics NOT indicated;** NB: Penicillin will → Rash (*Pathognomonic*)
    - **Self-Limiting Course;** Rest During Acute Phase Is Beneficial
    - **Supportive Treatment:** NSAIDS for fever, sore throat, malaise

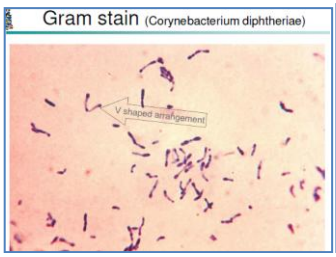
Other Notable Pharyngits's:

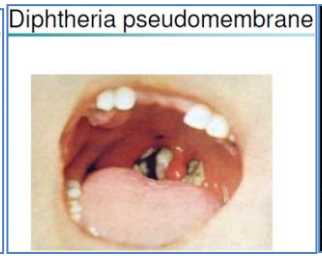
- **(Epstein Barr Virus) – Infectious Mononucleosis (Glandular Fever):**
  - **Aetiology:**
    - Epstein Barr Virus
  - **Pathogenesis:**
    - Transmitted through Saliva (Ie. Kissing Disease)
    - Incubation period <8wks.
    - **Preferentially Infects B-Cells → Reactive B-Lymphocytes → "Mononucleosis"**
  - **Morphology:**
    - Tender Cervical Lymphadeopathy
    - Blood Smear – Lymphocytosis with *Atypical Lymphocytes*

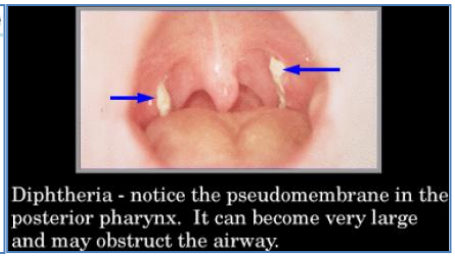


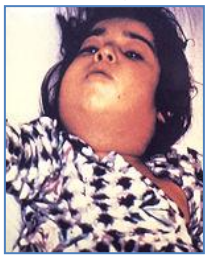
  - **Clinical Features:**
    - **Signs/Symptoms:**
      - **Fever +**
      - **Glandular Fever Triad:**
        - **Fatigue**/Malaise (Anorexia/Lethargy)
        - **Pharyngitis** (Sore Throat)
        - **Lymphadeopathy** (Especially Cervical)
      - **Others – (**Splenomegaly, Hepatitis, Haemolysis, Jaundice**)**
  - **Diagnosis:**
    - **Typically Clinical**
    - **Peripheral Blood Smear** – (Reactive Lymphocytes)
    - **"Monospot" Test** (I.E. The Latex Agglutination Assay, Or "Monospot")
    - **EBV Serology**
    - **+ LFTs**
  - **Treatment:**
    - **Antibiotics NOT indicated;** NB: Penicillin will → Rash (*Pathognomonic*)
    - **Self-Limiting Course;** Rest During Acute Phase Is Beneficial
    - **Supportive Treatment:** NSAIDS for fever, sore throat, malaise
  - **Complications:**
    - **EBV is an Oncogenic Herpesvirus → Tumours:**
      - **→Burkitt's Lymphoma**
      - **→Hodgkin's Lymphoma**
      - **→Nasopharyngeal Carcinoma**

- **Diptheria:**
  - **Aetiology:**
    - Gram Positive Bacterium – *Corynebacterium Diptheriae*
  - **Pathogenesis:**
    - **Transmission** – Aerosol, Physical Contact.
  - **Morphology:**
    - Adherent Whitish Pseudomembrane Over Pharynx & Tonsils (May → Obstruction)



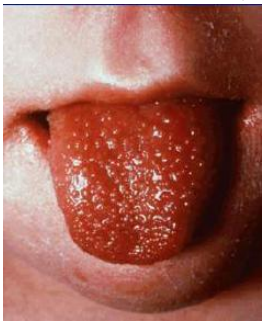
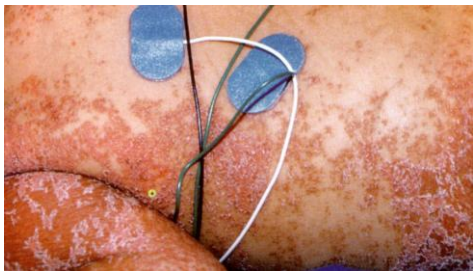






  - **Clinical Features:**
    - High Fever, Sore Throat, Fatigue, Nausea & Vomiting
    - Pseudomembrane on Tonsils & Pharynx - May have Airway Obstruction & Dysphagia
  - **Complications:**
    - **Systemic Exotoxin →**
      - Myocarditis (Potentially fatal toxigenic Cardiomyopathy → Heart Failure)
      - Peripheral Neuritis.
      - Chronic Non-Healing Ulcers
  - **Diagnosis:**
    - **Swab M/C/S**
    - **+ Toxin Detection**
  - **Treatment:**
    - ***Penicillin* or *Erythromycin* (if Penicillin Allergic)**

- **Scarlet Fever ("Strawberry Tongue"):**
  - **Aetiology:**
    - Certain strains of ***GABH-Strep "Pyogenes"*** *(Which are infected with a "Bacteriophage"* [Virus] → Produce an Eruthrogenic toxin)
  - **Pathogenesis:**
    - **GABH-Strep Infection → *Exotoxin* → Local effect on Tonsils/Pharynx/Skin**
      - **→Tongue**
        - Initially covered with white exudate
        - Exudate is shed
        - inflammation of underlying tissue
      - **→ Skin**
        - Diffuse, Erythematous Rash

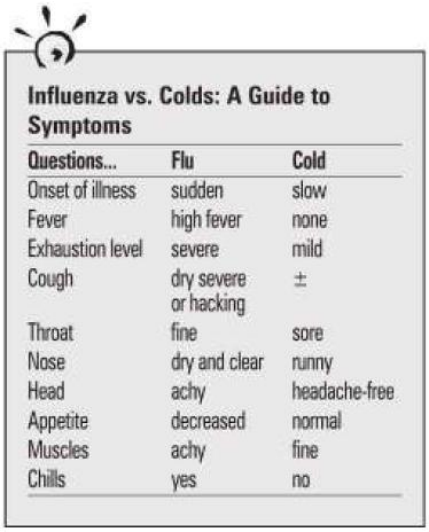



  - **Complications:**
    - **Rheumatic Heart Disease**
    - **PSGN**
  - **Diagnosis:**
    - ****Throat Swab if: Fever + Tonsil Exudate + Lymphadenopathy + <15yo**
  - **Treatment:**
    - **Antibiotics!!: *Penicillin-V/G* or *Erythromycin* if Penicillin Allergic**

RESPIRATORY Pathology:
URTI – RHINITIS

Common Cold (Acute Rhinitis)

- **Aetiology:**
  - **Rhinoviruses,** Adenoviruses, Paramyxoviruses, Influenza viruses, Myxoviruses,
- **Pathogenesis:**
  - **Transmission – (**Droplet Transmission/Contact Secretions**)**
  - **Viral Infection of URT Mucosa** → URT Inflammation → Mucous Hypersecretion
  - (NB: No Cross-Protection between Serotypes → Possibility of Repeated Infections)
- **Clinical Features**
  - **Short Incubation Period (2-3 days)**
  - **1wk Of Symptoms:**
    - **Local** - Nasal Congestion, Sneezing, Sore Throat, Hoarseness, Cough, Conjunctivitis
    - **General** - Malaise, Headache, Myalgias, Mild Fever
  - **Signs**
    - Rhinorrhea
    - Inflamed Nasal/Oropharyngeal Mucosa
    - Lymphadeopathy
    - **NB: Normal Chest Exam**
  - **Complications**
    - **Secondary Bacterial Infection:** (Otitis Media, Sinusitis, Tonsillitis, Bronchitis, Pneumonia)
    - **Asthma/COPD Exacerbation**
    - **Benign Inflammatory Nasal Polyps**
- **Diagnosis:**
  - **Differentials:**
    - Allergic Rhinitis, Pharyngitis, Influenza, Laryngitis, Croup, Sinusitis, Bacterial Infections
  - **Clinical Diagnosis** – (Symptoms + Nasal Exam + Inflamed Mucosa + Watery Discharge)
  - **Laboratory Diagnosis** – ONLY if *Other Conditions are Suspected*.
- **Management:**
  - **Patient Education**
    - **No Antibiotics Indicated Because Of Viral Etiology**
    - **Consider 2^{o} Bacterial Infection** if NO Resolution after 3-10 Days
  - ***Symptomatic Relief:**
    - ***Paracetamol***
    - **Decongestants *(Phenylephrine/Pseudoeffedrine)*, Antihistamines**
    - **+ Rest, Hydration, Gargling Warm Salt Water, Steam**
    - **+(↑Dependence On Bronchodilators/Inhaled Steroids For Asthmatics & COPD)**



Influenza vs. Colds: A Guide to Symptoms

Questions...	Flu	Cold
Onset of illness	sudden	slow
Fever	high fever	none
Exhaustion level	severe	mild
Cough	dry severe or hacking	±
Throat	fine	sore
Nose	dry and clear	runny
Head	achy	headache-free
Appetite	decreased	normal
Muscles	achy	fine
Chills	yes	no

Table 12. Nasal Discharge: Character and Associated Conditions

Character	Associated Conditions
Watery/mucoid	Allergic, viral, vasomotor, CSF leak (halo sign)
Mucopurulent	Bacterial, foreign body
Serosanguinous	Neoplasia
Bloody	Trauma, neoplasia, bleeding disorder, hypertension/vascular disease

RESPIRATORY Pathology:
URTI – SINUSITIS

ACUTE SUPPURATIVE SINUSITIS (<4wks):

- **Definition**
  - Acute Infection And Inflammation Of The Paranasal Sinuses – Up to 4wks in Duration
- **Etiology**
  - ****Viral (Most Common):**
    - ****Rhinovirus, Influenza, Parainfluenza**
  - **Bacterial:**
    - **S. *Pneumoniae* (35%), H. *Injluenzae* (35%),** M. *Catarrhalis,* Anaerobes (Dental)
- **Clinical Features:**
  - **Symptoms:**
    - Facial Pain / Pressure
    - Nasal Congestion
    - Purulent Nasal Discharge
    - Fever
  - **(Signs More Suggestive Of A Bacterial Etiology):**
    - >10day Duration
    - Mucopurulent Discharge
- **Investigations:**
  - **Clinical Diagnosis**
  - **Transillumination of Sinuses**
  - **+/- Skull XR – (**Opaque Sinuses & Fluid-Levels**)**
- **Management**
  - ***Paracetamol***
  - **Decongestants – (*Phenylephrine / Pseudoeffedrine*)**
  - **Intranasal Corticosteroid – (Nasonex [*Mometasone*])**
  - **+/- Antibiotics – (Augmentin [*Amoxicillin + Clavulanate*] or Rulide [*Roxithromycin*])**
  - (+ Supportive Mx)

CHRONIC SINUSITIS (>3MTHS):

- **Definition**
  - Inflammation Of The Paranasal Sinuses Lasting >3 Months → Irreversible Changes in Epithelium
- **Etiology – Any of the Following:**
  - Progression from Acute Sinusitis (Viral/Bacterial)
  - Untreated Nasal Allergy
  - Chronic Inflammatory Disorder E.G. Wegener's
- **Clinical Features (Similar To Acute, But Less Severe)**
  - Facial Pain / Pressure
  - Chronic Nasal Congestion
  - **+ Halitosis**
- **Investigations:**
  - **Clinical Diagnosis**
  - **+ Head CT –(**Pre-Surgical**)**
- **Management:**
  - **Antibiotics 3-6wks – (Augmentin [*Amoxicillin + Clavulanate*] or Rulide [*Roxithromycin*])**
  - **Intranasal Corticosteroid – (Nasonex [*Mometasone*])**
  - **Decongestants – (*Phenylephrine / Pseudoeffedrine*)**
  - **Surgery –(**If Medical Therapy Fails**)**

RESPIRATORY Pathology:
URTI – TONSILLITIS

ACUTE TONSILLITIS

- **Etiology**
  - **GABH-Strep (Pyogenes)**
  - **Or S. *pneumoniae,* S. *aureus,* H. *influenzae,*** M. *catarrhalis*
  - **Or Epstein-Barr virus (EBV)**
- **Clinical Features**
  - **Typically Children (5-10yrs) & Adolescents (15-25yrs)**
  - **Symptoms:**
    - Pharyngitis
    - Reffered Ear Pain
    - Headache
    - Dysphagia, Odynophagia, Trismus
    - Malaise, Fever
  - **Signs:**
    - Fever
    - Reddened Throat
    - Tonsils – (Enlarged, Inflamed ± Exudates / White Follicles)
    - Swollen, Tender Cervical Lymphadenopathy
    - **(If Scarlet Fever** → Strawberry Tongue & Scarletiniform Rash)
    - **(If EBV** → Palatal Petechiae)
- **Differentials:**
  - **Strep Pharyngitis**
  - Viral Pharyngitis
  - **EBV**
  - Peritonsillar Abscesses
- **Investigations**
  - **FBC – (**↑WCC + Differentials**)**
  - **Throat Swab MCS – (**?GABH-Strep Pyogenes**)**
    - **(Suspected if Fever + Tonsillar Exudate + Lymphadeopathy + NO Cough + <15yo)**
  - **ASOT – Anti-Streptolysin 'O' Titre – (**?GABH-Strep Pyogenes**).**
  - **Monospot Test –(**?EBV**)**
- **Treatment/Management:**
  - (Bed Rest, Soft Diet, Fluids)
  - ***Paracetamol***
  - **Antibiotics –(if Fever + Tonsillar Exudate + Lymphadeopathy + NO Cough + <15yo):**
    - ***Penicillin*** Or ***Amoxicillin*** (***Erythromycin*** If Penicillin Allergy) X 10 Days
- **Complications**
  - **Abscess:** Peritonsillar (a "Quinsy"), Intra Tonsillar
  - **Post-Streptococcal:**
    - Glomerulonephritis
    - Rheumatic Heart Disease
    - Scarlet Fever

Continue Reading For Bonus Supplementary Study Materials…

R Respirology

Alexander Kumachev and **Navjot Rai,** chapter editors
Hart Stadnick and **Kevin Yau,** associate editors
Alex Cressman, EBM editor
Dr. Meyer Balter and **Dr. Matthew Binnie,** staff editors

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Acronyms

A-a	alveolar-arterial
A-aDO_2	alveolar-arterial oxygen diffusion gradient
ABG	arterial blood gas
ACEI	angiotensin converting enzyme inhibitor
ACV	assist-control ventilation
AECOPD	acute exacerbation of COPD
AFB	acid-fast bacillus
AFP	alpha-fetoprotein
AHI	apnea hypopnea index
ALS	amyotrophic lateral sclerosis
ANA	antinuclear antibody
ANCA	anti-neutrophil cytoplasmic antibody
APTT	activated partial thromboplastin time
ARDS	acute respiratory distress syndrome
ASA	acetylsalicylic acid (Aspirin®)
ASD	atrial septal defect
AV	arteriovenous
AVM	arteriovenous malformation
AVN	avascular necrosis
BG	blood glucose
BiPAP	bilevel positive airway pressure
BOOP	bronchiolitis obliterans with organizing pneumonia
BSA	body surface area
CA	cancer
CCB	calcium channel blocker
CD	Crohn's disease
CF	cystic fibrosis
CHF	congestive heart failure
CI	cardiac index
CO	cardiac output
COP	cryptogenic organizing pneumonia
COPD	chronic obstructive pulmonary disease
CPAP	continuous positive airway pressure
CSA	central sleep apnea
CVD	cardiovascular disease
CVP	central venous pressure
CWP	coal worker's pneumoconiosis
DIC	disseminated intravascular coagulation
DL_{CO}	carbon monoxide diffusing capacity of lung
EBUS	endobronchial ultrasound
ECMO	extracorporeal membrane oxygenation
ERV	expiratory reserve volume
ETT	endotracheal tube
FEF	forced expiratory flow rate
FEV_1	forced expiratory volume in 1 second
FiO_2	fraction of oxygen in inspired air
FRC	functional residual capacity
GBM	glomerular basement membrane
GERD	gastroesophageal reflux disease
H/A	headache
HPA	hypothalamic-pituitary axis
HRT	hormone replacement therapy
IBD	inflammatory bowel disease
IC	inspiratory capacity
ICP	intracranial pressure
ICS	inhaled corticosteroid
ILD	interstitial lung disease
IPF	idiopathic pulmonary fibrosis
LAAC	long-acting anti-cholinergic
LABA	long-acting beta-agonist
LLN	lower limit of normal
LMWH	low molecular weight heparin
LTRA	leukotriene receptor antagonist
LV	left ventricle
LVEDP	left ventricular end diastolic pressure
LVF	left ventricular failure
MAC	*Mycobacterium avium* complex
MDI	metered dose inhaler
MEP	maximum expiratory pressure
MIP	maximum inspiratory pressure
MSA	mixed sleep apnea
MSK	musculoskeletal
NPPV	non-invasive positive pressure ventilation
NSCLC	non-small cell lung cancer
NTT	nasotracheal tube
OCP	oral contraceptive pill
OSA	obstructive sleep apnea
PA	posteroanterior
P_aCO_2	arterial partial pressure of carbon dioxide
P_aO_2	arterial partial pressure of oxygen
P_AO_2	alveolar partial pressure of oxygen
P_{atm}	atmospheric pressure
PCP	*Pneumocystis carinii* pneumonia
PCV	pressure control ventilation
PCWP	pulmonary capillary wedge pressure
PDA	patent ductus arteriosus
PE	pulmonary embolism
PEEP	positive end expiratory pressure
PEF	peak expiratory flow
PFT	pulmonary function tests
PMNs	polymorphonuclear cells
PP	pulse pressure
PSV	pressure support ventilation
PTH	parathyroid hormone
PTT	partial thromboplastin time
PUD	peptic ulcer disease
PVC	premature ventricular contraction
RA	rheumatoid arthritis
RAD	right axis deviation
RAP	right atrial pressure
RBBB	right bundle branch block
RF	rheumatoid factor
RV	residual volume
RVEDV	right ventricular end diastolic volume
RVH	right ventricular hypertrophy
RVSP	right ventricular systolic pressure
SCC	squamous cell carcinoma
SCLC	small cell lung cancer
$S_{cv}O_2$	central venous oxygen saturation
SIMV	synchronous intermittent mandatory ventilation
SIRS	systemic inflammatory response syndrome
SV	stroke volume
SVC	superior vena cava
SVRI	systemic vascular resistance index
TB	tuberculosis
TCA	tricyclic antidepressant
TLC	total lung capacity
TNM	tumour, node, metastasis
TPN	total parenteral nutrition
UC	ulcerative colitis
URTI	upper respiratory tract infection
V/Q	ventilation-to-perfusion
VATS	video-assisted thoracopic surgery
VC	vital capacity
VSD	ventricular septal defect
VTE	venous thromboembolism
V_T	tidal volume

Approach to the Respiratory Patient

Basic Anatomy Review

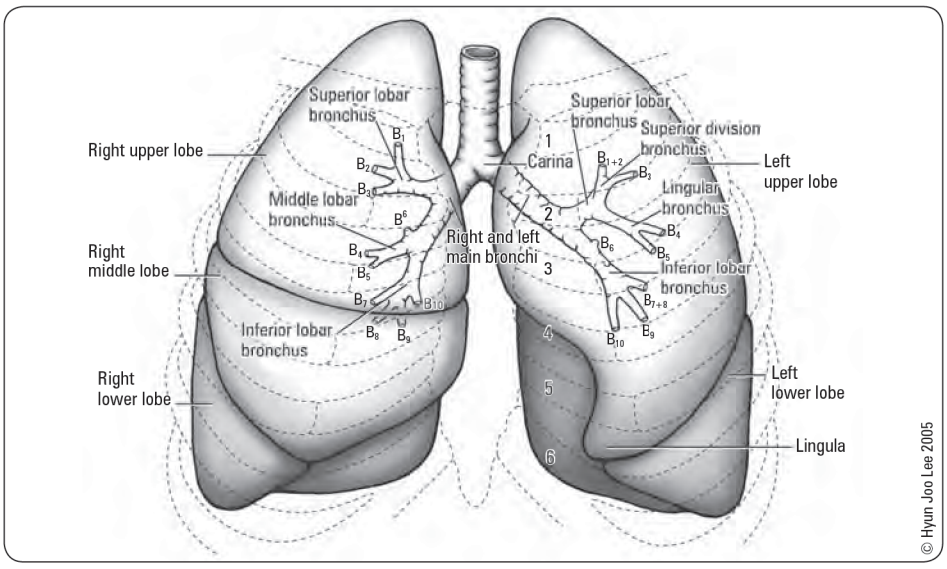

Figure 1. Lung lobes and bronchi

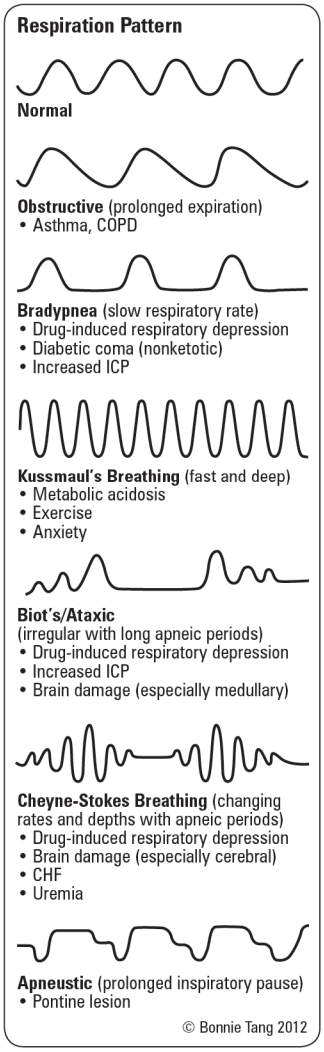

Figure 2. Respiration patterns in normal and disease states

Differential Diagnoses of Common Presentations

Table 1. Differential Diagnosis of Dyspnea

Acute Dyspnea (minutes-hours)
- **Cardiac causes**
  - Ischemic heart disease
  - CHF exacerbation
  - Cardiac tamponade
- **Pulmonary causes**
  - Upper airway obstruction (anaphylaxis, foreign body)
  - Airway disease (asthma, COPD exacerbation, bronchitis)
  - Parenchymal lung disease (ARDS, pneumonia)
  - Pulmonary vascular disease (PE, vasculitis)
  - Pleural disease (pneumothorax, tension pneumothorax)
  - Respiratory control (metabolic acidosis, ASA toxicity)
- **Psychiatric causes**
  - Anxiety/psychosomatic

Chronic Dyspnea (weeks-months)
- **Cardiac causes**
  - Valvular heart disease
  - Decreased CO
- **Respiratory causes**
  - Parenchymal lung disease (interstitial disease)
  - Pulmonary vascular disease (pulmonary HTN, vasculitis)
  - Pleural disease (effusion)
  - Airway disease (asthma, COPD)
- **Metabolic causes**
  - Severe anemia
  - Hyperthyroidism
- **Neuromuscular and chest wall disorders**
  - Deconditioning, obesity, pregnancy, neuromuscular disease

Table 2. Differential Diagnosis of Chest Pain

(see Cardiology and Cardiac Surgery C4 and Emergency Medicine ER21)

Nonpleuritic
- **Pulmonary**
  - Pneumonia
  - PE
  - Neoplasm
- **Cardiac**
  - MI
  - Myocarditis/pericarditis
- **Esophageal**
  - GERD
  - Spasm
  - Esophagitis
  - Ulceration
  - Achalasia
  - Neoplasm
  - Esophageal rupture
- **Mediastinal**
  - Lymphoma
  - Thymoma
- **Subdiaphragmatic**
  - PUD
  - Gastritis
  - Biliary colic
  - Pancreatitis
- **Vascular**
  - Dissecting aortic aneurysm
- **MSK**
  - Costochondritis
  - Skin
  - Breast
  - Ribs

Pleuritic
- **Pulmonary**
  - Pneumonia
  - PE
  - Pneumothorax
  - Hemothorax
  - Neoplasm
  - TB
  - Empyema
- **Cardiac**
  - Pericarditis
  - Dressler's syndrome
- **GI**
  - Subphrenic abscess
  - Pancreatitis
- **MSK**
  - Costochondritis
  - Fractured rib
  - Myositis
  - Herpes zoster

Common Causes of Clubbing
- Pulmonary: Lung CA, bronchiectasis, pulmonary fibrosis, abscess, CF, empyema (NOT COPD)
- Cardiac: Cyanotic heart disease, endocarditis, A-V fistula
- GI: IBD, celiac, cirrhosis
- Endocrine: Graves'
- Other: Other malignancy, primary hypertrophic osteoarthropathy

Clubbing is not seen in COPD – if present, think malignancy

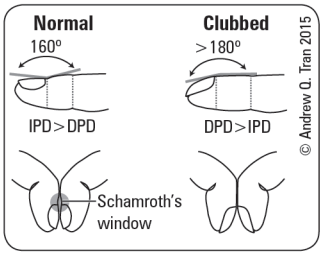

Figure 3. Signs of nail clubbing

Table 3. Differential Diagnosis of Hemoptysis

Airway Disease
- Acute or chronic bronchitis
- Bronchiectasis
- Bronchogenic CA
- Bronchial carcinoid tumour

Parenchymal Disease
- Pneumonia
- TB
- Lung abscess

Vascular Disease
- PE
- Elevated pulmonary venous pressure:
  - LVF
  - Mitral stenosis
- Vascular malformation
- Vasculitis
  - Goodpasture's syndrome
  - Idiopathic pulmonary hemosiderosis

Miscellaneous
- Impaired coagulation
- Pulmonary endometriosis

Table 4. Differential Diagnosis of Cough

Airway Irritants
- Inhaled smoke, dusts, fumes
- Postnasal drip (upper airway cough syndrome)
- Aspiration
  - Gastric contents (GERD)
  - Oral secretions
  - Foreign body

Airway Disease
- URTI including postnasal drip and sinusitis
- Acute or chronic bronchitis
- Bronchiectasis
- Neoplasm
- External compression by node or mass lesion
- Asthma
- COPD

Parenchymal Disease
- Pneumonia
- Lung abscess
- Interstitial lung disease

CHF

Drug-induced (e.g. ACEI)

Hemoptysis
- Most common cause is bronchitis
- 90% of massive hemoptysis is from the bronchial arteries
- Considered "massive" if >600 mL/24 h

Most Common Causes of Chronic Cough in the Non-smoking Patient (cough >3 mo with normal CXR)
- GERD
- Asthma
- Postnasal drip
- ACEI

Adapted from: Weinberger SE. Principles of pulmonary medicine, 5th ed. 2008. With permission from Elsevier

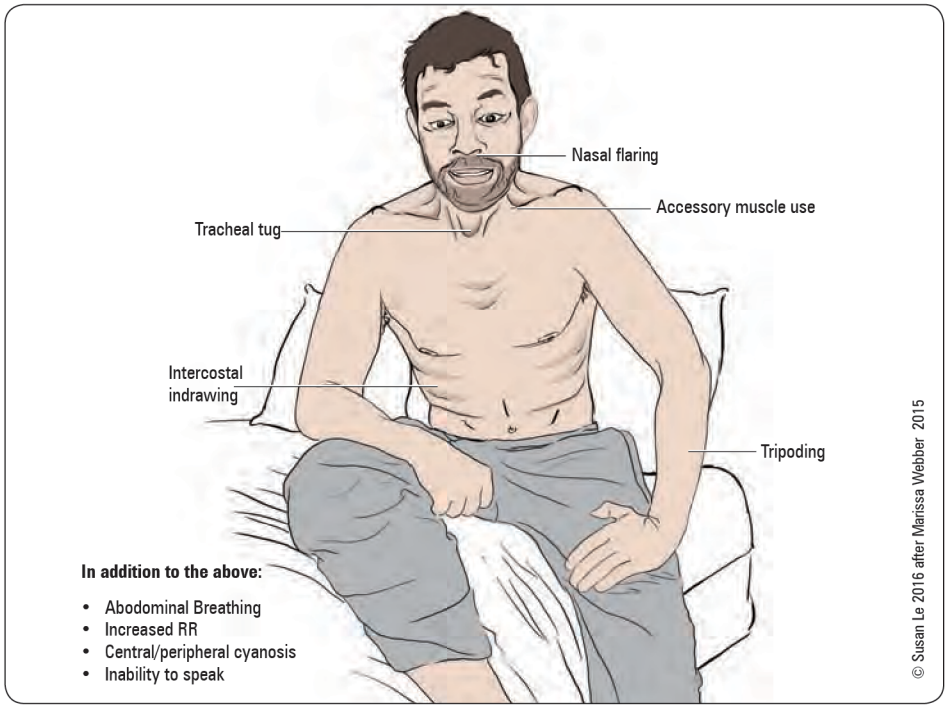

Figure 4. Signs of respiratory distress

Pulmonary Function Tests

- useful in differentiating the pattern of lung disease (obstructive vs. restrictive)
- assess lung volumes, flow rates, and diffusion capacity (Figures 5A and 5B)
- **note**: normal values for FEV_1 are approximately ±20% of the predicted values (for age, sex, and height); ethnicity may affect predicted values

Table 5. Comparison of Lung Flow and Volume Parameters in Obstructive vs. Restrictive Lung Disease

	Obstructive	Restrictive
	• Decreased flow rates (most marked during expiration) • Air trapping (increased RV/TLC) • Hyperinflation (increased FRC, TLC)	• Decreased lung compliance • Decreased lung volumes
DDx	Asthma, COPD, CF, bronchiolitis, bronchiectasis*	ILD, pleural disease, neuromuscular disease, chest wall disease
FEV_1/FVC	↓	↑ or N
TLC RV RV/TLC	↑ or N ↑ or N ↑ or N	↓ ↓ N
DL_{CO}	↓/↑ or N	↓ or N

*Bronchiectasis can be obstructive or mixed

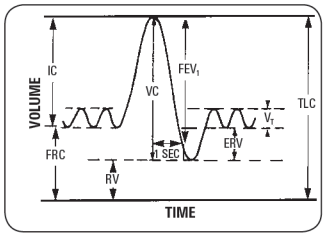

Figure 5A. Subcompartments of lung volumes

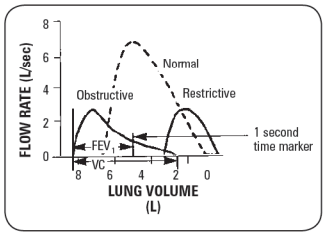

Figure 5B. Expiratory flow volume curves

Adapted with permission from Elsevier. Weinberger SE. Principles of pulmonary medicine, 5th ed. 2008

Table 6. Common Respirology Procedures

Technique	Purpose	Description
Plethysmography ("body box")	Measure FRC	• After a normal expiration the patient inhales against a closed mouthpiece • Resultant changes in the volume and pressure of the plethysmograph are used to calculate the volume of gas in the thorax • Useful for patients with air trapping
He dilution	Measure FRC	• A patient breathes from a closed circuit containing a known concentration and volume of helium • Since the amount of helium remains constant, FRC is determined based on the final concentration of the helium in the closed system • Only includes airspaces that communicate with the bronchial tree
Bronchoscopy	Diagnosis and therapy	• A flexible or rigid bronchoscope is used for visualization of a patient's airways Allows for: ▪ Bronchial and broncho-alveolar lavage (washings) for culture and cytology ▪ Endobronchial or transbronchial tissue biopsies ▪ Removal of secretions/foreign bodies/blood ▪ Laser resections ▪ Airway stenting • Mediastinal lymph nodes can also be sampled using a special bronchoscope equipped with an U/S probe (EBUS)

Lung Volumes
ERV – Expiratory Reserve Volume
FEF – Forced Expiratory Flow Rate
FEV_1 – Forced Expiratory Volume (in one second)
FRC – Functional Residual Capacity
IC – Inspiratory Capacity
RV – Residual Volume
TLC – Total Lung Capacity
VC – Vital Capacity
V_T – Tidal Volume

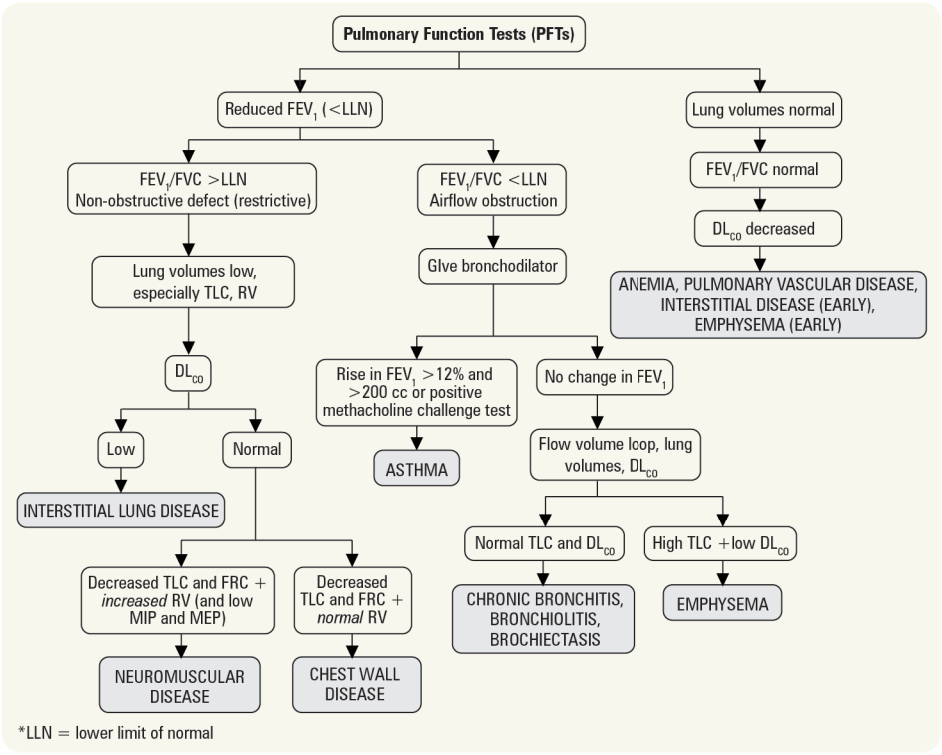

Figure 6. Interpreting PFTs

Chest X-Rays

- see Medical Imaging, MI4

Table 7. CXR Patterns and Differential Diagnosis

Pattern	Signs	Common DDx
Consolidation ("Airspace disease")	Air bronchogram Silhouette sign Less visible blood vessels	Acute: water (pulmonary edema), pus (pneumonia), blood (hemorrhage) Chronic: neoplasm (lymphoma), inflammatory (eosinophilic pneumonia), infection (TB, fungal)
Reticular ("Interstitial disease")	Increased pulmonary markings Honeycombing (IPF)	ILD (IPF, collagen vascular disease, asbestos, drugs)
Nodular	Cavitary vs. non-cavitary	Cavitary: neoplasm (primary vs. metastatic lung cancer), infectious (anaerobic or Gram negative, TB, fungal), inflammatory (RA, Granulomatosis with Polyangiitis [GPA]) Non-cavitary: above + sarcoid, Kaposi's sarcoma (in HIV), silicosis and other pneumoconioses

Arterial Blood Gases

- provides information on acid-base and oxygenation status
- see Nephrology, NP14

Approach to Acid-Base Status

1. Is the pH acidemic (pH <7.35), alkalemic (pH >7.45), or normal (pH 7.35-7.45)?
2. What is the primary disturbance?
   - metabolic: change in HCO_3^- and pH in same direction
   - respiratory: change in HCO_3^- and pH in opposite directions
3. Is there appropriate compensation? (see Table 8)
   - metabolic compensation occurs over 2-3 d reflecting altered renal HCO_3^- production and excretion
   - respiratory compensation through ventilatory control of P_aCO_2 occurs immediately
   - inadequate compensation may indicate a second acid-base disorder

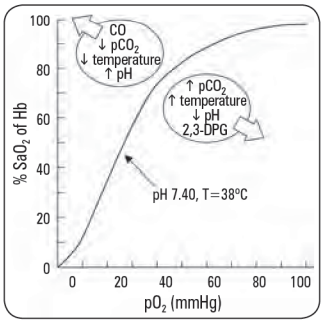

Figure 7. Oxygen-Hb dissociation curve

Factors that Shift the Oxygen-Hb Dissociation Curve to the Right

"**CADET, face right!**"
CO_2
Acid
2,3-**D**PG
Exercise
Temperature (increased)

Table 8. Expected Compensation for Specific Acid-Base Disorders

Disturbance	P_aCO_2 (mmHg) (normal ~40)	HCO_3^- (mmHg) (normal ~24)
Respiratory Acidosis		
Acute	↑ 10	↑ 1
Chronic	↑ 10	↑ 3
Respiratory Alkalosis		
Acute	↓ 10	↓ 2
Chronic	↓ 10	↓ 5
Metabolic Acidosis	↓ 1	↓ 1
Metabolic Alkalosis	↑ 5-7	↑ 10

4. If there is metabolic acidosis, what is the anion gap and osmolar gap?
   - anion gap = $[Na^+]-([Cl^-]+[HCO_3^-])$; normal ≤10-15 mmol/L
   - osmolar gap = measured osmolarity – calculated osmolarity = measured – (2[Na^+] + glucose + urea); normal ≤10 mmol/L
5. If anion gap is increased, is the change in bicarbonate the same as the change in anion gap?
   - if not, consider a mixed metabolic picture

Table 9. Differential Diagnosis of Respiratory Acidosis

Increased P_aCO_2 secondary to hypoventilation

Respiratory Centre Depression (Decreased RR)
- Drugs (anesthesia, sedatives, narcotics)
- Trauma
- Increased ICP
- Encephalitis
- Stroke
- Central apnea
- Supplemental O_2 in chronic CO_2 retainers (e.g. COPD)

Neuromuscular Disorders (Decreased Vital Capacity)
- Myasthenia gravis
- Guillain-Barré syndrome
- Poliomyelitis
- Muscular dystrophies
- ALS
- Myopathies
- Chest wall disease (obesity, kyphoscoliosis)

Airway Obstruction (Asthma, COPD)

Parenchymal Disease
- COPD
- Pulmonary edema
- Pneumothorax
- Pneumonia
- ILD (late stage)
- ARDS

Mechanical Hypoventilation (Inadequate Mechanical Ventilation)

Table 10. Differential Diagnosis of Respiratory Alkalosis

Decreased P_aCO_2 secondary to hyperventilation

Hypoxemia
- Pulmonary disease (pneumonia, edema, PE, interstitial fibrosis)
- Severe anemia
- Heart failure
- High altitude

Respiratory Centre Stimulation
- CNS disorders
- Hepatic failure
- Gram-negative sepsis
- Drugs (ASA, progesterone, theophylline, catecholamines, psychotropics)
- Pregnancy
- Anxiety
- Pain

Mechanical Hyperventilation (Excessive Mechanical Ventilation)

ABG Normal Values
pH 7.35-7.45
HCO_3 22-26 mEq/L
P_aCO_2 35-45 mm Hg
P_aO_2 80-100 mm Hg

Acidosis ←→ Hyperkalemia
Alkalosis ←→ Hypokalemia

Note: Mixed acid-base disturbances can still have a "normal" pH

Osmolar Gap = measured osmolarity – calculated osmolarity; for calculated osmolarity think "2 salts and a sticky BUN" (2Na + glucose + urea)

Anion Gap Metabolic Acidosis
MUDPILESCAT
Methanol
Uremia
Diabetic ketoacidosis/starvation ketoacidosis
Phenformin/**P**araldehyde
Isoniazid, **I**ron, **I**buprofen
Lactate
Ethylene glycol
Salicylates
Cyanide, **C**arbon dioxide
Alcoholic ketoacidosis
Toluene, **T**heophylline

• see Nephrology, NP15 for differential diagnosis of metabolic acidosis and alkalosis

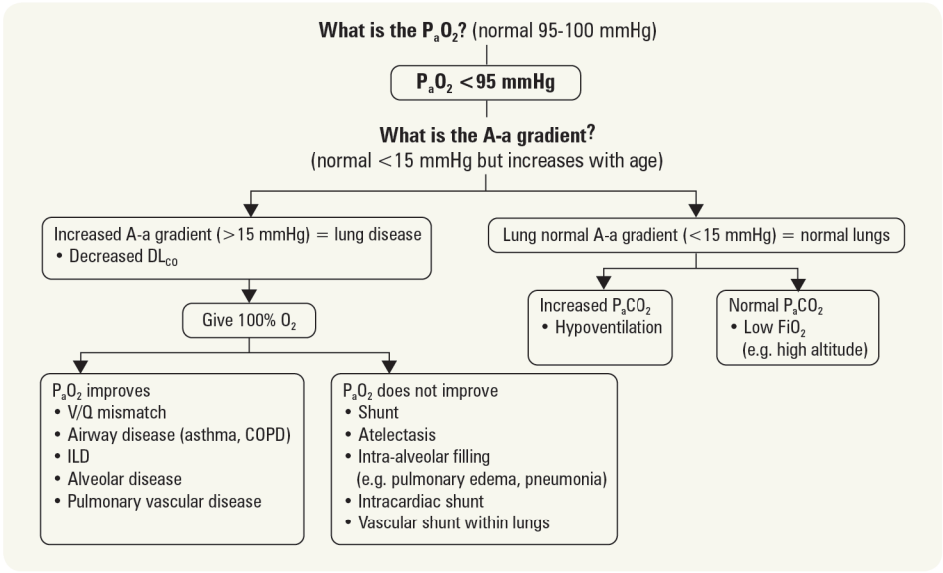

Figure 8. Approach to hypoxemia

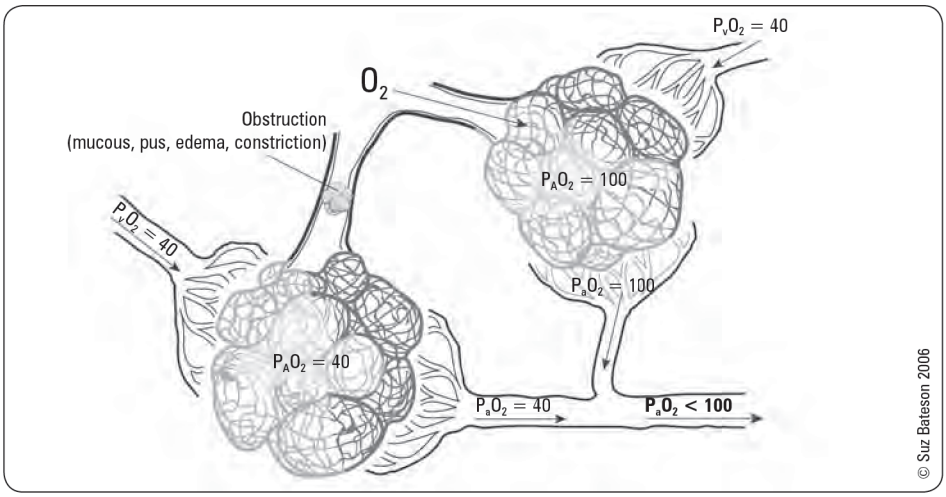

Figure 9. Pathophysiology of shunt

Diseases of Airway Obstruction

Pneumonia

- see Infectious Diseases, ID7

Asthma

- see Family Medicine, FM16 and Pediatrics, P89

Definition

- chronic inflammatory disorder of the airways resulting in episodes of reversible bronchospasm causing airflow obstruction
- associated with reversible airflow limitation and airway hyper-responsiveness to endogenous or exogenous stimuli

Epidemiology

- common, 7-10% of adults, 10-15% of children
- most children with asthma significantly improve in adolescence
- often family history of atopy (asthma, allergic rhinitis, eczema)
- occupational asthma (organic allergies, isocyanates, animals, etc.)

At Sea Level on Room Air
FiO_2 = 0.21
P_{atm} = 760 mmHg
PH_2O = 47 mmHg
RQ = 0.8
Thus, A-aDO_2 Gradient on Room Air
A-aDO_2 = (150 – 1.25 [P_aCO_2]) – P_aO_2

Diffusion Capacity for Carbon Monoxide (DL_{CO})

DL_{CO} decreases with:
- Decreased surface area (e.g. emphysema)
- Decreased hemoglobin
- Interstitial lung disease
- Pulmonary vascular disease

DL_{CO} increases with:
- Asthma
- Pulmonary hemorrhage
- Polycythemia
- Increased pulmonary blood volume

Pulmonary Shunt
Occurs when the capillary networks of the alveoli are perfused, yet there is a lack of adequate ventilation (and thus oxygenation) in that alveolus or group of alveoli. Thus this blood enters the pulmonary venous system without being oxygenated

Airway Obstruction (decreased FEV_1)
- Asthma
- COPD (chronic bronchitis, emphysema)
- Bronchiectasis
- Cystic fibrosis

Red Flags
Severe tachypnea/tachycardia, respiratory muscle fatigue, diminished expiratory effort, cyanosis, silent chest, decreased LOC

Central cyanosis is not detectable until SaO_2 is <85%. It is more easily detected in polycythemia and less readily detectable in anemia

Asthma Action Plan
Is a written plan developed by patients and their physicians which includes signs and symptoms for patients to recognize their current level of respiratory distress (denoted as 'green', 'yellow', or 'red/emergency' zones) and the personalized treatment options for each zone

Pathophysiology
- airway obstruction → V/Q mismatch → hypoxemia → ↑ ventilation → ↓ P_aCO_2 → ↑ pH and muscle fatigue → ↓ ventilation, ↑ P_aCO_2/↓ pH

Signs and Symptoms
- dyspnea, wheezing, chest tightness, cough (especially nocturnal), sputum
- symptoms can be paroxysmal or persistent
- signs of respiratory distress (see Figure 4)
- pulsus paradoxus

Table 11. Criteria for Determining if Asthma is Well Controlled

Daytime symptoms <4 d/wk	No asthma-related absence from work/school
Night-time symptoms <1 night/wk	β_2-agonist use <4 times/wk
Physical activity normal	FEV_1 or PEF >90% of personal best
Exacerbations mild, infrequent	PEF diurnal variation <10-15%

Adapted from: *Can Respir J* 2012; 19:127-164

Investigations
- O_2 saturation
- ABGs (consider in acute exacerbation, along with peak flows, in Emergency Department)
  - decreased P_aO_2 during attack (V/Q mismatch)
  - decreased P_aCO_2 in mild asthma (hyperventilation)
  - normal or increased P_aCO_2 is an ominous sign: patient is no longer able to hyperventilate (worsened airway obstruction or respiratory muscle fatigue)
- PFTs (do when stable)

Table 12. Pulmonary Function Criteria for Diagnosis of Asthma

Preferred Measurement	Alternative Measurements
Spirometry Showing Reversible Airway Obstruction (1) ↓ FEV_1/FVC below lower limit of normal (<0.75 to 0.8 in adults, <0.8-0.9 in children age 6+) AND (2) ↑ FEV_1 ≥12% (min. 200 mL in adults) after bronchodilator or controller therapy	**Peak Expiratory Flow Variability** (1) ↑ in PEF after a bronchodilator or course of controller therapy • Adults: PEF ↑ 60 L/min (min. 20%) OR Diurnal variation >8% for twice daily readings (20% for multiple daily readings) • Children age 6+: PEF ↑ 20% **Positive Challenge Test** (1) Methacholine challenge: PC_{20} <4 mg/mL (4-16 mg/mL is borderline; >16 mg/mL is negative) OR (2) Post-exercise: ↓ FEV_1 ≥10-15%

Adapted from: *Can Respir J* 2012; 19:127-164

Treatment
- environment: avoid triggers
- patient education: features of the disease, goals of treatment, self-monitoring
- pharmacological
  - symptomatic relief in acute episodes: short-acting β_2-agonist, anticholinergic bronchodilators, oral steroids, addition of a long acting β_2-agonist
  - long-term prevention: inhaled/oral corticosteroids, anti-allergic agents, long-acting β_2-agonists, methylxanthine, LTRA, anti-IgE antibodies (e.g. Xolair®)

Emergency Management of Asthma (see Emergency Medicine, ER29)
1. inhaled β_2-agonist first line (MDI route and spacer device recommended)
2. systemic steroids (PO or IV if severe)
3. if severe add anticholinergic therapy ± magnesium sulphate
4. rapid sequence intubation in life-threatening cases (plus 100% O_2, monitors, IV access)
5. SC/IV adrenaline if caused by anaphylaxis, IV salbutamol if unresponsive
6. corticosteroid therapy at discharge

Asthma Triggers
- URTIs
- Allergens (pet dander, house dust, molds, cockroach)
- Irritants (cigarette smoke, air pollution)
- Drugs (NSAIDs, β-blockers)
- Preservatives (sulphites, MSG)
- Other (emotion/anxiety, cold air, exercise, GERD)

Signs of Poor Asthma Control

DANGERS
Daytime Sx ≥4 times/wk
Activities reduced
Nightime Sx ≥1 time/wk
GP visits
ER visits
Rescue puffer (SABA) use ≥4 times/wk
School and work absences

Consider LABA for night-time symptoms

LTRA in Addition to Usual Care for Acute Asthma in Adults and Children
Cochrane DB Syst Rev 2012;CD006100
Purpose: To determine if the addition of LTRA is beneficial to patients with acute asthma receiving inhaled bronchodilators and systemic corticosteroids.
Methods: RCTs in Cochrane Airway Group's Specialised Register of trials that compared LTRA and standard vs. placebo and standard in people with acute asthma of any age.
Results: 8 trials, 1,470 adults and 470 children. For oral treatment, no significant difference between LTRAs and control in hospital admission (RR 0.86; 95% CI 0.21-3.52) or requirement for additional care (RR 0.87; 95% CI 0.60-1.68). LTRAs improved FEV1 in adults (mean difference 0.08; 95% CI 0.01-0.14) but not in children. No significant difference in adverse events between LTRAs and control (RR 0.81; 95% CI 0.22-2.99). Similar results were found for intravenous treatment.
Conclusions: Currently, there is no evidence to support routine use of LTRAs in acute asthma.

Natural Progression of COPD

40s	Chronic productive cough, wheezing occasionally
50s	1st acute chest illness
60s	Dyspnea on exertion, increasing sputum, more frequent exacerbations
Late Stage	Hypoxemia with cyanosis, polycythemia, hypercapnia (morning headache), cor pulmonale, weight loss

GOLD Classification of the Severity of COPD

GOLD 1	Mild FEV_1 ≥80% of predicted
GOLD 2	Moderate 50% ≤ FEV_1 <80% of predicted
GOLD 3	Severe 30% ≤ FEV_1 <50% of predicted
GOLD 4	Very Severe FEV_1 <30% of predicted

Guidelines for Asthma Management

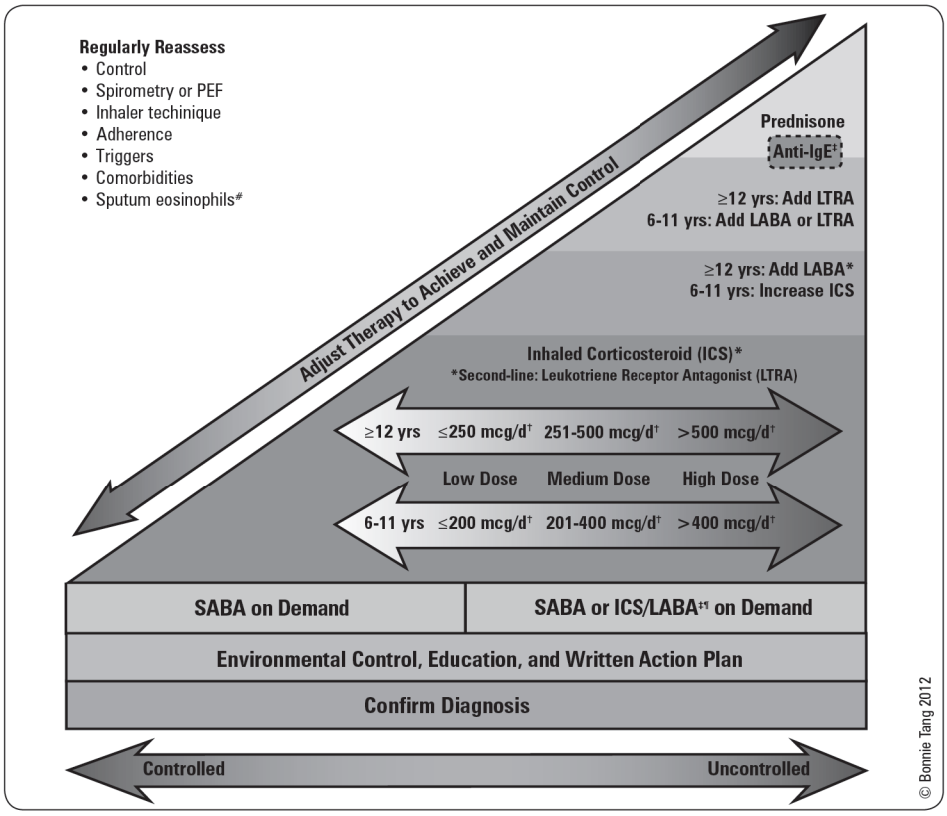

Figure 10. Guidelines for asthma management

†HFA Becolmethasone or equivalent; *Second-line: LTRA; ‡Approved for 12 yr and over; ¶Using a formulation approved for use as a reliever; #In adults 18 yr and older with moderate to severe asthma

Adapted from: *Can Respir J* 2012;19:127-164

Chronic Obstructive Pulmonary Disease

• see Family Medicine, FM16

Definition

- progressive and irreversible condition of the lung characterized by chronic obstruction to airflow with many patients having periodic exacerbations, gas trapping, lung hyperinflation, and weight loss
- 2 subtypes: chronic bronchitis and emphysema (usually coexist to variable degrees)
- gradual decrease in FEV_1 over time with episodes of acute exacerbations

Table 13. Clinical and Pathologic Features of COPD*

Chronic Bronchitis	Emphysema
Defined Clinically Productive cough on most days for at least 3 consecutive months in 2 successive years Obstruction is due to narrowing of the airway lumen by mucosal thickening and excess mucus	**Defined Pathologically** Dilation and destruction of air spaces distal to the terminal bronchiole without obvious fibrosis Decreased elastic recoil of lung parenchyma causes decreased expiratory driving pressure, airway collapse, and air trapping **2 Types** 1) **Centriacinar** (respiratory bronchioles predominantly affected) • Typical form seen in smokers, primarily affects upper lung zones 2) **Panacinar** (respiratory bronchioles, alveolar ducts, and alveolar sacs affected) • Accounts for about 1% of emphysema cases • α_1-antitrypsin deficiency, primarily affects lower lobes

*Note that both chronic bronchitis and emphysema can exist without obstruction. Only if obstruction is also present is it termed COPD

Risk Factors

- smoking is #1 risk factor
- others
  - environmental: air pollution, occupational exposure, exposure to wood smoke or other biomass fuel for cooking
  - treatable factors: α_1-antitrypsin deficiency, bronchial hyperactivity
  - demographic factors: age, family history, male sex, history of childhood respiratory infections, low socioeconomic status

Remember, first line therapy for COPD is smoking cessation

α-1-Antitrypsin Deficiency
Inherited disorder of defective production of α_1-antitrypsin, a protein produced by hepatocytes. Acts in the alveolar tissue by inhibiting the action of proteases from destroying alveolar tissue. When deficient, proteases can destroy lung alveoli resulting in emphysema

CO_2 Retainers
On ABG, retainers have chronically elevated CO_2 levels with a normal pH. Maintain O_2 Sat between 88-92% to prevent Haldane effect and decreased respiratory drive

Pulmonary Embolism in Patients with Unexplained Exacerbation of COPD: Prevalence and Risk Factors
Ann Intern Med 2006;144:390-396
Study: Prospective cohort study of 211 patients with COPD (all current and former smokers) admitted to hospital for severe COPD exacerbation of unknown origin.
Measurements: All patients received spiral CT angiogram (CTA) and venous compression ultrasonography of both legs.
Results: 25% of patients met diagnostic criteria for PE (+ CTA or + U/S).
Conclusions: Prevalence of PE in patients hospitalized for COPD exacerbation of unknown origin is 25%. Therefore, all patients presenting to hospital with COPD exacerbation without obvious cause require PE workup (leg dopplers or CTA – decision of which to use depends on pre-test probability of the patient).

Non-Invasive Positive Pressure Ventilation for Treatment of Respiratory Failure due to Exacerbations of COPD
Cochrane DB Syst Rev 2004;CD004104
Study: Cochrane Systematic Review. 14 RCTs.
Population: 758 adult patients with COPD and acute respiratory failure due to COPD exacerbation.
Intervention: Usual medical care (UMC) and Non-invasive positive ventilation (NPPV) vs. UMC alone.
Primary Outcome: Treatment failure, mortality, and tracheal intubation.
Results: The risks for all primary outcomes were reduced with NPPV use: treatment failure (RR 0.48); mortality (RR 0.52); and intubation use (RR 0.61). Length of hospital stay was a significant mean 3.24 d shorter, but no difference between ICU length of stay. There is a small and significant improvement in pH (weight mean difference (WMD)=0.04), P_aCO_2 (WMD=0.40 kPa), and respiratory rate (WMD=-3.08 bpm) within 1 h post-treatment with NPPV. Complications associated with treatment were reduced in the NPPV treatment arm (RR 0.38).
Conclusion: For patients in respiratory failure due to a COPD exacerbation, NPPV is effective in reducing treatment failure, mortality, and need for intubation when used as a first line treatment adjunct to UMC.

Signs and Symptoms

Table 14. Clinical Presentation and Investigations for Chronic Bronchitis and Emphysema

	Symptoms	Signs	Investigations
Bronchitis (Blue Bloater*)	Chronic productive cough Purulent sputum Hemoptysis Mild dyspnea initially	Cyanosis (2° to hypoxemia and hypercapnia) Peripheral edema from RVF (cor pulmonale) Crackles, wheezes Prolonged expiration if obstructive Frequently obese	**PFT:** ↓ FEV_1, ↓ FEV_1/FVC N TLC, ↓ or N DL_{CO} **CXR:** AP diameter normal ↑ bronchovascular markings Enlarged heart with cor pulmonale
Emphysema (Pink Puffer*)	Dyspnea (± exertion) Minimal cough Tachypnea Decreased exercise tolerance	Pink skin Pursed-lip breathing Accessory muscle use Cachectic appearance due to anorexia and increased work of breathing Hyperinflation/barrel chest, hyperresonant percussion Decreased breath sounds Decreased diaphragmatic excursion	**PFT:** ↓ FEV_1, ↓ FEV_1/FVC ↑ TLC (hyperinflation) ↑ RV (gas trapping) ↓ DL_{CO} **CXR:** ↑ AP diameter Flat hemidiaphragm (on lateral CXR) ↓ heart shadow ↑ retrosternal space Bullae ↓ peripheral vascular markings

*Note that the distinction between "blue bloaters" and "pink puffers" is more of historical than practical interest as most COPD patients have elements of both

Table 15. Treatment of Stable COPD

Treatment	Details
PROLONG SURVIVAL	
Smoking cessation	Nicotine replacement, bupropion, varenicline
Vaccination	Influenza, pneumococcal vaccine
Home oxygen	Prevents cor pulmonale and decreases mortality if used >15h/d; indicated if (1) P_aO_2 <55 mmHg or (2) <60 mmHg with cor pulmonale or polycythemia
SYMPTOMATIC RELIEF (no mortality benefit)	
Bronchodilators (mainstay of current drug therapy, used in combination)	Short-acting anticholinergics (e.g. ipratropium bromide) and short-acting β_2-agonists (e.g. salbutamol, terbutaline) • SABAs: rapid onset but significant side effects at high doses (e.g. hypokalemia) • Short-acting anticholinergics more effective than SABAs with fewer side effects but slower onset; take regularly rather than PRN LABAs (e.g. salmeterol, formoterol, indacaterol) and long-acting anticholinergics (e.g. tiotropium bromide, glycopyrronium bromide) • More sustained effects for moderate to severe COPD Inhaled corticosteroid (ICS) + LABA combination (e.g. Advair®: fluticasone + salmeterol, Symbicort®: budesonide + formoterol) • ICS/LABA increases effectiveness vs. LABA alone Theophylline: weak bronchodilator; limited evidence to suggest combination with bronchodilator • Side effects: nervous tremor, nausea/vomiting/diarrhea, tachycardia, arrhythmias, sleep changes PDE4 inhibitor: roflumilast (Daxas®) anti-inflammatory medication useful in COPD with chronic bronchitis, severe airflow obstruction, frequent exacerbations
Corticosteroids	ICS monotherapy is contraindicated and ICS should only be used with a LABA in combination in patients with a history of exacerbations COPD airways are usually inflamed but often not responsive to steroids, therefore avoid chronic systemic glucocorticoids (although oral steroids are very important when treating exacerbations)
Surgical	Lung volume reduction surgery (resection of emphysematous parts of lung, associated with higher mortality if FEV_1 <20%), lung transplant
Other	Patient education, eliminate respiratory irritants/allergens (occupational/environmental), exercise rehabilitation to improve physical endurance

Remember to step down therapy to lowest doses which control symptoms/signs of bronchoconstriction

Influenza Vaccine for Patients with Chronic Obstructive Pulmonary Disease
Cochrane DB Syst Rev 2006;1:CD002733
Study: Cochrane Systematic Review. 11 RCTs included, 6 specifically in COPD patients.
Population: Six of the studies were done on COPD patients in particular, while the others were on elderly and high-risk individuals. Asthma patients were excluded.
Intervention: Live or inactivated virus vaccines vs. placebo.
Outcome: Exacerbation rates, hospitalizations, mortality, lung function and adverse effects.
Results: In patients with COPD, inactive vaccine correlated with fewer exacerbations per vaccinated subject than placebo (weighted mean difference (WMD) -0.37, 95% CI -0.64 to -0.11). Inactivated vaccine resulted in fewer influenza-related infections than placebo (WMD 0.19, 95% CI 0.07-0.48). There was also an increased risk of local mild, transient adverse reactions with the vaccine.
Conclusions: There appears to be a reduction in influenza-related infections, as well as exacerbations in patients with COPD receiving the vaccine.

Different Durations of Corticosteroid Therapy for Exacerbations of Chronic Obstructive Pulmonary Disease
Cochrane DB Syst Rev 2014:CD006897
Study: Cochrane systematic review. 8 studies.
Population: 582 patients, with severe or very severe COPD.
Intervention: Corticosteroids given at equivalent daily doses for 3-7 d (short duration) vs. 10-15 d (longer-duration).
Outcome: treatment failure, risk of relapse, time to next COPD exacerbation, likelihood of adverse event, length of hospital stay, and lung function at end of treatment.
Results: In four studies there was no difference in risk of treatment failure between short-duration and longer-duration systemic corticosteroid treatment (n = 457; odds ratio (OR) 0.72, 95% confidence interval (CI) 0.36 to 1.46)), which was equivalent to 22 fewer per 1000 for short-duration treatment (95% CI 51 fewer to 34 more). No difference in risk of relapse (a new event) was observed between short-duration and longer-duration systemic corticosteroid treatment (n = 457; OR 1.04, 95% CI 0.70 to 1.56), which was equivalent to nine fewer per 1,000 for short-duration treatment (95% CI 68 fewer to 100 more). Time to the next COPD exacerbation did not differ in one large study that was powered to detect non-inferiority and compared five days versus 14 d of systemic corticosteroid treatment (n = 311; hazard ratio 0.95, 95% CI 0.66 to 1.37). In five studies no difference in the likelihood of an adverse event was found between short-duration and longer-duration systemic corticosteroid treatment (n = 503; OR 0.89, 95% CI 0.46 to 1.69, or nine fewer per 1000 [95% CI 44 fewer to 51 more]). Length of hospital stay (n = 421; mean difference (MD) -0.61 days, 95% CI -1.51 to 0.28) and lung function at the end of treatment (n = 185; MD FEV1 -0.04 L; 95% CI -0.19 to 0.10) did not differ between short-duration and longer-duration treatment.
Conclusion: 5 d of oral corticosteroids is likely to be sufficient for treatment of adults with acute exacerbations of COPD, and this review suggests that the likelihood is low that shorter courses of systemic corticosteroids (of around five days) lead to worse outcomes than are seen with longer (10 to 14 d) courses.

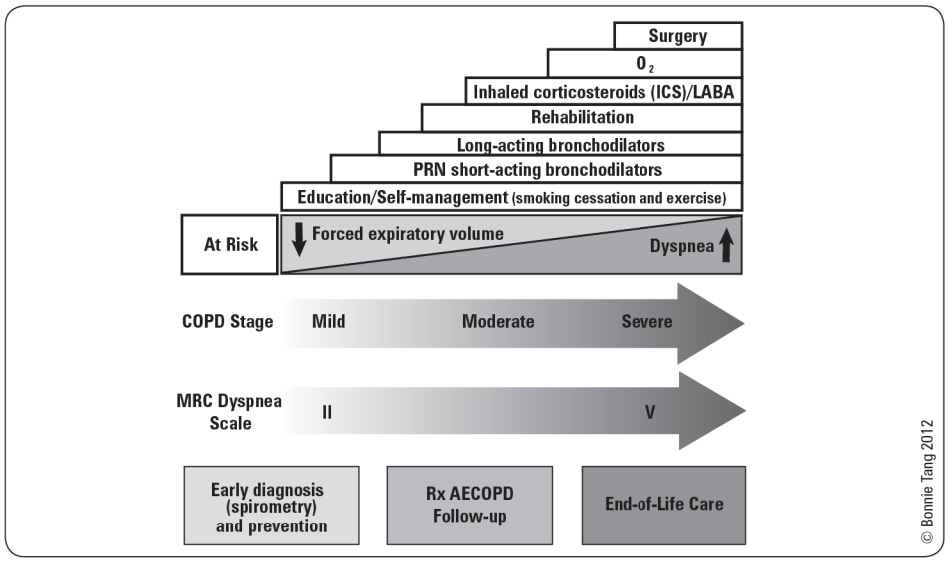

Figure 11. Guidelines for COPD Management
Adapted from: Canadian Thoracic Society recommendations for management of chronic obstructive pulmonary disease. *Can Respir J* 2008;(Suppl A):15

Acute Exacerbations of COPD

- **definition**
  - sustained (>24-48 h) worsening of dyspnea, cough, or sputum production leading to an increased use of medications
- **etiology**: viral URTI, bacteria, air pollution, CHF, PE, MI must be considered
- **management**
  - ABCs, consider assisted ventilation if decreasing LOC or poor ABGs
  - O_2: target 88-92% SaO_2 for CO_2 retainers
  - bronchodilators by MDI with spacer or nebulizer
    - SABA + anticholinergic, e.g. salbutamol and ipratropium bromide via nebulizers x 3 back-to-back q15min
  - systemic corticosteroids: IV solumedrol or oral prednisone
  - antibiotics for exacerbations with increased sputum production and at least one of the following: increased dyspnea or sputum purulence
    - simple exacerbation (no risk factors): amoxicillin, 2nd or 3rd generation cephalosporin, macrolide, or TMP/SMX
    - complicated exacerbation (one of: FEV_1 ≤50% predicted, ≥4 exacerbations per year, ischemic heart disease, home O_2 use, chronic oral steroid use): fluoroquinolone or β-lactam + β-lactamase inhibitor (amoxicillin/clavulanate)
  - post exacerbation: rehabilitation with general conditioning to improve exercise tolerance
- ICU admission
  - for life threatening exacerbations
  - ventilatory support
    - non-invasive: NPPV, BiPAP
    - conventional mechanical ventilation

Prognosis in COPD

- prognostic factors
  - level of dyspnea is the single best predictor
  - development of complications, e.g. hypoxemia or cor pulmonale
- 5 yr survival
  - FEV_1 <1 L = 50%
  - FEV_1 <0.75 L = 33%
- BODE index for risk of death in COPD
  - greater score = higher probability the patient will die from COPD; score can also be used to predict hospitalization
  - 10 point index consisting of four factors
    - **B**ody mass index (BMI): <21 (+1 point)
    - **O**bstruction (FEV_1): 50-64% (+1), 36-49% (+2), <35% (+3)
    - **D**yspnea (MRC scale): walks slower than people of same age on level surface, stops occasionally (+1), stops at 100 yards or a few minutes on the level (+2), too breathless to leave house or breathless when dressing/undressing (+3)
    - **E**xercise capacity (6 minute walk distance): 250-349 m (+1), 150-249 m (+2), <149 m (+3)

Complications of COPD
- Polycythemia 2° to hypoxemia
- Chronic hypoxemia
- Pulmonary HTN from vasoconstriction
- Cor pulmonale
- Pneumothorax due to rupture of emphysematous bullae

Systemic Corticosteroids for Acute Exacerbations of Chronic Obstructive Pulmonary Disease
Cochrane DB Syst Rev 2014: CD001228
Study: Cochrane systematic review 16 studies.
Population: 1,787 patients with acute COPD exacerbations.
Intervention: Oral or parenteral corticosteroids vs. placebo.
Outcome: treatment failure, risk of relapse, time to next COPD exacerbation, likelihood of adverse event, length of hospital stay, and lung function at end of treatment.
Results: Systemic corticosteroids reduced the risk of treatment failure by over half compared with placebo in nine studies (n = 917) with median treatment duration 14 d, odds ratio (OR) 0.48 (95% CI 0.35-0.67). The evidence was graded as high quality and it would have been necessary to treat nine people (95% CI 7-14) with systemic corticosteroids to avoid one treatment failure. There was moderate-quality evidence for a lower rate of relapse by one month for treatment with systemic corticosteroid in two studies (n = 415) (hazard ratio (HR) 0.78; 95% CI 0.63-0.97). Mortality up to 30 d was not reduced by treatment with systemic corticosteroid compared with control in 12 studies (n = 1,319; OR 1.00; 95% CI 0.60-1.66). FEV_1, measured up to 72 hours, showed significant treatment benefits (7 studies; n = 649; mean difference (MD) 140 mL; 95% CI 90-200); however, this benefit was not observed at later time points. The likelihood of adverse events increased with corticosteroid treatment (OR 2.33; 95% CI 1.59-3.43). The risk of hyperglycemia was significantly increased (OR 2.79; 95% CI 1.86-4.19). For general inpatient treatment, duration of hospitalization was significantly shorter with corticosteroid treatment (MD -1.22 d; 95% CI -2.26 to -0.18), with no difference in length of stay in the intensive care unit (ICU) setting. Comparison of parenteral versus oral treatment showed no significant difference in the primary outcomes of treatment failure, relapse or mortality or for any secondary outcomes.
Conclusion: There is high-quality evidence to support treatment of exacerbations of COPD with systemic corticosteroid by the oral or parenteral route in reducing the likelihood of treatment failure and relapse by 1 mo, shortening length of stay in hospital inpatients not requiring assisted ventilation in ICU and giving earlier improvement in lung function and symptoms. There is no evidence of benefit for parenteral treatment compared with oral treatment with corticosteroid on treatment failure, relapse or mortality. There is an increase in adverse drug effects with corticosteroid treatment, which is greater with parenteral administration compared with oral treatment.

Bronchiectasis

Definition
- irreversible dilatation of airways due to inflammatory destruction of airway walls resulting from persistently infected mucus
- usually affects medium sized airways
- *P. aeruginosa* is the most common pathogen; *S. aureus, H. influenzae,* and nontuberculous mycobacteria also common

Table 16. Etiology and Pathophysiology of Bronchiectasis

Obstruction	**Post-Infectious** (results in dilatation of bronchial walls)	**Impaired Defenses** (leads to interference of drainage, chronic infections, and inflammation)
Tumour Foreign body Thick mucus	Pneumonia TB Measles Pertussis Allergic bronchopulmonary aspergillosis MAC	Hypogammaglobulinemia CF Defective leukocyte function Ciliary dysfunction (Kartagener's syndrome: bronchiectasis, sinusitis, situs inversus)

Signs and Symptoms
- chronic cough, purulent sputum (but 10-20% have dry cough), hemoptysis (can be massive), recurrent pneumonia, local crackles (inspiratory and expiratory), wheezes
- clubbing
- may be difficult to differentiate from chronic bronchitis

Investigations
- PFTs: often demonstrate obstructive pattern but may be normal
- CXR
  - nonspecific: increased markings, linear atelectasis, loss of volume in affected areas
  - specific: "tram tracking" – parallel narrow lines radiating from hilum, cystic spaces, honeycomb like structures
- high-resolution thoracic CT (diagnostic, gold standard)
  - 87-97% sensitivity, 93-100% specificity
  - "signet ring": dilated bronchi with thickened walls where diameter bronchus > diameter of accompanying artery
- sputum cultures (routine + AFB)
- serum Ig levels
- sweat chloride if cystic fibrosis suspected (upper zone predominant)

Treatment
- vaccination: influenza and Pneumovax®
- antibiotics (oral, IV, inhaled): routinely used for mild exacerbations, driven by sputum sensitivity; macrolides may be used chronically for an anti-inflammatory effect
- inhaled antibiotics (tobramycin) used chronically to suppress pseudomonas and reduce exacerbations
- inhaled corticosteroids: decrease inflammation and improve FEV_1
- oral corticosteroids for acute, major exacerbations
- chest physiotherapy, breathing exercises, physical exercise
- pulmonary resection: in selected cases with focal bronchiectasis

Cystic Fibrosis

- see Pediatrics, P90

Pathophysiology
- chloride transport dysfunction: thick secretions from exocrine glands (lung, pancreas, skin, reproductive organs) and blockage of secretory ducts

Clinical Features
- results in severe lung disease, pancreatic insufficiency, diabetes, and azoospermia
- other manifestations: meconium ileus in infancy, distal ileal obstruction in adults, sinusitis, liver disease
- chronic lung infections
  - *S. aureus*: early
  - *P. aeruginosa*: most common
  - *B. cepacia*: worse prognosis but less common
  - *Aspergillus fumigatus*

Usually presents in childhood as recurrent lung infections that become persistent and chronic

Investigations
- sweat chloride test
  - increased concentrations of NaCl and K^+ ($[Cl^-]$ >60 mmol/L is diagnostic in children)
  - heterozygotes have normal sweat tests (and no symptoms)

- PFTs
  - early: airflow limitation in small airways
  - late: severe airflow obstruction, hyperinflation, gas trapping, decreased DL_{CO} (very late)
- ABGs
  - hypoxemia, hypercapnia later in disease with eventual respiratory failure and cor pulmonale
- CXR
  - hyperinflation, increased pulmonary markings (especially upper lobes)

Treatment
- chest physiotherapy and postural drainage
- bronchodilators (salbutamol ± ipratropium bromide)
- inhaled mucolytic (reduces mucus viscosity), hypertonic saline DNase
- inhaled tobramycin
- antibiotics (e.g. ciprofloxacin)
- lung transplant
- pancreatic enzyme replacements

Prognosis
- depends on: infections (cepacia colonization), FEV_1, acute pulmonary exacerbations, lung transplant vs. non-lung transplant

Interstitial Lung Disease

Definition
- a group of disorders which cause progressive scarring of lung tissue
- this scarring can eventually impair lung function and gas exchange

Pathophysiology
- inflammatory and/or fibrosing process in the alveolar walls → distortion and destruction of normal alveoli and microvasculature
- typically associated with
  - lung restriction (decrease in TLC and VC)
  - decreased lung compliance (increased or normal FEV_1/FVC)
  - impaired diffusion (decreased DL_{CO})
  - hypoxemia due to V/Q mismatch (usually without hypercapnia until end stage)
  - pulmonary HTN and cor pulmonale occur with advanced disease secondary to hypoxemia and blood vessel destruction

Etiology
- >100 known disorders can cause ILD
- majority due to unknown agents or cause

Table 17. Interstitial Lung Diseases

UNKNOWN ETIOLOGY	
Idiopathic interstitial pneumonias UIP (usual interstial pneumonia e.g. IPF) NSIP (non-specific interstitial pneumonia) LIP (lymphocytic interstitial pneumonia) COP (cryptogenic organizing pneumonia e.g. BOOP) DIP (desquamative interstitial pneumonia) IPPFE (idiopathic pleuroparenchymal fibroelastosis) AFOP (acute fibrinous and organizing pneumonia)	Sarcoidosis Langerhans-cell histiocytosis (eosinophilic granuloma) Lymphangioleiomyomatosis

KNOWN ETIOLOGY		
ILD Associated with Systemic Rheumatic Disorders Scleroderma Rheumatoid arthritis SLE Polymyositis/dermatomyositis Anti-synthetase syndromes Mixed connective tissue disease **Environment/Occupation Associated ILD** Hypersensitivity pneumonitis (usually organic antigen) Farmer's lung Air conditioner/humidifier lung Bird breeder's lung Pneumoconioses (inorganic dust) Silicosis Asbestosis Coal worker's pneumoconiosis Chronic beryllium disease Pneumonitis from gases/fumes/vapour	**ILD Associated with Drugs or Treatments** Antibiotics (nitrofurantoin) Anti-inflammatory agents (methotrexate) Cardiovascular drugs (amiodarone) Antineoplastic agents (chemotherapy agents) Illicit drugs Radiation **ILD Associated with Pulmonary Vasculitis** Granulomatosis with Polyangiitis (GPA) Goodpasture's syndrome Idiopathic pulmonary hemosiderosis	**Inherited Disorders** Familial IPF Telomerase mutations Neurofibromatosis Tuberous sclerosis Gaucher's disease **Alveolar Filling Disorders** Chronic eosinophilic pneumonia Pulmonary alveolar proteinosis

In ILD think
FASSTEN and **BAD RASH**

Upper Lung Disease (FASSTEN)
Farmer's lung (hypersensitivity pneumonitis)
Ankylosing spondylitis
Sarcoidosis
Silicosis
TB
Eosinophilic granuloma (Langerhans-cell histiocytosis)
Neurofibromatosis

Lower Lung Disease (BADRASH)
Bronchiolitis obliterans with organizing pneumonia (BOOP)
Asbestosis
Drugs (nitrofurantoin, hydralazine, INH, amiodarone, many chemo drugs)
Rheumatologic disease
Aspiration
Scleroderma
Hamman Rich (acute interstitial pneumonia) and IPF

Signs and Symptoms
- dyspnea, especially on exertion
- nonproductive cough
- crackles (dry, fine, end-inspiratory)
- clubbing (especially in IPF and asbestosis)
- features of cor pulmonale
- note that signs and symptoms vary with underlying disease process
  - e.g. sarcoidosis is seldom associated with crackles and clubbing

Investigations
- CXR/high resolution CT (see Medical Imaging, MI7)
  - usually decreased lung volumes
  - reticular, nodular, or reticulonodular pattern (nodular <3 mm)
  - hilar/mediastinal adenopathy (especially in sarcoidosis)
- PFTs
  - restrictive pattern: decreased lung volumes and compliance
  - normal or increased FEV_1/FVC (>70-80%), e.g. flow rates are often normal or high when corrected for absolute lung volume
  - DL_{CO} decreased due to V/Q mismatch (less surface area for gas exchange ± pulmonary vascular disease)
- ABGs
  - hypoxemia and respiratory alkalosis may be present with progression of disease
- other
  - bronchoscopy, bronchoalveolar lavage, lung biopsy
  - ESR, ANA (lupus), RF (RA), serum-precipitating antibodies to inhaled organic antigens (hypersensitivity pneumonitis), c-ANCA (GPA), anti-GBM (Goodpasture's)

The CXR can be normal in up to 15% of patients with interstitial lung disease

Unknown Etiologic Agents

IDIOPATHIC PULMONARY FIBROSIS

Definition
- also known as usual interstitial pneumonia or cryptogenic fibrosing alveolitis
- a progressive, irreversible condition characterized by fibrosis of lung parenchyma with no known cause
  - chest CT usually shows honeycomb lung, lung biopsy shows UIP (usual interstitial pneumonia) pattern
    - commonly presents over age 50, incidence rises with age; males > females
- DDx
  - other idiopathic interstitial pneumonia, especially NSIP, but also COP and
    - desquamative interstitial pneumonitis (DIP)
    - lymphocytic interstitial pneumonitis (LIP): usually 2° to immune conditions such as HIV (mostly in children), Sjögren's

IPF Prevalence
- Age 35-44: 2-7 per 100,000
- Age >75: 175 per 100,000

Signs and Symptoms
- commonly presents over age 50, incidence rises with age; males > females
- dyspnea on exertion, nonproductive cough, constitutional symptoms, late inspiratory fine crackles at lung bases, clubbing

Investigations
- labs (nonspecific, autoimmune serology usually negative)
- CXR: reticular or reticulonodular pattern with lower lung predominance; may appreciate honeycombing in advanced disease
- high resolution CT: lower zone peripheral reticular markings, traction bronchiectasis, honeycombing; ground glass, consolidation, or nodules should not be prominent in IPF
- biopsy: rarely for UIP as honeycombing makes radiologic diagnosis possible

Treatment
- O_2
- N-acetylcysteine (anti-oxidant)
- pirfenidone and nintedanib may slow disease progression
- lung transplantation for advanced disease
- mean survival of 3-5 yr after diagnosis

SARCOIDOSIS

Definition
- idiopathic non-infectious granulomatous multi-system disease with lung involvement in 90%
- characterized pathologically by non-caseating granulomas
- numerous HLA antigens have been shown to play a role and familial sarcoidosis is now recognized

Epidemiology
- typically affects young and middle-aged patients
- higher incidence among African Americans and people at northern latitudes e.g. Scandinavia, Canada

Signs and Symptoms
- asymptomatic, cough, dyspnea, fever, arthralgia, malaise, erythema nodosum, chest pain
- chest exam often normal
- common extrapulmonary manifestations
  - cardiac (arrhythmias, sudden death)
  - eye involvement (anterior or posterior uveitis)
  - skin involvement (skin papules, erythema nodosum, lupus pernio)
  - peripheral lymphadenopathy
  - arthralgia
  - hepatomegaly ± splenomegaly
- less common extra-pulmonary manifestations involve bone, CNS, kidney
- two acute sarcoid syndromes
  - Lofgren's syndrome: fever, erythema nodosum, bilateral hilar lymphadenopathy, arthralgias
  - Heerfordt-Waldenstrom syndrome: fever, parotid enlargement, anterior uveitis, facial nerve palsy

Investigations
- CBC (cytopenias from spleen or marrow involvement)
- serum electrolytes, creatinine, liver enzymes, calcium (hypercalcemia/hypercalciuria due to vitamin D activation by granulomas)
- hypergammaglobulinemia, occasionally RF positive
- elevated serum ACE (non-specific and non-sensitive)
- CXR: predominantly nodular opacities especially in upper lung zones ± hilar adenopathy
- PFTs: normal, obstructive pattern, restrictive pattern with normal flow rates and decreased DL_{CO}, or mixed obstructive/restrictive pattern
- ECG: to rule out conduction abnormalities
- slit-lamp eye exam: to rule out uveitis

Most common presentation: asymptomatic CXR finding

Diagnosis
- biopsy
  - transbronchial lung biopsy, transbronchial lymph node aspiration, endobronchial ultrasound guided surgical (EBUS) biopsy, or mediastinoscopic lymph node biopsy for granulomas
  - in ~75% of cases, transbronchial biopsy shows granulomas in the parenchyma even if the CXR is normal

Hilar adenopathy refers to enlargement of mediastinal lymph nodes which is most often seen by standard CXR as spherical/ellipsoidal and/or calcified nodes. If unilateral - think neoplasia, TB, or sarcoid. If bilateral - think sarcoid or lymphoma

Staging
- radiographic, based on CXR
  - Stage 0: normal radiograph
  - Stage I: bilateral hilar lymphadenopathy ± right paratracheal lymphadenopathy
  - Stage II: bilateral hilar lymphadenopathy and diffuse interstitial disease
  - Stage III: interstitial disease only (reticulonodular pattern or nodular pattern)
  - Stage IV: pulmonary fibrosis (honeycombing)

Treatment
- 85% of stage I resolve spontaneously
- 50% of stage II resolve spontaneously
- steroids for symptoms, declining lung function, hypercalcemia, or involvement of eye, CNS, kidney, or heart (not for abnormal CXR alone)
- methotrexate or other immunosuppressives occasionally used

Corticosteroids for Pulmonary Sarcoidosis
Cochrane DB Syst Rev 2005;CD001114
Study: Meta-analysis of 13 RCTs involving 1,066 participants examining the use of steroids (oral or inhaled) in sarcoidosis.
Results: Oral steroids demonstrated an improvement in CXR (RR 1.46, 95% CI 1.01-2.09). For inhaled corticosteroids, two studies showed no improvement in lung function and one study showed an improvement in diffusing capacity. No data on side-effects.
Conclusions: Oral steroids improve CXR findings and global scores of CXR, symptoms, and spirometry over 3-24 mo, but do not improve lung function or modify disease course. Oral steroids may be of benefit for patients with Stage 2 and 3 disease.

Prognosis
- approximately 10% mortality secondary to progressive fibrosis of lung parenchyma

Known Etiologic Agents

HYPERSENSITIVITY PNEUMONITIS
- also known as extrinsic allergic alveolitis
- non-IgE mediated inflammation of lung parenchyma (acute, subacute, and chronic forms)
- caused by sensitization to inhaled agents, usually organic dust
- pathology: airway-centered, poorly formed granulomas and lymphocytic inflammation
- exposure usually related to occupation or hobby
  - Farmer's Lung (*Thermophilic actinomycetes*)
  - Bird Breeder's/Bird Fancier's Lung (immune response to bird IgA)
  - Humidifier Lung (*Aureobasidium pullulans*)
  - Sauna Taker's Lung (*Aureobasidium* spp.)

Signs and Symptoms
- acute presentation: (4-6 h after exposure)
  - dyspnea, cough, fever, chills, malaise (lasting 18-24 h)
  - CXR: diffuse infiltrates
  - type III (immune complex) reaction
- subacute presentation: more insidious onset than acute presentation
- chronic presentation
  - insidious onset
  - dyspnea, cough, malaise, anorexia, weight loss
  - PFTs: progressively restrictive
  - CXR: predominantly upper lobe reticulonodular pattern
  - type IV (cell mediated, delayed hypersensitivity) reaction (see Rheumatology, RH2)
- in both acute and chronic reactions, serum precipitins may be detectable (neither sensitive nor specific)

Calcified diaphragmatic plaques are highly suggestive of asbestosis, especially if bilateral

CXR Fibrotic Patterns
- Asbestosis: lower > upper lobes
- Silicosis: upper > lower lobes
- Coal: upper > lower lobes

Treatment
- early diagnosis: avoidance of further exposure is critical as chronic changes are irreversible
- systemic corticosteroids can relieve symptoms and speed resolution

Remember to involve occupational health and place of work for data collection and treatment plan. Also counsel re: worker's insurance as per jurisdiction (e.g. Workers Safety Insurance Board [WSIB] in Ontario)

PNEUMOCONIOSES
- reaction to inhaled inorganic dusts 0.5–5 μm in size
- no effective treatment, therefore key is exposure prevention through the use of protective equipment
- smoking cessation, annual influenza and pneumococcal vaccination, rehabilitation, lung transplant for endstage disease

Table 18. Pneumoconioses

Diagnosis	Etiology	Symptoms	Investigations	Complications
Asbestosis	Exposure risks: insulation, shipyard, construction, brake linings, pipe fitters, plumbers Slowly progressive diffuse interstitial fibrosis induced by inhaled asbestos fibres Usually >10-20 yr of exposure; may develop with shorter but heavier exposure; typically prolonged interval (20-30 yr) between exposure and clinical disease	Insidious onset Dyspnea Cough: paroxysmal, non-productive Fine end-expiratory crackles (increased at bases) Clubbing (much more likely in asbestosis than silicosis or CWP)	CXR Lower > upper lobe Reticulonodular pattern, may develop IPF-like honeycombing Asbestos exposure can also cause pleural and diaphragmatic plaques (± calcification), pleural effusion, round atelectasis Microscopic examination reveals ferruginous bodies: yellow-brown rod-shaped structures which represent asbestos fibres coated in macrophages	Asbestos exposure increases risk of bronchogenic CA and malignant mesothelioma Risk of lung cancer dramatically increased for smokers
Silicosis	At risk population: sandblasters, rock miners, stone cutters, quarry and highway workers Generally requires >20 yr exposure; may develop with much shorter but heavier exposure	Dyspnea, cough, and wheezing	CXR Upper > lower lobe Early: nodular disease (simple pneumoconiosis), lung function usually normal Late: nodules coalesce into masses (progressive massive fibrosis) Possible hilar lymph node enlargement (frequently calcified), especially "egg shell" calcification	Mycobacterial infection (e.g. TB)
Coal Worker's Pneumoconiosis (CWP)	At risk population: coal workers, graphite workers Coal and silica, coal is less fibrogenic than silica	Pathologic hallmark is coal macule Simple CWP No signs or symptoms, usually normal lung function Complicated CWP (also known as progressive massive fibrosis) Dyspnea Course: few patients progress to complicated CWP	Simple CWP CXR: multiple nodular opacities, mostly upper lobe Complicated CWP CXR: opacities larger and coalesce	Caplan's syndrome: rheumatoid arthritis and CWP present as larger nodules

INTERSTITIAL LUNG DISEASE ASSOCIATED WITH DRUGS OR TREATMENTS
Drug-Induced
- antineoplastic agents: bleomycin, mitomycin, busulfan, cyclophosphamide, methotrexate, chlorambucil, BCNU (carmustine)
- antibiotics: nitrofurantoin, penicillin, sulfonamide
- cardiovascular drugs: amiodarone, tocainide
- anti-inflammatory agents: methotrexate, penicillamine
- gold salts
- illicit drugs (heroin, methadone)
- rituximab, anti-TNF-α agents (infliximab, etanercept, adalimumab)

Radiation-Induced
- early pneumonitis: approximately 6 wk post-exposure
- late fibrosis: 6-12 mo post-exposure
- infiltrates conform to the shape of the radiation field

Pulmonary Vascular Disease

Pulmonary Hypertension

Definition

- mean pulmonary arterial pressure >25 mmHg at rest and >30 mmHg with exercise, or a systolic pulmonary artery pressure of >40 mmHg at rest
- in the past, pulmonary HTN was classified as primary or secondary pulmonary HTN, but this classification was modified to a more clinically useful, treatment based classification

Table 19. World Health Organization Classification of Pulmonary Hypertension

Classification	Some Causes	Treatment Options	Consider in All Patients with PH
I. Pulmonary Arterial HTN	Idiopathic Collagen vascular disease (scleroderma, SLE, RA) Congenital systemic-to-pulmonary shunts (Eisenmenger syndrome) Portopulmonary HTN HIV infection Drugs and toxins (e.g. anorexigens) Pulmonary veno-occlusive disease Schistosomiasis Pulmonary capillary hemangiomatosis Sickle cell disease	No effective treatment CCBs or advanced therapy often needed The latter includes: prostanoids, endothelin receptor antagonists, PDE5 inhibitors Lung transplantation	Oxygen therapy Exercise Consider anticoagulation
II. Pulmonary HTN due to Left Heart Disease	Left-sided atrial or ventricular heart disease (e.g. LV dysfunction) Left-sided valvular heart disease (e.g. aortic stenosis, mitral stenosis)	Treat underlying heart disease	
III. Pulmonary HTN due to Lung Disease and/or Hypoxia	Parenchymal lung disease (COPD, interstitial fibrosis, cystic fibrosis) Chronic alveolar hypoxia (chronic high altitude, alveolar hypoventilation disorders, sleep-disordered breathing)	Treat underlying cause of hypoxia and correct with supplemental oxygen (proven mortality benefit)	
IV. Chronic Thromboembolic Pulmonary HTN (CTEPH)	Thromboembolic obstruction of proximal pulmonary arteries Obstruction of distal pulmonary arteries – PE (thrombus, foreign material, tumour, *in situ* thrombosis)	Anticoagulation, thromboendarterectomy	
V. Pulmonary HTN with Unclear Multifactorial Mechanisms	Hematologic disorders Systemic disorders (e.g. sarcoidosis) Metabolic disorders Extrinsic compression of central pulmonary veins (tumour, adenopathy, fibrosing mediastinitis)	Treat underlying cause	

Adapted from: Simonneau G, et al. *J Am Coll Cardio* 2009;54(1 Suppl):S43-S54

Mechanisms of Pulmonary Hypertension (simplified)

- hypoxic vasoconstriction
  - chronic hypoxia causes pulmonary vasoconstriction by a variety of actions on the pulmonary artery endothelium and smooth muscle cells, such as: down regulation of endothelial nitric oxide synthase and alteration of voltage gated potassium channels leading to vasoconstriction
  - causes: COPD, chronic alveolar hypoxia
- decreased area of pulmonary vascular bed
  - leads to a rise in resting pulmonary arterial pressure
  - causes: collagen vascular disease, HIV infection, drugs and toxins, thrombotic or embolic disease, inflammatory, pulmonary capillary hemangiomatosis, interstitial fibrosis, CF
- volume and pressure overload
  - significant HTN only occurs with excessive volume overload, since pulmonary artery pressure will not rise in otherwise normal lung until pulmonary blood flow exceeds 2.5x the basal rate
  - causes: congenital systemic-to-pulmonary shunts (e.g. VSD, ASD, PDA), portopulmonary HTN, left-sided heart conditions, pulmonary veno-occlusive disease, extrinsic compression of central pulmonary veins

Pulmonary arterial pressures are measured by pulmonary artery catheters (i.e. Swan-Ganz catheter) which are inserted into a large vein (often internal jugular). A balloon at the end of the catheter tip is inflated causing the catheter to advance through the right side of the heart and into the pulmonary artery. This allows for the measurement of RA, RV, PA, and pulmonary capillary wedge pressures as well as sampling of mixed venous blood. A thermistor near the end of the catheter also allows for assessment of cardiac output by thermodilution

IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION (PRIMARY PULMONARY HYPERTENSION)

Definition
- pulmonary HTN in the absence of a demonstrable cause
- exclude:
  - left-sided cardiac valvular disease
  - myocardial disease
  - congenital heart disease
  - any clinically significant parenchymal lung disease
  - systemic connective-tissue disease
  - chronic thromboembolic disease

Epidemiology
- usually presents in young females (20-40 yr); mean age of diagnosis is 36 yr
- most cases are sporadic; familial predisposition in 10% of cases, some linked to mutations in BMPR2
- may be associated with the use of anorexic drugs (e.g. Aminorex®, Fenfluramine®), amphetamines, and cocaine

Signs and Symptoms

Table 20. Signs and Symptoms of Pulmonary Hypertension

Symptoms	Signs
Dyspnea	Loud, palpable P_2
Fatigue	RV heave
Retrosternal chest pain	Right-sided S_4 (due to RVH)
Syncope	Systolic murmur (tricuspid regurgitation [TR])
Symptoms of underlying disease	If RV failure: right sided S_3, increased JVP, positive HJR, peripheral edema, TR
	Reynaud's phenomenon

Investigations
- CXR: enlarged central pulmonary arteries, cardiac changes due to RV enlargement (filling of retrosternal air space)
- ECG
  - RVH/right-sided strain (see Cardiology and Cardiac Surgery, C36)
- 2-D echo doppler assessment of right ventricular systolic pressure
- cardiac catheterization: direct measurement of pulmonary artery pressures (necessary to confirm diagnosis)
- PFTs to asses for underlying lung disease: DL_{CO} usually reduced; volumes and flows normal
- CT angiogram to assess lung parenchyma and possible PE
- V/Q scan ± pulmonary angiogram to rule out thromboembolic disease
- serology: ANA positive in 30% of patients with primary pulmonary HTN; other serologic markers can be used in the appropriate clinical setting

Treatment
- see Table 19

Prognosis
- 2-3 yr mean survival from time of diagnosis
- survival decreases to approximately 1 yr if severe pulmonary HTN or right-heart failure

Guidelines for Vasodilator Response in Pulmonary Arterial HTN
- Patients with IPAH that respond to vasodilators acutely, have an improved survival with long-term use of CCBs
- Vasoreactivity testing: short-acting agent such as IV epoprostenol, IV adenosine, or inhaled NO
- Positive vasodilator response: mean PAP fall of at least 10 mmHg to ≤40 mmHg with an increased or unchanged cardiac output (European Society of Cardiology)
- Positive vasodilator response: should be considered as candidate for trial of oral CCB therapy

Medical Therapy for Pulmonary Arterial Hypertension. ACCP Evidence-Based Clinical Practice Guidelines. *Chest* 2004;(Suppl)06:126

Virchow's Triad
- Venous stasis
- Endothelial cell damage
- Hypercoagulable states

Pulmonary Embolism

Definition
- lodging of a blood clot in the pulmonary arterial tree with subsequent increase in pulmonary vascular resistance, impaired V/Q matching, and possibly reduced pulmonary blood flow

Etiology and Pathophysiology
- one of the most common causes of preventable death in the hospital
- proximal leg thrombi (popliteal, femoral, or iliac veins) are the source of most clinically recognized pulmonary emboli
- thrombi often start in calf, but must propagate into proximal veins to create a sufficiently large thrombus for a clinically significant PE
- fewer than 30% of patients have clinical evidence of DVT (e.g. leg swelling, pain, or tenderness)
- always suspect PE if patient develops fever, sudden dyspnea, chest pain, or collapse 1-2 wk after surgery

Multidetector Computed Tomography for Acute Pulmonary Embolism (PIOPED II Trial)
NEJM 2006;354:2317-2327
Study: Multicentre, prospective study investigating accuracy of computed tomography angiography (CTA) alone and combined with venous phase imaging (CTA-CTV) for the diagnosis of PE.
Patients: 824 patients of several thousand eligible for study received reference diagnosis to confirm absence or presence of PE (V/Q scan, venous compression U/S of lower extremities, and pulmonary digital-subtraction angiography (DSA) if necessary). To confirm absence, patients in whom PE was excluded were telephoned 3-6 mo after enrollment. Any deaths were reviewed by an outcome committee. All patients enrolled also underwent clinical assessment of PE (including a Wells' score) prior to imaging.
Outcomes: Diagnosis of pulmonary embolism.
Results: 773 of 824 patients had adequate CTAs for interpretation. PE was diagnosed in 192 of the 824 patients. Sensitivity was 83% (150 of 181 patients, 95% CI 0.76-0.92) and specificity was 96% (567 of 592 patients, 95% CI 0.93-0.97). However, the predictive value of CTA-CTV varied when clinical pre-test probability was taken into account. PPV of CTA for high, intermediate and low clinical probability were 96% (95% CI 0.78-0.99), 92% (95% CI 0.84-0.96), and 58% (95% CI 0.40-0.73), respectively. NPV of CTA for high, intermediate and low clinical probability were 60% (95% CI 0.32-0.83), 89% (95% CI 0.82-0.93), and 96% (95% CI 0.92-0.98) respectively.
Conclusion: CTA is effective for diagnosing or excluding PE in accordance with assessment of clinical pretest probability. When clinical probability is inconsistent with imaging results, further investigations are required to rule out PE.

Risk Factors

- stasis
  - immobilization: paralysis, stroke, bed rest, prolonged sitting during travel, immobilization of an extremity after fracture
  - obesity, CHF
  - chronic venous insufficiency
- endothelial cell damage
  - post-operative injury, trauma
- hypercoagulable states
  - underlying malignancy (particularly adenocarcinoma)
  - cancer treatment (chemotherapy, hormonal)
  - exogenous estrogen administration (OCP, HRT)
  - pregnancy, post-partum
  - prior history of DVT/PE, family history
  - nephrotic syndrome
  - coagulopathies: Factor V Leiden, Prothrombin 20210A variant, inherited deficiencies of antithrombin/protein C/protein S, antiphospholipid antibody, hyperhomocysteinemia, increased Factor VIII levels, and myeloproliferative disease
- increasing age

Clinical Prediction Rule for Pulmonary Embolism
J Thromb Hemost 2000;83:416-420
Wells' Criteria

Risk Factors	Points
Clinical signs of DVT	3.0
No more likely alternative diagnosis (using H&P, CXR, ECG)	3.0
Immobilization or surgery in the previous 4 wk	1.5
Previous PE/DVT	1.5
HR >100 beats/min	1.5
Hemoptysis	1.0
Malignancy	1.0
Clinical Probability	
Low (0-2)	3%
Intermediate (3-6)	28%
High (>6)	78%
Modified Wells": >4 PE likely; ≤4 PE unlikely	

JAMA 2006

Investigations (if highly suspicious, go straight to CT angiogram)

- see Emergency Medicine, ER32

Table 21. Common Investigations for Pulmonary Embolism

Investigation	Purpose/Utility
Pulmonary Angiogram (Gold Standard)	Filling defect indicative of embolus; negative angiogram excludes clinically relevant PE More invasive, and harder to perform than CT, therefore done infrequently
D-Dimer	Highly sensitive D-dimer result can exclude DVT/PE if pretest probability is already low Little value if pretest probability is high If D-dimer positive, will need further evaluation with compression U/S
CT Angiogram	Both sensitive and specific for PE Diagnosis and management uncertain for small filling defects CT may identify an alternative diagnosis if PE is not present CT scanning of the proximal leg and pelvic veins can be done at the same time and may be helpful
Venous Duplex U/S or Doppler	With leg symptoms Positive test rules in proximal DVT Negative test rules out proximal DVT Without leg symptoms Positive test rules in proximal DVT Negative test does not rule out a DVT: patient may have non-occlusive or calf DVT
ECG	Findings not sensitive or specific Sinus tachycardia most common; may see non-specific ST segment and T wave changes RV strain, RAD, RBBB, S1-Q3-T3 with massive embolization
CXR	Frequently normal; no specific features Atelectasis (subsegmental), elevation of a hemidiaphragm Pleural effusion: usually small Hampton's hump: cone-shaped area of peripheral opacification representing infarction Westermark's sign: dilated proximal pulmonary artery with distal oligemia/decreased vascular markings (difficult to assess without prior films) Dilatation of proximal PA: rare
V/Q Scan	Very sensitive but low specificity Order scan if CXR normal, no COPD Contraindication to CT (contrast allergy, renal dysfunction, pregnancy) Avoid V/Q scan if CXR abnormal or COPD Inpatient Suspect massive PE Results Normal: excludes the diagnosis of PE High probability: most likely means PE present, unless pre-test probability is low 60% of V/Q scans are nondiagnostic
Echocardiogram	Useful to assess massive or chronic PE Not routinely done
ABG	No diagnostic use in PE (insensitive and nonspecific) May show respiratory alkalosis (due to hyperventilation)

D-dimer is elevated in patients with recent surgery, cancer, inflammation, infection, and severe renal dysfunction. It has good sensitivity and negative predictive value, but poor specificity and positive predictive value

Classic ECG finding of PE is S_1-Q_3-T_3 (inverted T_3), but most commonly see only sinus tachycardia

Evaluation of a Suspected Pulmonary Embolism

Low clinical probability of embolism

D-dimer (+ve) → **CT scan (+ve)** → ruled in
(–ve) → ruled out (–ve) → ruled out

Intermediate or high probability

CT scan (–ve) → ruled out
(+ve) → ruled in

Notes
- Use D-dimers only if low clinical probability, otherwise, go straight to CT
- If using V/Q scans (CT contrast allergy or renal failure):
  - Negative V/Q scan rules out the diagnosis
  - High probability V/Q scan only rules in the diagnosis if have high clinical suspicion
  - Inconclusive V/Q scan requires leg U/S to look for DVT or CT

Treatment

- admit for observation (patients with DVT only are often sent home on LMWH)
- oxygen: supplemental O_2 if hypoxemic or short of breath
- pain relief: analgesics if chest pain – narcotics or acetominophen
- acute anticoagulation: therapeutic-dose SC LMWH or IV heparin – start ASAP
  - anticoagulation stops clot propagation, prevents new clots and allows endogenous fibrinolytic system to dissolve existing thromboemboli over months
  - get baseline CBC, INR, aPTT ± renal function ± liver function
  - for SC LMWH: dalteparin 200 U/kg once daily, enoxaparin 1 mg/kg bid or 1.5mg/kg once daily, or tinzaparin 175 U/kg once daily – no lab monitoring – avoid or reduce dose in renal dysfunction
  - for IV heparin: bolus of 75 U/kg (usually 5,000 U) followed by infusion starting at 20 U/kg/h – aim for aPTT 2-3x control
- long-term anticoagulation
  - warfarin: start the same day as LMWH/heparin – overlap warfarin with LMWH/heparin for at least 5 d and until INR in target range of 2-3 for at least 2 d
  - LMWH instead of warfarin for pregnancy, active cancer, or high bleeding risk patients
  - direct thrombin inhibitors: can treat from outset with rivaroxaban; dabigatran has been shown to have lower bleeding risk than warfarin; no monitoring required, however agents not reversible, so avoid if bleeding concerns
- IV thrombolytic therapy
  - if patient has massive PE (hypotension or clinical right heart failure) and no contraindications
  - hastens resolution of PE but may not improve survival or long-term outcome and doubles risk of major bleeding
- interventional thrombolytic therapy
  - massive PE is preferentially treated with catheter-directed thrombolysis by an interventional radiologist
  - works better than IV thrombolytic therapy and fewer contraindications
- IVC filter: only if recent proximal DVT + absolute contraindication to anticoagulation
- duration of long-term anticoagulation: individualized, however generally
  - if reversible cause for PE (surgery, injury, pregnancy, etc.): 3-6 mo
  - if PE unprovoked: 6 mo to indefinite
  - if ongoing major risk factor (active cancer, antiphospholipid antibody, etc.): indefinite

Thromboprophylaxis

- mandatory for most hospital patients: reduces DVT, PE, all-cause mortality, cost-effective
- start ASAP
- continue at least until discharge or recommend extending for 35 d post-operatively, if major orthopedic surgery

Table 22. VTE Risk Categories and Prophylaxis (see Hematology, H35)

Risk Group	Prophylaxis Options
Low Thrombosis Risk	
Medical patients: fully mobile	No specific prophylaxis
Surgery: <30 min, fully mobile	Frequent ambulation
Moderate Thrombosis Risk	
Most general, gynecologic, urologic surgery	LMWH
Sick medical patients	Low dose unfractionated heparin
	Fondaparinux
High Thrombosis Risk	LMWH
Arthoplasty, hip fracture surgery	Fondaparinux
Major trauma, spinal cord injury	Warfarin (INR 2-3)
	Dabigatran
	Apixaban
	Rivaroxaban
	Low dose unfractionated heparin
High Bleeding Risk	
Neurosurgery, intracranial bleed	TED stockings, pneumatic compression devices
Active bleeding	LMWH or low dose heparin when bleeding risk decreases

PE Rule Out Criteria (PERC)
Prospective Multicentre Evaluation of the Pulmonary Embolism Rule Out Criteria
J Thromb Hemost 2008;6:772

- Age less than 50 yr
- Heart rate less than 100 bpm
- Oxyhemoglobin saturation ≥95 percent
- No hemoptysis
- No estrogen use
- No prior DVT or PE
- No unilateral leg swelling
- No surgery or trauma requiring hospitalization within the past 4 wk

Acute PE can probably be excluded without further diagnostic testing if the patient meets all PERC criteria AND there is a low clinical suspicion for PE, according to either the Wells' criteria or a low gestalt probability determined by the clinician prior to diagnostic testing for PE.

Extended Use of Dabigatran, Warfarin or Placebo in Venous Thromboembolism
NEJM 2013;368:709-718
Study: Two double blind, RCTs; one comparing against placebo, the other against active treatment.
Population: 4,199 patients (2,856 in active-control study, 1,343 in placebo-control study) with VTE who had completed at least 3 mo of therapy.
Intervention: In the active-control study, patients randomized to either 150 mg dabigatran or warfarin (INR 2.0-3.0). Patients in the placebo-control study received either 150 mg dabigatran or placebo.
Outcome: Recurrence of VTE, risk of major or clinically relevant bleed.
Results: In the active-control study, there was a hazard ratio (HR) of 1.44 (95% CI 0.78-2.64 for non-inferiority) of recurrent VTE with dabigatran vs. warfarin. HR of major or clinically relevant bleed was 0.54 (95% CI 0.41-0.71). In the placebo-control study, the HR of VTE with dabigatran vs. placebo was 0.08 (95% CI 0.02-0.25). HR of major or clinically relevant bleed was 2.92 (95% CI 1.52-5.60).
Conclusions: Dabigatran appears to be non-inferior to warfarin in the prevention of VTE recurrence. Dabigatran is associated with a lower risk of major or clinically relevant bleed than warfarin, but greater than placebo.

Workup for Idiopathic VTE
Thrombophilia Workup: recurrent or idiopathic DVT/PE, age <50, FHx, unusual location, massive

Malignancy Workup: 12% of patients with idiopathic VTE will have a malignancy

The Use of Unfractionated Heparin Should Be Limited to:

- Patients with severe renal dysfunction (CrCl <30 ml/min) in whom LMWH and novel oral anticoagulation should be avoided
- Patients at elevated risk of bleeding that may need rapid reversal of anticoagulation
- Patients who receive thrombolytic therapy

Pulmonary Vasculitis

Table 23. Pulmonary Vasculitis

Disease	Definition	Pulmonary Features	Extra-pulmonary Features	Investigations	Treatment
Granulomatosis with Polyangiitis (Wegener's Granulomatosis) (see Nephrology, NP23)	Systemic vasculitis of medium and small arteries	Necrotizing granulomatous lesions of the upper and lower respiratory tract	Focal necrotizing lesions of arteries and veins; crescentic glomerulonephritis	CXR: nodules, cavities, and alveolar opacities c-ANCA Tissue confirmation	Corticosteroids and cyclophosphamide or rituximab
Churg-Strauss Syndrome (eosinophilic granulomatosis with polyangiitis)	Multisystem disorder characterized by allergic rhinitis, asthma, and prominent peripheral eosinophilia	Asthma Infiltrates	Life-threatening systemic vasculitis involving the lungs, pericardium and heart, kidneys, skin, and PNS (mononeuritis multiplex)	Peripheral eosinophilia is the most common finding p-ANCA may be positive Biopsy involved tissue	Corticosteroids
Goodpasture's Disease (see Nephrology, NP23)	A disorder characterized by diffuse alveolar hemorrhage and glomerulonephritis caused by anti-GBM antibodies, which cross-react with basement membranes of the kidney and lung	Hemoptysis May follow an influenza infection	Anemia	CXR: may see alveolar infiltrates if hemorrhage is profuse ELISA test with anti-GBM antibodies Renal biopsy/indirect immunofluorescence shows linear staining	Acutely: corticosteroids, plasmapheresis Immunosuppressive therapy Severe cases: bilateral nephrectomy
Systemic Lupus Erythematosus, Rheumatoid Arthritis, Scleroderma	See Rheumatology, RH8				

Pulmonary Edema

- see Cardiology and Cardiac Surgery, C37

Scleroderma is the most common collagen vascular disease affecting the lung

Diseases of the Mediastinum and Pleura

Mediastinal Masses

Definition
- mediastinum: bound by the thoracic inlet, diaphragm, sternum, vertebral bodies, and the pleura
- can be broken down into 3 compartments: anterior, middle, and posterior

Etiology and Pathophysiology
- diagnosis is aided by location and patient's age
- anterior compartment: more likely to be malignant
  - "Four Ts" (see sidebar), lymphoma, lipoma, pericardial cyst
- middle compartment
  - pericardial cyst, bronchogenic cyst/tumour, lymphoma, lymph node enlargement, aortic aneurysm
- posterior compartment
  - neurogenic tumours, meningocele, enteric cysts, lymphoma, diaphragmatic hernias, esophageal tumour, aortic aneurysm

Differential of an Anterior Compartment Mass

4 Ts
Thymoma
Thyroid enlargement (goitre)
Teratoma
Tumours
(lymphoma, parathyroid, esophageal, angiomatous)

Signs and Symptoms
- 50% asymptomatic (mainly benign); when symptomatic, 50% are malignant
- chest pain, cough, dyspnea, recurrent respiratory infections
- hoarseness, dysphagia, Horner's syndrome, facial/upper extremity edema (SVC compression)
- paraneoplastic syndromes (e.g. myasthenia gravis [thymomas])

Mediastinal Components
Anterior: sternum to pericardium and great vessels. Includes: thymus, extrapericardial aorta and branches, great veins, lymphatic tissues
Middle: pericardium (anteriorly) posterior pericardial reflection, diaphragm, thoracic inlet. Includes: heart, intrapericardial great vessels, pericardium, trachea
Posterior: posterior pericardial reflection, posterior border of vertebral bodies, first rib to the diaphragm. Includes: esophagus, vagus nerve, thoracic duct, sympathetic chain, azygous venous system

Investigations
- CXR (compare to previous)
- CT with contrast (anatomic location, density, relation to mediastinal vascular structures)
- MRI: specifically indicated in the evaluation of neurogenic tumours
- U/S (best for assessment of structures in close proximity to the heart and pericardium)
- radionuclide scanning: ^{131}I (for thyroid), gallium (for lymphoma)
- biochemical studies: thyroid function, serum calcium, phosphate, PTH, AFP, β-hCG
- biopsy (mediastinoscopy, percutaneous needle aspiration)

Horner's Syndrome
Ptosis, Miosis, Anhydrosis

Management
- excision if symptomatic enlarging benign masses or concerns of malignancy
- resect bronchogenic cysts and localized neurogenic tumours via minimally invasive video assisted procedures
- exploration via sternotomy or thoracotomy
- diagnostic biopsy rather than major operation if mass is likely to be a lymphoma, germ cell tumour, or unresectable invasive malignancy
- ± post-operative radiotherapy/chemotherapy if malignant

Mediastinitis

- most common causes: post-operative complications of cardiovascular or thoracic surgical procedures

Acute
- etiology
  - complication of endoscopy (e.g. esophageal perforation providing entry point for infection)
  - esophageal or cardiac surgery
  - tumour necrosis
- signs and symptoms
  - fever, substernal pain
  - pneumomediastinum, mediastinal compression
  - Hamman's sign (auscultatory "crunch" during cardiac systole)
- treatment
  - antibiotics, drainage, ± surgical closure of perforation

Chronic
- usually granulomatous process or fibrosis related to previous infection (e.g. histoplasmosis, TB, sarcoidosis, syphilis)

Pleural Effusions


Definition
- excess amount of fluid in the pleural space (normally up to 25 mL)

Etiology
- disruption of normal equilibrium between pleural fluid formation/entry and pleural fluid absorption/exit
- pleural effusions are classified as transudative or exudative
  - distinguish clinically using Light's Criteria, which has a sensitivity of 98% and specificity of 83% for identifying exudative pleural effusions

Table 24. Laboratory Values in Transudative and Exudative Pleural Effusion

	Light's Criteria	Modified Light's Criteria
Protein – Pleural/Serum	>0.5	>0.5
LDH – Pleural/Serum	>0.6	>0.6
Pleural LDH	>2/3 upper limit of N serum LDH	>0.45 upper limit of N serum LDH
Exudate = at Least One Criterion Met		

Ann Intern Med 1979;77:507-513 *Chest* 1997;111:970-980

All criteria for transudate must be fulfilled to be considered a transudative effusion. If any one of the criteria for exudates is met – it is an exudate

Transudative Pleural Effusions
- pathophysiology: alteration of systemic factors that affect the formation and absorption of pleural fluid (e.g. increased capillary hydrostatic pressure, decreased plasma oncotic pressure)
- etiology
  - CHF: usually right-sided or bilateral cirrhosis
  - nephrotic syndrome, protein losing enteropathy, cirrhosis
  - pulmonary embolism (may cause transudative but more often causes exudative effusion)
  - peritoneal dialysis, hypothyroidism, CF, urinothorax

Transudative effusions are usually bilateral, not unilateral

Exudative effusions can be bilateral or unilateral

Exudative Pleural Effusions
- pathophysiology: increased permeability of pleural capillaries or lymphatic dysfunction
- etiology (see Table 25)

Table 25. Exudative Pleural Effusion Etiologies

Etiology	Examples
Infectious	Parapneumonic effusion (associated with bacterial pneumonia, lung abscess) Empyema (bacterial, fungal, TB) TB pleuritis Viral infection
Malignancy	Lung carcinoma (35%) Lymphoma (10%) Metastases: breast (25%), ovary, kidney Mesothelioma
Inflammatory	Collagen vascular diseases: RA, SLE Pulmonary embolism Post-CABG Drug reaction
Intra-Abdominal	Subphrenic abscess Pancreatic disease (elevated pleural fluid amylase) Meigs' syndrome (ascites and hydrothorax associated with an ovarian fibroma or other pelvic tumour)
Intra-Thoracic	Esophageal perforation (elevated fluid amylase)
Trauma	Chylothorax: thoracic duct disrupted and chyle accumulates in the pleural space due to trauma, tumour Hemothorax: rupture of a blood vessel, commonly by trauma or tumours Pneumothorax (spontaneous, traumatic, tension)

Appearance of Pleural Fluid
- Bloody: trauma, malignancy
- White: chylothorax, empyema
- Black: aspergillosis, amoebic liver abscess
- Yellow-green: rheumatoid pleurisy
- Viscous: malignant mesothelioma
- Ammonia odour: urinothorax
- Food particles: esophageal rupture

Signs and Symptoms
- often asymptomatic
- dyspnea: varies with size of effusion and underlying lung function
- pleuritic chest pain
- inspection: trachea deviates away from effusion, ipsilateral decreased expansion
- percussion: decreased tactile fremitus, dullness
- auscultation: decreased breath sounds, bronchial breathing and egophony at upper level, pleural friction rub

Investigations
- CXR
  - must have >200 mL of pleural fluid for visualization on PA film
  - lateral: >50 mL leads to blunting of posterior costophrenic angle
  - PA: blunting of lateral costophrenic angle
  - dense opacification of lung fields with concave meniscus
  - decubitus: fluid will shift unless it is loculated
  - supine: fluid will appear as general haziness
- CT may be helpful in differentiating parenchymal from pleural abnormalities, may identify underlying lung pathology
- U/S: detects small effusions and can guide thoracentesis
- thoracentesis: indicated if pleural effusion is a new finding; be sure to send off blood work (LDH, glucose, protein) at the same time for comparison
  - risk of re-expansion pulmonary edema if >1.5 L of fluid is removed
  - inspect for colour, character, and odour of fluid
  - analyze fluid
- pleural biopsy: indicated if suspect TB, mesothelioma, or other malignancy (and if cytology negative)
- ± U/S: detects small effusions and can guide thoracentesis
- treatment depends on cause, ± drainage if symptomatic
- CT can be helpful in differentiating parenchymal from pleural abnormalities

Role of CT in Pleural Effusion
- To assess for fluid loculation, pleural thickening and nodules, parenchymal abnormalities and adenopathy
- Helps to distinguish benign from malignant effusion and transudative from exudative effusion
- May not distinguish empyema from parapneumonic effusion

Features of Malignant Effusion
- Multiple pleural nodules
- Nodular pleural thickening

Features of Exudative Effusion
- Loculation
- Pleural thickening
- Pleural nodules
- Extrapleural fat of increased density

Table 26. Analysis of Pleural Effusion

Measure	Purpose
Protein, LDH	Transudate vs. exudate
Gram stain, Ziehl-Nielsen stain (TB), culture	Looking for specific organisms
Cell count differential	Neutrophils vs. lymphocytes (lymphocytic effusion in TB, cancer, lymphoma, serositis)
Cytology	Malignancy, infection
Glucose (low)	RA, TB, empyema, malignancy, esophageal rupture
Rheumatoid factor, ANA, complement	Collagen vascular disease
Amylase	Pancreatitis, esophageal perforation, malignancy
pH	Empyema <7.2, TB, and mesothelioma <7.3
Blood	Mostly traumatic, malignancy, PE with infarction, TB
Triglycerides	Chylothorax from thoracic duct leakage, mostly due to trauma, lung CA, or lymphoma

Appearance of Pleural Fluid
- Bloody: trauma, malignancy
- White: chylothorax, empyema
- Black: aspergillosis, amoebic liver abscess
- Yellow-green: rheumatoid pleurisy
- Viscous: malignant mesothelioma
- Ammonia odour: urinothorax
- Food particles: esophageal rupture

Treatment
- thoracentesis
- treat underlying cause
- consider indwelling pleural catheter or pleurodesis in refractory effusions

Complicated Parapneumonic Effusion

- persistent bacteria in the pleural space but fluid is non-purulent
- neutrophils, pleural fluid acidosis (pH <7.00), and high LDH
- often no bacteria grown since rapidly cleared from pleural space
- fibrin layer leading to loculation of pleural fluid
- treatment: antibiotics and drainage, treat as an empyema

Pleural Effusions

Simple Effusion
pH >7.2, LDH <1/2 serum, glucose >2.2

Complicated Effusion
pH <7.2, LDH >1/2 serum, glucose <2.2, positive Gram stain
Needs drainage

Empyema

Definition
- pus in pleural space or an effusion with organisms seen on a Gram stain or culture (e.g. pleural fluid is grossly purulent)
- positive culture is not required for diagnosis

Etiology
- contiguous spread from lung infection (most commonly anaerobes) or infection through chest wall (e.g. trauma, surgery)

Signs and Symptoms
- fever, pleuritic chest pain

Investigations
- CT chest
- thoracentesis
- PMNs (lymphocytes in TB) ± visible organisms on Gram stain

Treatment
- antibiotic therapy for at least 4-6 wk (rarely effective alone)
- complete pleural drainage with chest tube
- if loculated, more difficult to drain – may require surgical drainage with video-assisted thoracopic surgery (VATS), or surgical removal of fibrin coating to allow lung re-expansion (decortication)

When possible, organism-directed therapy, guided by culture sensitivities or local patterns of drug resistance, should be utilized

Atelectasis

- see General Surgery, GS10

Pneumothorax

Definition
- presence of air in the pleural space

Pathophysiology
- entry of air into pleural space raises intrapleural pressure causing partial lung deflation

Etiology
- traumatic: penetrating or non-penetrating chest injuries
- iatrogenic (central venous catheter, thoracentesis, mechanical ventilation with barotrauma)
- spontaneous (no history of trauma)
  - primary (no underlying lung disease)
    - spontaneous rupture of apical subpleural bleb of lung into pleural space
    - predominantly tall, healthy, young males
  - secondary (underlying lung disease)
    - rupture of subpleural bleb which migrates along bronchioalveolar sheath to the mediastinum then to the intrapleural space
    - necrosis of lung tissue adjacent to pleural surface (e.g. pneumonia, abscess, PCP, lung CA, emphysema)

Need to Rule Out Life-Threatening Tension Pneumothorax

If pneumothorax with:
- Severe respiratory distress
- Tracheal deviation to contralateral side
- Distended neck veins (↑ JVP)
- Hypotension

Do not perform CXR
Needs immediate treatment
See Emergency Medicine, ER11

Signs and Symptoms
- can be asymptomatic
- acute-onset pleuritic chest pain, dyspnea

- tachypnea, tachycardia
- tracheal deviation (contralateral deviation in tension pneumothorax)
- ipsilateral diminished chest expansion
- decreased tactile/vocal fremitus
- hyperresonance
- ipsilateral diminished breath sounds

Investigations
- CXR
  - small: separation of visceral and parietal pleura seen as fine crescentic line parallel to chest wall at apex
  - large: increased density and decreased volume of lung on side of pneumothorax
  - see Medical Imaging, MI8

Treatment
- small pneumothoraces (<20% with no signs of respiratory/circulatory collapse) resolve spontaneously; breathing 100% oxygen accelerates resorption of air
- small intercostal tube with Heimlich valve for most spontaneous pneumothoraces
- large pneumothoraces or those complicating underlying lung disease require placement of a chest tube connected to underwater seal ± suction
- for repeated episodes: pleurodesis with sclerosing agent or apical bullectomy and abrasion
- treat underlying cause (e.g. antibiotic for PCP)

Asbestos-Related Pleural Disease and Mesothelioma

Etiology and Pathophysiology
- benign manifestations of asbestos exposure
  - "benign asbestos pleural effusion"
    - exudative effusion, typically ~10 yr after exposure, resolves
  - pleural plaques, usually calcified
    - marker of exposure; usually an asymptomatic radiologic finding
- mesothelioma
  - primary malignancy of the pleura
  - decades after asbestos exposure (even with limited exposure)
  - smoking not a risk factor, but asbestos and smoking synergistically increase risk of lung cancer

Signs and Symptoms
- persistent chest pain, dyspnea, cough, bloody pleural effusion, weight loss

Investigations
- biopsy (pleuroscopic or open)
- needle biopsy may seed needle tract with tumour

Treatment
- resection (extrapleural pneumonectomy) requires careful patient selection; rarely successful (average survival <1 yr)

Respiratory Failure

Definition
- failure of respiratory system to maintain normal blood gases
- hypoxemic (P_aO_2 <60 mmHg)
- hypercapnic (P_aCO_2 >50 mmHg)
- acute vs. chronic (compensatory mechanisms activated)

Signs and Symptoms
- signs of underlying disease
- hypoxemia: restlessness, confusion, cyanosis, coma, cor pulmonale
- hypercapnia: headache, dyspnea, drowsiness, asterixis, warm periphery, plethora, increased ICP (secondary to vasodilatation)

Investigations
- serial ABGs
- CXR and/or CT, bronchoscopy to characterize underlying cause if unclear

Hypoxemic Respiratory Failure

Definition
- P_aO_2 decreased, P_aCO_2 normal or decreased

Treatment
- reverse the underlying pathology
- oxygen therapy: maintain oxygenation (if shunt present, supplemental O_2 is less effective; see Anesthesia, A9, for oxygen delivery systems)
- ventilation, BiPAP, and PEEP/CPAP (see Anesthesia, A10): positive pressure can recruit alveoli and redistribute lung fluid
- improve cardiac output: ± hemodynamic support (fluids, vasopressors, inotropes), reduction of O_2 requirements

Table 27. Approach to Hypoxemia

Type of Hypoxemia	Settings	P_aCO_2	A-aDO_2	Oxygen Therapy	Ventilation, BiPAP and PEEP	Improved Cardiac Output
1. Low F_iO_2	Postop, high altitude	N or ↓	N	Improves	No change	No change
2. Hypoventilation	Drug overdose	↑	N	Improves	Improves with ventilation	No change
3a. Shunt	ARDS, pneumonia	N or ↓	↑	No change	Improves (except if one-sided)	Improves
3b. Shunt (Right to Left)	Pulmonary HTN	N or ↓	↑	No change	Worsens	Worsens
4. Low Mixed Venous O_2 Content	Shock	↓	↑	Improves or no change	Worsens	Improves
5. V/Q Mismatch	COPD	N or ↑	↑	Improves (small amounts)	Often improves	Improves
6. Diffusion Impairment	ILD, emphysema	N	↑	Improves	Improves with positive pressure	No change or worsens

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Hypercapnic Respiratory Failure

- P_aCO_2 increased, P_aO_2 decreased

Pathophysiology
- increased CO_2 production: fever, sepsis, seizure, acidosis, carbohydrate load
- alveolar hypoventilation: COPD, asthma, CF, chest wall disorder, dead space ventilation (rapid shallow breathing)
  - inefficient gas exchange results in inadequate CO_2 removal in spite of normal or increased minute volume
- hypoventilation
  - central: brainstem stroke, hypothyroidism, severe metabolic alkalosis, drugs (opiates, benzodiazepines)
  - neuromuscular: myasthenia gravis, Guillain-Barré, phrenic nerve injury, muscular dystrophy, polymyositis, kyphoscoliosis
  - muscle fatigue

Treatment
- reverse the underlying pathology
- if P_aCO_2 >50 mmHg and pH is acidemic consider noninvasive or mechanical ventilation
- correct exacerbating factors
  - NTT/ETT suction: clearance of secretions
  - bronchodilators: reduction of airway resistance
  - antibiotics: treatment of infections
- maintain oxygenation (see above)
- diet: increased carbohydrate can increase P_aCO_2 in those with mechanical or limited alveolar ventilation; high lipids decrease P_aCO_2

Dead Space
- Ventilation without perfusion
- The opposite of shunt

Causes of Hypercapnia
- High Inspired CO_2
- Low Total Ventilation
- High Deadspace Ventilation
- High CO_2 Production

In chronic hypercapnia, supplemental O_2 may decrease the hypoxic drive to breathe, but do not deny oxygen if the patient is hypoxic

In COPD patients with chronic hypercapnia ("CO_2 retainers"), provide supplemental oxygen to achieve target SaO_2 from 88-92%

Acute Respiratory Distress Syndrome

- clinical syndrome characterized by severe respiratory distress, hypoxemia, and noncardiogenic pulmonary edema
- The Berlin Criteria (*JAMA* 2012; 307:2526-2533) for ARDS
  - acute onset
    - within 7 d of a defined event, such as sepsis, pneumonia, or patient noticing worsening of respiratory symptoms
      - – usually occurs within 72 h of presumed trigger
    - bilateral opacities consistent with pulmonary edema on either CT or CXR
    - not *fully* explained by cardiac failure/fluid overload, but patient may have concurrent heart failure
    - objective assessment of cardiac function (e.g. echocardiogram) should be performed even if no clear risk factors

Etiology

- direct lung injury
  - airway: aspiration (**gastric contents**, drowning), **pneumonia**, inhalation injury (oxygen toxicity, nitrogen dioxide, smoke)
  - circulation: embolism (fat, amniotic fluid), reperfusion injury
- indirect lung injury
  - circulation: **sepsis, shock, trauma**, blood transfusion, pancreatitis
  - neurogenic: head trauma, intracranial hemorrhage, drug overdose (narcotics, sedatives, TCAs)

Pathophysiology

- disruption of alveolar capillary membranes → leaky capillaries → interstitial and alveolar pulmonary edema → reduced compliance, V/Q mismatch, shunt, hypoxemia, pulmonary HTN

Clinical Course

A. Exudative Phase

- first 7 d of illness after exposure to ARDS precipitant
- alveolar capillary endothelial cells and type I pneumocytes are injured, resulting in loss of normally tight alveolar barrier
- patients develop dyspnea, tachypnea, increased work of breathing
  - these result in respiratory fatigue and eventually respiratory failure (see *Hypoxemic Respiratory Failure*, R26)

B. Fibroproliferative Phase

- after day 7
- may still experience dyspnea, tachypnea, fatigue, and hypoxemia
- most patients clinically improve and are able to wean off mechanical ventilation
- some patients develop fibrotic lung changes that may require long-term support on supplemental oxygen or even mechanical ventilation
- if fibrosis present, associated with increased mortality

Treatment

- based on ARDS network (see *Landmark Respirology Trials*, R36)
- treat underlying disorder (e.g. antibiotics if infection present)
- mechanical ventilation using low tidal volumes (<6 mL/kg) to prevent barotrauma
  - use optimal amount of PEEP (positive end-expiratory pressure) to keep airways open and allow the use of lower F_iO_2
  - may consider using prone ventilation, and/or inhaled nitric oxide, high frequency oscillator or ECMO (extracorpeal membrane oxygenation) if conventional treatment is failing
- fluids and inotropic therapy (e.g. dopamine, vasopressin) if cardiac output inadequate
- pulmonary-arterial catheter now seldom used for monitoring hemodynamics
- mortality: 30-40%, usually due to non-pulmonary complications
- sequelae of ARDS include residual pulmonary impairment, severe debilitation, polyneuropathy and psychologic difficulties, which gradually improve over time
- most survivors eventually regain near-normal lung function, often with mildly reduced diffusion capacity

ALI vs. ARDS: Definition is the same, except ALI is a $P_aO_2/F_iO_2 \leq 300$, while ARDS is a $P_aO_2/F_iO_2 \leq 200$

Categorization of ARDS as Mild, Moderate or Severe – The Berlin Criteria

ARDS Severity	P_aO_2/FiO_2 (mmHg)*	Mortality (95% CI)#
Mild	200-300	27 (24-30)%
Moderate	100-200	32 (29-34)%
Severe	<100	45 (42-48)%

*on ≥5 cm H_2O PEEP, #P<0.001

JAMA 2012;307:2526-2533

Risk Factors for Aspiration Pneumonia

Categories	Examples
Decreased level of consciousness	Alcoholism
Upper GI tract disorders	Dysphagia, esophageal disorders
Mechanical instrumentation	Intubation, nasogastric tube, feeding tubes
Neurologic conditions	Dementia, Parkinson disease
Others	Protracted vomiting

Neoplasms

Lung Cancer

Classification

- lung tumours can be classified as primary or secondary, benign or malignant, endobronchial or parenchymal
- bronchogenic carcinoma (epithelial lung tumours) are the most common type of primary lung tumour (other types make up less than 1%)
  - small cell lung cancer (SCLC): 10-15%
  - non-small-cell lung cancer (NSCLC): 85-90%
    - squamous cell carcinoma: arise from the proximal respiratory epithelium
    - adenocarcinoma: incidence is increasing; most common subtype in nonsmokers
      - bronchoalveolar carcinoma: grows along the alveolar wall in the periphery; may arise at sites of previous lung scarring
    - large cell undifferentiated cancer: diagnosis of exclusion
- benign epithelial lung tumours can be classified as papillomas or adenomas

Table 28. Characteristics of Bronchogenic Cancer

Cell Type	Incidence	Correlation with Smoking	Location	Histology	Metastasis	5 Yr Survival Rates
SCLC	10-15%	Strong	Central	Oat cell, neuroendocrine	Disseminated at presentation Origin in endobronchial cells	1% (poorest prognosis)
Adenocarcinoma	M: 35% F: 40%	Weak	Peripheral	Glandular, mucin producing	Early, distant	12% (60% for bronchoalveolar carcinoma, a subtype, with a resectable solitary lesion)
Squamous Cell Carcinoma (SCC)	30%	Strong	Central	Keratin, intercellular bridges	Local invasion and distant spread, may cavitate	25%
Large Cell Carcinoma	10-15%	Strong	Peripheral	Anaplastic, undifferentiated	Early, distant	13%

Risk Factors

- cigarette smoking: the relative risk of developing lung cancer is 10-30 times higher for smokers than for nonsmokers
- other risk factors include cigar smoking, pipe smoking, second-hand smoke, asbestos without smoking (relative risk is 5), asbestos with smoking (relative risk is 92), metals (e.g. chromium, arsenic, nickel), radon gas, ionizing radiation, genetics

Signs and Symptoms

- may be due to primary lesion, metastasis, or paraneoplastic syndrome
- primary lesion
  - cough (75%): beware of chronic cough that changes in character
  - dyspnea (60%)
  - chest pain (45%)
  - hemoptysis (35%)
  - other pain (25%)
  - clubbing (21%)
  - constitutional symptoms: anorexia, weight loss, fever, anemia
- metastasis
  - lung, hilum, mediastinum, pleura: pleural effusion, atelectasis, wheezing
  - pericardium: pericarditis, pericardial tamponade
  - esophageal compression: dysphagia
  - phrenic nerve: paralyzed diaphragm
  - recurrent laryngeal nerve: hoarseness
  - superior vena cava syndrome:
    - obstruction of SVC causing neck and facial swelling, as well as dyspnea and cough
    - other symptoms: hoarseness, tongue swelling, epistaxis, and hemoptysis
    - physical findings: dilated neck veins, increased number of collateral veins covering the anterior chest wall, cyanosis, edema of the face, arms, and chest, Pemberton's sign (facial flushing, cyanosis, and distension of neck veins upon raising both arms above head)
    - milder symptoms if obstruction is above the azygos vein
  - lung apex (Pancoast tumour): Horner's syndrome, brachial plexus palsy (most commonly C8 and T1 nerve roots)
  - rib and vertebrae: erosion
  - distant metastasis to brain, bone, liver, adrenals
- paraneoplastic syndromes
  - a group of disorders associated with malignant disease, not related to the physical effects of the tumour itself
  - most often associated with SCLC

Summary of Recommendations on Screening for Lung Cancer

American College of Chest Physicians (2013)

Screening with CXR
Not recommended

Screening with low-dose CT
Recomended for high-risk patients (current or former smokers quit within last 15 yr, aged 55-74, ≥30 pack yr smoking Hx)

American Lung Association (2013)

Screening with CXR
Not recommended

Screening with low-dose CT
Recomended for high-risk patients (current or former smokers aged 55-74, ≥30 pack yr smoking Hx, no Hx of lung cancer)

Reduced Lung Cancer Mortality with Low-Dose CT Screening
NEJM 2011;365:395-409
Study: Multicentre, RCT.
Methods: 53,454 participants at high risk for lung cancer (55-74 yr, >30 yr smoking, and smoking cessation for <5 y) were assigned to undergo three annual screenings with either low dose CT or single-view PA CXR.
Results: A relative reduction in mortality from lung cancer with low-dose CT screening of 20.0% (95% CI 6.8-26.7; p=0.004). Rate of death from any cause was reduced in the low-dose CT group as compared to the CXR group by 6.7% (95% CI 1.2-13.6; p=0.02).

	Low-dose CT	CXR
Rate of positive screening test	24.2%	6.9%
False positives	96.4%	94.5%
Incidence of lung cancer	645/100 K person yr	572/100 K person yr
Deaths from lung cancer	247/100 K person yr	309/100 K person yr

Conclusions: Screening with low-dose CT reduces mortality from lung cancer.

Horner has a MAP of the Coast
A Pan**coast** tumour compresses the cervical sympathetic plexus causing a **Horner's** syndrome:
Miosis
Anhydrosis
Ptosis

Table 29. Paraneoplastic Syndromes

System	Clinical Presentation	Associated Malignancy
Skeletal	Clubbing, hypertrophic pulmonary osteoarthropathy (HPOA)	NSCLC
Dermatologic	Acanthosis nigricans Dermatomyositis	Bronchogenic cancer Bronchogenic cancer
Endocrine	Hypercalcemia (osteolysis or PTHrP) Hypophosphatemia Hypoglycemia Cushing's syndrome (ACTH) Somatostatinoma syndrome SIADH	Squamous cell cancer Squamous cell cancer Sarcoma SCLC Bronchial carcinoid SCLC
Neuromyopathic	Lambert-Eaton syndrome Polymyositis Subacute cerebellar degeneration Spinocerebellar degeneration Peripheral neuropathy	SCLC
Vascular/ Hematologic	Nonbacterial endocarditis Trousseau's syndrome (migratory thrombophlebitis) DIC	Bronchogenic cancer NSCLC
Renal	Nephrotic syndrome	

Malignant lung tumours are the most common cause of cancer mortality throughout the world in both men and women

Investigations

- initial diagnosis
  - imaging: CXR, CT chest + upper abdomen, PET scan, bone scan
  - cytology: sputum
  - biopsy: bronchoscopy, EBUS, CT-guided percutaneous needle biopsy, mediastinoscopy
- staging workup
  - TMN staging system: T – primary tumour (size); N – regional lymph nodes; M – distant metastasis
  - blood work: electrolytes, LFTs, calcium, ALP
  - imaging: CXR, CT thorax and upper abdomen, bone scan, neuroimaging
  - invasive: bronchoscopy (EBUS), mediastinoscopy, mediastinotomy, thoracotomy
  - screen adenocarcinoma for EGFR and ALK mutations

Endobronchial Ultrasound (EBUS)
- Allows visualization of peri-bronchial structures and distal peripheral lung lesions
- Provides detailed assessment of the airway wall layers
- Allows for guided biopsies of lymph nodes and tumours
- Used for diagnosis and staging

Table 30. SCLC vs. NSCLC

	Stage	Definition	Treatment	Median Survival
SCLC	Limited stage	Confined to single radiation port (one hemithorax and regional lymph nodes)	Radiation ± chemotherapy ± prophylactic to brain	1-2 yr (12 wk without treatment)
	Extensive stage	Extension beyond a single radiation port	Chemotherapy	6 mo (5 wk without treatment)
	Stage	**TNM**	**Treatment**	**5 Yr Survival (%)***
NSCLC	IA	T1a-1bN0M0	1st line is complete surgical resection with possible post-operative adjuvant chemotherapy with stage IB and stage II; radiotherapy for non-surgical candidates	50-73
	IB	T2aN0M0		43-58
	IIA	T1a-T2a,N1M0 or T2bN0M0		36-46
	IIB	T2bN1M0 or T3N0M0		25-36
	IIIA	T1a-T2bN2M0 or T3N1-2M0 or T4N0-1M0	Combined modality approach (concurrent chemotherapy followed by surgery)	19-24
	IIIB	T4N2M0 or T1-4N3M0		7-9
	IV	T1-4N0-3M1a-1b	Systemic therapy or molecularly targeted therapy or symptom-based palliative management (radiation); isolated metastasis may be resected	2-13

* Depends on clinical vs. pathologic stage
Refer to *AJCC Cancer Staging Manual*, 7th ed. 2010 for complete TNM classification

2/3 of primary lung cancer is found in the upper lung; 2/3 of metastases occur in the lower lung (hematogenous spread secondary to increased blood flow to the base of the lung)

Treatment

- options include surgery, radiotherapy, chemotherapy, and palliative care for end-stage disease
- surgery not usually performed for SCLC since it is generally non-curable
- contraindications for surgery
  - spread to contralateral lymph nodes or distant sites
    - patients with potentially resectable disease must undergo mediastinal node sampling since CT thorax is not accurate in 20-40% of cases
  - poor pulmonary status (e.g. unable to tolerate resection of lung)

Prevention
Smoking cessation
Avoidance of exposures
Early detection

- chemotherapy (used in combination with other treatments)
  - common agents: etoposide, platinum agents (e.g. cisplatinum), ifosfamide, vincristine, anthracyclines, paclitaxel, irinotecan, gefitinib (an endothelial growth factor receptor inhibitor)
  - complications
    - acute: tumour lysis syndrome, infection, bleeding, myelosuppression, hemorrhagic cystitis (cyclophosphamide), cardiotoxicity (doxorubicin), renal toxicity (cisplatin), peripheral neuropathy (vincristine)
    - chronic: neurologic damage, leukemia, additional primary neoplasms

Approach to the Solitary Pulmonary Nodule

- see Medical Imaging, MI7

Definition

- a round or oval, sharply circumscribed radiographic lesion up to 3-4 cm, which may or may not be calcified, and is surrounded by normal lung
- can be benign or malignant

Terminology
- "nodule" <3 cm
- "mass" >3 cm

Table 31. Differential Diagnosis for Benign vs. Malignant Solitary Nodule

Benign (70%)	Malignant (30%)
Infectious granuloma (histoplasmosis, coccidiomycosis, TB, atypical mycobacteria)	**Bronchogenic carcinoma**
Other infections (bacterial abscess, PCP, aspergilloma)	Adenocarcinoma
Benign neoplasms (hamartoma, lipoma, fibroma)	Squamous cell carcinoma
Vascular (AV malformation, pulmonary varix)	Large cell carcinoma
Developmental (bronchogenic cyst)	Small cell carcinoma
Inflammatory (granulomatosis with polyangiitis, rheumatoid nodule, sarcoidosis)	**Metastatic lesions**
Other (infarct, pseudotumour, rounded atelectasis, lymph nodes, amyloidoma)	Breast
	Head and neck
	Melanoma
	Colon
	Kidney
	Sarcoma
	Germ cell tumours
	Pulmonary carcinoid

Hamartomas
- 10% of benign lung lesions
- Composed of tissues normally present in lung (fat, epithelium, fibrous tissue, and cartilage), but they exhibit disorganized growth
- Peak incidence is age 60, more common in men
- Usually peripheral and clinically silent
- CXR shows clustered "popcorn" pattern of calcification (pathognomonic for hamartoma)

Investigations

- CXR: always compare with previous CXR
- CT densitometry and contrast enhanced CT of thorax
- sputum cytology: usually poor yield
- biopsy (bronchoscopic or percutaneous) or excision (thoracoscopy or thoracotomy): if clinical and radiographic features do not help distinguish between benign or malignant lesion
  - if at risk for lung cancer, biopsy may be performed regardless of radiographic features
  - if a biopsy is non-diagnostic, whether to observe, re-biopsy, or resect will depend on the level of suspicion
- watchful waiting: repeat CXR and/or CT scan at 3, 6, 12 mo
- PET scan can help distinguish benign from malignant nodules

Pulmonary neoplasms may present as a solitary pulmonary nodule identified incidentally on a radiographic study (~10% of cases) or as symptomatic disease (most cases)

Adenocarcinoma present in a non-smoker may be due to endothelial growth factor receptor mutation

Table 32. CXR Characteristics of Benign vs. Malignant Solitary Nodule

Parameters	Benign	Malignant
Size	<3 cm, round, regular	>3 cm, irregular, spiculated
Margins	Smooth margin	Ill-defined or nctched margin
Features	Calcified pattern: central, "popcorn" pattern if hamartoma, usually no cavitation; if cavitating, wall is smooth and thin, no other lung pathology	Usually not calcified; if calcified, pattern is eccentric, no satellite lesions, cavitation with thick wall, may have pleural effusions, lymphadenopathy
Doubling Time	Doubles in <1 mo or >2 yr	Doubles in >1 mo or <2 yr

Corona Radiata Sign on Chest CT
- Fine striations that extend linearly from a nodule in a spiculated fashion
- Highly associated with malignancy

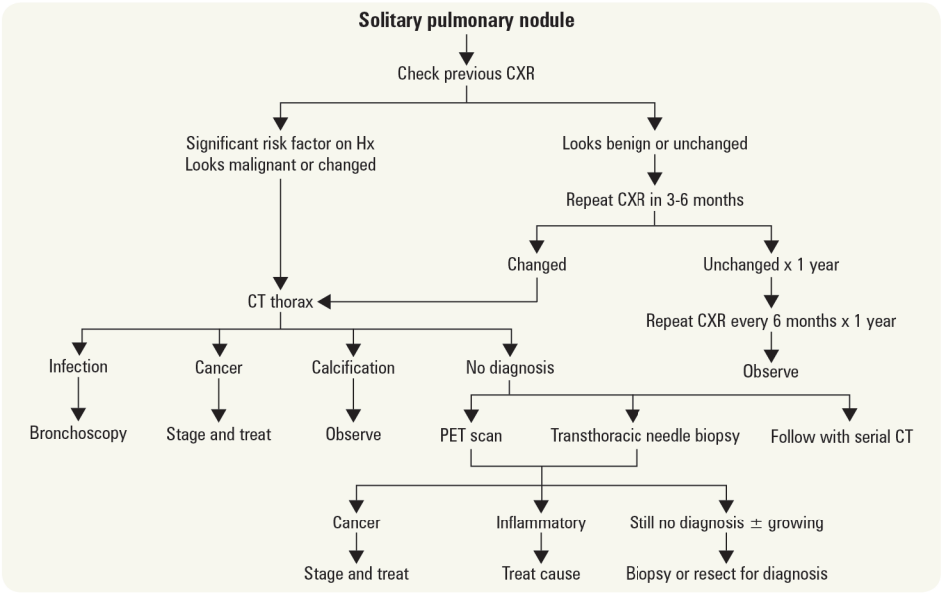

Figure 12. Evaluation of a solitary pulmonary nodule

Carcinoids
- Early onset (40-60 yr)
- Most are central and can produce symptoms and signs of bronchial obstruction
- Hemoptysis is present in ~50% of cases

Sleep-Related Breathing Disorders

Hypoventilation Syndromes

- primary alveolar hypoventilation: idiopathic
- obesity-hypoventilation syndrome (Pickwickian syndrome)
- respiratory neuromuscular disorders

Sleep Apnea

Definition
- episodic decreases in airflow during sleep
- quantitatively measured by the Apnea/Hypopnea Index (AHI) = # of apneic and hypopneic events per hour of sleep
- sleep apnea generally accepted to be present if AHI >15

Classification
- obstructive (OSA)
  - caused by transient, episodic obstruction of the upper airway
  - absent or reduced airflow despite persistent respiratory effort
- central (CSA) (see Neurology, N49)
  - caused by transient, episodic decreases in CNS drive to breathe
  - no airflow because no respiratory effort
  - Cheyne-Stokes Respiration: a form of CSA in which central apneas alternate with hyperpneas to produce a crescendo-decrescendo pattern of tidal volume; seen in severe LV dysfunction, brain injury, and other settings (see Figure 2)
- mixed (MSA)
  - features of both OSA and CSA
  - loss of hypoxic and hypercapnic drives to breathe secondary to "resuscitative breathing": overcompensatory hyperventilation upon awakening from OSA induced hypoxia

Normal Respiratory Changes during Sleep
- Tidal volume decreases
- Arterial CO_2 increases (due to decreased minute ventilation)
- Pharyngeal dilator muscles relax causing increased upper airway resistance

Apnea: absence of breathing for ≥10 s

Hypopnea: excessive decrease in rate or depth of breathing (>50% reduction in ventilation)

Hyperpnea: excessive increase in rate or depth of breathing

Risk Factors
- for OSA: obesity, upper airway abnormality, neuromuscular disease, hypothyroidism, alcohol/sedative use, nasal congestion, sleep deprivation
- for CSA: LV failure, brainstem lesions, encephalitis, encephalopathy, myxedema, high altitude

Signs and Symptoms
- obtain history from spouse/partner
- secondary to repeated arousals and fragmentation of sleep: daytime somnolence, personality and cognitive changes, snoring
- secondary to hypoxemia and hypercapnia: morning headache, polycythemia, pulmonary/systemic HTN, cor pulmonale/CHF, nocturnal angina, arrhythmias

- the typical presentation for OSA is a middle-aged obese male who snores
- CSA can be due to neurological disease

Investigations
- sleep study (polysomnography)
  - evaluates sleep stages, airflow, ribcage movement, ECG, SaO_2, limb movements
  - indications
    - excessive daytime sleepiness
    - unexplained pulmonary HTN or polycythemia
    - daytime hypercapnia
    - titration of optimal nasal CPAP
    - assessment of objective response to other interventions

Treatment
- modifiable factors: weight loss, decreased alcohol/sedatives, nasal decongestion, treatment of underlying medical conditions
- OSA or MSA: nasal CPAP, postural therapy (e.g. no supine sleeping), dental appliance, uvulopalatopharyngoplasty, tonsillectomy
- CSA or hypoventilation syndromes: nasal BiPAP/CPAP, respiratory stimulants (e.g. progesterone) in select cases
- tracheostomy rarely required and should be used as last resort for OSA

Complications
- depression, weight gain, decreased quality of life, workplace and vehicular accidents, cardiac complications (e.g. HTN), reduced work/social function

CPAP has been shown to reduce cardiovascular risk and cardiovascular related deaths in patients with obstructive sleep apnea

Continuous Positive Airways Pressure for Obstructive Sleep Apnea
Cochrane DB Syst Rev 2006;CD001106
Study: Pooled analysis of 36 RCTs (n=1,718) comparing nocturnal CPAP with an inactive control or oral appliances in adults with OSA.
Conclusions: The use of CPAP showed significant improvements in objective and subjective measures including cognitive function, sleepiness, measures of quality of life, and a lower average systolic and diastolic blood pressure. People who responded equally well to CPAP and oral appliances expressed a strong preference for oral appliances; however, participants on oral appliances were more likely to withdraw from therapy.

Introduction to Intensive Care

- goal is to provide stabilization for critically ill patients: hemodynamic, respiratory or cardiac instability, or need for close monitoring

Intensive Care Unit Basics

Lines and Catheters
- arterial lines
  - monitor beat-to-beat blood pressure variations, obtain blood for routine ABGs
  - common sites are the radial and femoral arteries
- central venous catheter (central line)
  - administer IV fluids, monitor CVP, insert pulmonary artery catheters
  - administer TPN and agents too irritating for peripheral line
  - common sites: internal jugular vein, subclavian vein, femoral vein
- pulmonary arterial catheter
  - balloon guides the catheter from a major vein to the right heart
  - measures pulmonary capillary wedge pressure (PCWP) via a catheter wedged in distal pulmonary artery
  - PCWP reflects the LA and LV diastolic pressure (barring pulmonary venous or mitral valve disease)
  - indications (now used infrequently due to associated complications)
    - diagnosis of shock states, primary pulmonary HTN, valvular disease, intracardiac shunts, cardiac tamponade, PE
    - assessment of hemodynamic response to therapies
    - differentiation of high- versus low-pressure pulmonary edema
    - management of complicated MI, multiorgan system failure and/or severe burns, or hemodynamic instability after cardiac surgery
  - absolute contraindications
    - tricuspid or pulmonary valve mechanical prosthesis
    - right heart mass (thrombus or tumour)
    - tricuspid or pulmonary valve endocarditis

Table 33. Useful Equations and Cardiopulmonary Parameters

BSA = [Ht (cm) + Wt (kg) – 60]/100	PCWP = LVEDP
SV = CO / HR	SVI = CI / HR
CI = CO / BSA	RV Ejection Fraction = SV / RVEDV
SVRI = [(MAP – RAP) 80]/CI	PP = sBP – dBP
P:F ratio = P_aO_2 / F_IO_2	MAP = 1/3 sBP + 2/3 dBP = dBP + 1/3 PP

BSA = body surface area; CI = cardiac index; CO = cardiac output; dBP = diastolic blood pressure; HR = heart rate; LVEDP = left ventricular end diastolic pressure; MAP = mean arterial pressure; PCWP = pulmonary capillary wedge pressure; PP = pulse pressure; RAP = right atrial pressure; RVEDV = right ventricular end diastolic volume; sBP = systolic blood pressure; SV = stroke volume; SVI = stroke volume index; SVRI = systemic vascular resistance index

Organ Failure

Table 34. Types of Organ Failure

Type of Failure	Clinical Presentation	Treatment
Respiratory Failure (see *Respiratory Failure*, R26)	Hypoxemia Hypercapnea	Treat underlying cause (e.g. lung disease, shunt, V/Q mismatch, drug-related, cardiac) Manage mechanical ventilation settings Supplemental oxygen
Cardiac Failure (see Cardiology and Cardiac Surgery, C36)	Hypotension Decreased urine output Altered mental status Arrhythmia Hypoxia	Treat underlying cause (e.g. bradycardia, tachycardia, blood loss, adrenal insufficiency) Volume resuscitation Vasopressors Inotropes Intra-aortic balloon pump
Coagulopathy (see Hematology, H32)	Increased INR or PTT Low platelet count Bleeding, bruising	Treat underlying cause (e.g. thrombocytopenia, drug-related, immune-related, DIC) Transfusion of blood products, clotting factors
Liver Failure (see Gastroenterology, G36)	Elevated transaminases, bilirubin Coagulopathy Jaundice Mental alteration (encephalopathy) Hypoglycemia	Treat underlying cause (e.g. viral hepatitis, drug related, metabolic) Liver transplant Lactulose
Renal Failure (see Nephrology, NP17)	Elevated creatinine Reduced urine output Signs of volume overload (e.g. CHF, effusions)	Treat underlying cause (e.g. shock, drug-related, obstruction) Correct volume and electrolyte status, eliminate toxins Diuretics Dialysis

Intensive Insulin Therapy in Critically Ill Patients
NEJM 2001;345:1359-1367
Study: Prospective, randomized controlled clinical outcome study.
Patients: 1,548 patients admitted to the ICU.
Intervention: At admission, patients were randomly assigned to either intensive insulin therapy or conventional therapy. Those in the intensive group had an infusion started if BG exceeded 6.1 mmol/L, and maintained to keep BG between 4.4-6.1 mmol/L. Those in the conventional group were started on insulin only if BG exceeded 11.9, and the infusion was adjusted for a target between 10.0 and 11.1 mmol/L.
Primary Outcome: Death from any cause during ICU stay.
Results: 35 patients (4.6%) died in the intensive group in the ICU, vs. 63 patients (8.0%) in the conventional group. This represents a 32% mortality reduction (p=0.04). Intensive insulin therapy also reduced overall in-hospital mortality, lowered deaths due to sepsis, multi-organ failure. Most of the mortality benefit was seen in long stay patients (>5 d).
Conclusion: Intensive insulin therapy in the ICU reduces mortality by 32%, and improves in-hospital mortality and morbidity.

Shock

- see Emergency Medicine, ER3
- inadequate tissue perfusion potentially resulting in end organ injury
  - categories of shock
    - hypovolemic: hemorrhage, dehydration, vomiting, diarrhea, interstitial fluid redistribution
    - cardiogenic: myopathic (myocardial ischemia ± infarction), mechanical, arrhythmic, pharmacologic
    - obstructive: massive PE (saddle embolus), pericardial tamponade, constrictive pericarditis, increased intrathoracic pressure (e.g. tension pneumothorax)
    - distributive: sepsis, anaphylactic reaction, neurogenic, endocrinologic, toxic

Shock: Clinical Correlation

Hypovolemic: patients have cool extremities due to peripheral vasoconstriction

Cardiogenic: patients usually have signs of left-sided heart failure

Obstructive: varied presentation

Distributive: patients have warm extremities due to peripheral vasodilation

Table 35. Changes Seen in Different Classes of Shock

	Hypovolemic	Cardiogenic	Obstructive	Distributive
HR	↑	↑, N, or ↓	↑	↑ or ↓
BP	↓	↓	↓	↓
JVP	↓	↑	↑	↓
Extremities	Cold	Cold	N or Cold	Warm
Other	Look for visible hemorrhage or signs of dehydration	Bilateral crackles on chest exam	Depending on cause, may see pulsus paradoxus, Kussmaul's sign, or tracheal deviation	Look for obvious signs of infection or anaphylaxis

Causes of SHOCK

Spinal (neurogenic), **S**eptic
Hemorrhagic
Obstructive (e.g. tension pneumothorax, cardiac tamponade, PE)
Cardiogenic (e.g. arrhythmia, MI)
Anaphyla**K**tic

- treat underlying cause
- treatment goal is to return critical organ perfusion to normal (e.g. normalize BP)
- common treatment modalities include
  - fluid resuscitation
  - inotropes (e.g. dobutamine), vasopressors (e.g. norepinephrine), vasopressin
  - revascularization or thrombolytics for ischemic events

Sepsis

- the leading cause of death in noncoronary ICU settings is multi-organ failure due to sepsis
- the predominant theory is that sepsis is attributable to uncontrollable immune system activation

Definitions

- sepsis: the presence of both infection and SIRS (see Table 36)
- severe sepsis: sepsis associated with organ dysfunction, hypoperfusion or hypotension
- septic shock: sepsis with arterial hypotension despite adequate fluid resuscitation

Systemic Inflammatory Response Syndrome (SIRS): generalized inflammatory reaction caused by infectious and noninfectious entities, manifested by two or more of:
- Body temperature >38°C or <36°C
- Heart rate >90/min
- Respiratory rate >20/min or P_aCO_2 <32 mmHg
- WBC >12,000 cells/mL or <4,000 cells/mL or >10% bands

- multiorgan dysfunction syndrome: sepsis in the presence of altered organ function such that homeostasis cannot be maintained without intervention

Signs and Symptoms

Table 36. Clinical Manifestations of Sepsis

General Variables	Organ Dysfunction Variables
Fever (>38°C) or hypothermia (<36°C)	Arterial hypoxemia (P_aO_2/F_iO_2 <300)
Heart rate >90/min	Acute oliguria (urine output <0.5 mL/kg/h)
sBP <90 mmHg, MAP <70, or a sBP decrease >40 mmHg	Creatinine increase >40 μmol/L
Tachypnea	Coagulation abnormalities (INR >1.5 or aPTT >60 s)
Altered mental status	Ileus (absent bowel sounds)
Positive fluid balance (>20 mL/kg over 24 h)	Thrombocytopenia (platelet count <100,000/L)
Hyperglycemia (BG >7.7 mmol/L) in the absence of diabetes	Hyperbilirubinemia (plasma total bilirubin >70 mmol/L)
Leukopenia (WBC <4,000/L)	Leukocytosis (WBC >12,000/L)
Normal WBC count with >10% immature forms	**Tissue Perfusion Variables**
Plasma C-reactive protein >2 SD above the normal value	Hyperlactatemia (>1 mmol/L)
	Decreased capillary refill or mottling

Table adapted with permission from Levy MM, Fink MP, Marshall JC, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Critical Care Medicine* 2003;31:1250-1256

Treatment

- identify the cause and source of infection: blood, sputum, urine Gram stain, and C&S
- initiate empiric antibiotic therapy
- monitor, restore, and maintain hemodynamic function

Early Goal Directed Therapy

- adjustments of cardiac preload, afterload, and contractility to balance oxygen delivery with demand
- should be started immediately and completed within 6 h of recognition of severe sepsis or septic shock
- patient should meet SIRS criteria and sBP <90 mmHg or lactate >4 mmol/L
  1. supplemental oxygen ± intubation and mechanical ventilation
  2. central venous and arterial catheterization
  3. maintain CVP 8-12 mmHg with IV crystalloids/colloids
  4. MAP maintained 65-90 mmHg with the use of vasoactive agents
  5. $S_{cv}O_2$ <70% then
     - transfusion of red cells until Hct >30%
     - if $S_{cv}O_2$ <70% after transfusion then use inotropic agents
- supportive oxygenation and ventilation using lung-protective regimen
- early nutritional support: enteral route is used to preserve function of intestinal mucosal barrier
- control hyperglycemia with insulin to decrease infectious complications
- physiologic dose corticosteroid replacement therapy in patients with relative adrenal insufficiency (nonresponders to corticotropin stimulation test)
  - consider in mechanically ventilated septic shock patients with organ dysfunction requiring vasopressors, despite early goal-directed therapy and appropriate antibiotic therapy
- recombinant activated protein C may be considered in patients with severe sepsis or septic shock with an APACHE II score >25 despite early goal-directed therapy and appropriate antibiotic therapy
- DVT/PE prophylaxis
- advanced care planning, including the communication of likely outcomes and realistic goals of treatment with patients and families

Corticosteroids for Treating Severe Sepsis and Septic Shock
Cochrane DB Syst Rev 2010;CD002243
Study: Meta-analysis of 25 RCTs and quasi-RCTs examining the efficacy of corticosteroids on death at one month in patients with severe sepsis and septic shock.
Results: Overall, there was no difference in 28-d all-cause mortality but there was significant heterogeneity in dosing strategy between the studies. Treatment with long course of low dose corticosteroids significantly reduced 28-d mortality, increased the proportion of shock reversal by day 7 and day 28, reduced the sepsis-related organ failure assessment score by day 7, and survivors' length of stay in the ICU, without inducing gastroduodenal bleeding, superinfection, or neuromusular weakness. Corticosteroids increased the risk of hyperglycemia and hypernatremia.
Conclusions: Corticosteroids did not change mortality in severe sepsis and septic shock. A long course of low dose corticosteroids reduced 28-d mortality without major complications.

Common Medications

Table 37. Common Medications for Respiratory Diseases

	Drug	Typical Adult Dose	Indications	Side Effects
β_2-AGONISTS				
Short-Acting	salbutamol/albuterol (Ventolin®) (light blue/navy), terbutaline (Bricanyl®)	1-2 puffs q4-6h prn	Bronchodilator in acute reversible airway obstruction	CV (angina, flushing, palpitations, tachycardia, can precipitate atrial fibrillation), CNS (dizziness, H/A, insomnia, anxiety), GI (diarrhea, N/V), rash, hypokalemia, paroxysmal bronchospasm
Long-Acting	salmeterol (Serevent®), formoterol (Oxeze®) indacaterol (Onbrez®)	1-2 puffs bid 1 puff daily	Maintenance treatment (prevention of bronchospasm) in COPD, asthma	
Combination Long-Acting β_2-Agonist and Inhaled Corticosteroid	fluticasone and salmeterol (Advair®) (purple MDI or diskus) Budesonde and formoterol (Symbicort®) (red turbuhaler) Mometasone and formoterol (Zenhale®) (blue MDI)	1 puff bid 2 puffs bid	COPD and asthma	Common: CNS, H/A, dizziness Resp: URTI, GI (N/V, diarrhea, pain/discomfort, oral candidiasis)
ANTICHOLINERGICS				
	ipratropium bromide (Atrovent®) (clear/green), tiotropium bromide (Spiriva®) glycopyrronium bromide	2-3 puffs qid 1 puff qam 1 puff daily	Bronchodilator used in COPD, bronchitis and emphysema	Palpitations, anxiety, dizziness, fatigue, H/A, N/V, dry mucous membranes, urinary retention, increased toxicity in combination with other anticholinergic drugs
CORTICOSTEROIDS				
Inhaled	fluticasone (Flovent®) (orange/peach) budesonide (Pulmicort®) ciclesonide (Alvesco®) beclomethasone (QVAR®, Vanceril®) Mometasone (Asmanex®)	2-4 puffs bid 2 puffs bid 1-4 puffs OD 1-4 puffs bid (40 μg), 1-2 puffs bid (80 μg) 1 puff daily or bid	Maintenance treatment of asthma	H/A, fever, N/V, MSK pain, URTI, throat irritation, growth velocity reduction in children/adolescents, HPA axis suppression, increased pneumonia risk in COPD
Systemic	prednisone (Apo-prednisone®, Deltasone®) methylprednisolone (Depo-Medrol®, Solu-Medrol®)	Typically 40-60 mg per day PO 125 mg q8h IV (sodium succinate) loading dose 2 mg/kg then 0.5-1 mg/kg q6h for 5 d	Acute exacerbation of COPD; severe, persistent asthma, PCP Status asthmaticus	Endocrine (hirsutism, DM/glucose intolerance, Cushing's syndrome, HPA axis suppression), GI (increased appetite, indigestion), ocular (cataracts, glaucoma), edema, AVN, osteoporosis, H/A, psychiatric (anxiety, insomnia), easy bruising
ADJUNCT AGENTS				
	theophylline (Uniphyll®)	400-600 mg OD	Treatment of symptoms of reversible airway obstruction due to COPD	GI upset, diarrhea, N/V, anxiety, H/A, insomnia, muscle cramp, tremor, tachycardia, PVCs, arrhythmias Toxicity: persistent, repetitive vomiting, seizures
LEUKOTRIENE ANTAGONISTS				
	montelukast (Singular®) zafirlukast (Accolate®)	10 mg PO qhs, now only available as once daily slow release 20 mg bid	Prophylaxis and chronic treatment of asthma	H/A, dizziness, fatigue, fever, rash, dyspepsia, cough, flu-like symptoms
MONOCLONAL ANTIBODIES				
	omalizumab (Xolair®)	150-375 mg SC q2-4wk	Moderate-severe persistant asthma	H/A, sinusitis, pharyngitis, URTI, viral infection, thrombocytopenia, anaphylaxis
PDE5 INHIBITORS				
	roflumilast (Daxas®)	500 μg PO OD	Severe emphysema, with frequent exacerbations	Weight loss, suicidal ideation
ANTIBIOTICS – COMMUNITY ACQUIRED PNEUMONIA				
Macrolide	erythromycin azithromycin clarithromycin	250-500 mg PO tid x 7-10 d 500 mg PO x 1 dose, then 250 mg OD x 4 1,000 mg od or 500 mg PO bid x 7-10 d	Alternate to doxycycline or fluoroquinolone	GI (abdominal pain, diarrhea, N/V), H/A, prolonged QT, ventricular arrhythmias, hepatic impairment GI (diarrhea, N/V, abdominal pain), renal failure, deafness H/A, rash, GI (diarrhea, N/V, abnormal taste, heartburn, abdominal pain), increased urea
Doxycycline		100 mg PO bid x 7-10 d	Alternate to macrolide or fluoroquinolone	Photosensitivity, rash, urticaria, anaphylaxis, diarrhea, entercolitis, tooth discolouration in children
Fluoroquinolone	levofloxacin (Levaquin®) moxifloxacin (Avelox®)	500 mg PO OD x 7-10 d 400 mg PO OD x 7 d	Alternate to macrolide or doxycycline	CNS (dizziness, fever, H/A), GI (N/V, diarrhea, constipation), prolonged QT

Table 37. Common Medications for Respiratory Diseases (continued)

	Drug	Typical Adult Dose	Indications	Side Effects
ANTIBIOTICS – HOSPITAL ACQUIRED PNEUMONIA				
3rd gen Cephalosporin	ceftriaxone (Rocephin®)	1-2 g IV OD x 7-10 d	Combine with fluoroquinolone or macrolide	Rash, diarrhea, eosinophilia, thrombocytosis, leukopenia, elevated transaminases
Fluoroquinolone	levofloxacin moxifloxacin	750 mg PO OD x 5 d 400 mg PO OD x 7 d (5 d for AECOPD)	Combine with 3rd gen cephalosporin	See above
Piperacillin/ Tazobactam (Tazocin®)		4.5 g IV q6-8h x 7-10 d	Suspect Pseudomonas	CNS (confusion, convulsions, drowsiness), rash, Hematologic (abnormal platelet aggregation, prolonged PT, positive Coombs)
Vancomycin (Vancocin®)		1 g IV bid x 7-10 d	Suspect MRSA	CNS (chills, drug fever), hematologic (eosinophilia), rash, red man syndrome, interstitial nephritis, renal failure, ototoxicity
Macrolide	azithromycin clarithromycin	500 mg IV OD x 2 d, then 500 mg PO OD x 5 d 1,000 mg od or 500 mg PO bid x 7-10 d	Suspect Legionella	See above See above
ICU MEDICATIONS				
Pressors/Inotropes	norepinephrine (Levophed®) phenylephrine dobutamine	0.5-30 μg/min IV 0.5 μg/kg/min IV 2-20 μg/kg/min IV	Acute hypotension Severe hypotension Inotropic support	Angina, bradycardia, dyspnea, hyper/hypotension, arrhythmias See above See above
Sedatives/Analgesia	fentanyl (opioid class) propofol (anesthetic)	50-100 μg then 50-unlimited μg/h IV 1-3 mg/kg then 0.3-5 mg/kg/h IV	Sedation and/or analgesia Sedation and/or analgesia	Bradycardia, respiratory depression, drowsiness, hypotension Apnea, bradycardia, hypotension (good for ventilator sedation)

See Infectious Diseases, ID26 – for the management of pulmonary tuberculosis

Landmark Respirology Trials

Trial	Reference	Results
ARDS Network	*NEJM* 2000; 342:1301-8	Mortality decreased in ARDS patients ventilated with a low tidal volume strategy
Berlin Criteria	*JAMA* 2012; 307:2526-33	The new definition of ARDS, better predicts mortality
CPAP and Apnea	*NEJM* 2005; 353:2025-33	CPAP ameliorates symptoms of sleep apnea but does not affect mortality in CHF
EINSTEIN-PE	*NEJM* 2012; 366:1287-97	Fixed dose of rivoxabarin was non-inferior to standard therapy (Vit K antagonist) initial and long-term treatment of PE
Emphysema Treatment Trial	*NEJM* 2003; 348:2059-73	Lung volume reduction surgery benefits patients with upper lobe disease and low exercise capacity
IELCAP	*NEJM* 2006; 355:1763-71	High survival rate in patients with early stage lung cancer detected by low dose CT screening
Lung Health	*JAMA* 1994; 272:1497-505	Aggressive smoking intervention significantly decreases the age-related decline in FEV_1 in middle-aged smokers with mild airways obstruction
OSCILLATE	*NEJM* 2013; 368: 795-805	Early high-frequency oscillatory ventilation in patients with moderate to severe ARDS might increase in-hospital mortality
Pneumonia	*NEJM* 1978; 298:801-9	Interstitial lung disease subsets have different prognoses and response to treatment (e.g. desquamative but not usual interstitial pneumonia respond well to corticosteroids)
POET-COPD	*NEJM* 2011; 364:1093-103	Tiotropium decreases the number of moderate-to-severe exacerbations in comparison to salmeterol
REDUCE	*JAMA* 2013; 309: 2223-2231	5 d course of glucocorticoids is non-inferior to a 14 d course for treatment of acute COPD exacerbations
ROFLUMILAST	*Lancet* 2009; 374:695-703	Leukotriene inhibitors improve FEV_1 when used as add-on therapy in COPD patients on tiotropium or salmeterol
TORCH	*NEJM* 2007; 356:775-89	Combination of inhaled steroids and long-acting β_2-agonists improves COPD symptoms, reduces exacerbations, and shows a trend to lowers mortality
UPLIFT	*NEJM* 2008; 359:1543-54	Tiotropium improves symptoms of COPD with fewer exacerbations, but does not affect FEV_1 decline

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OT Otolaryngology – Head & Neck Surgery

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Acronyms

ABR	auditory brainstem response	FNA	fine needle aspiration	OSA	obstructive sleep apnea
AC	air conduction	GERD	gastroesophageal reflux disease	RA	rheumatoid arthritis
AOM	acute otitis media	GPA	granulomatosis with polyangiitis	SCC	squamous cell carcinoma
BAHA	bone anchored hearing aid	H&N	head and neck	SCM	sternocleidomastoid
BC	bone conduction	HL	hearing loss	SNHL	sensorineural hearing loss
CHL	conductive hearing loss	HPV	human papillomavirus	SRT	speech reception threshold
CPA	cerebellopontine angle	INCS	intranasal corticosteroids	TEF	tracheoesophageal fistula
EAC	external auditory canal	MEE	middle ear effusion	TM	tympanic membrane
EBV	Epstein-Barr virus	MEI	middle ear inflammation	TNM	tumour, node, metastases
FAP	familial adenomatous polyposis	OE	otitis externa	URTI	upper respiratory tract infection
FESS	functional endoscopic sinus surgery	OME	otitis media with effusion		

Basic Anatomy Review

Ear

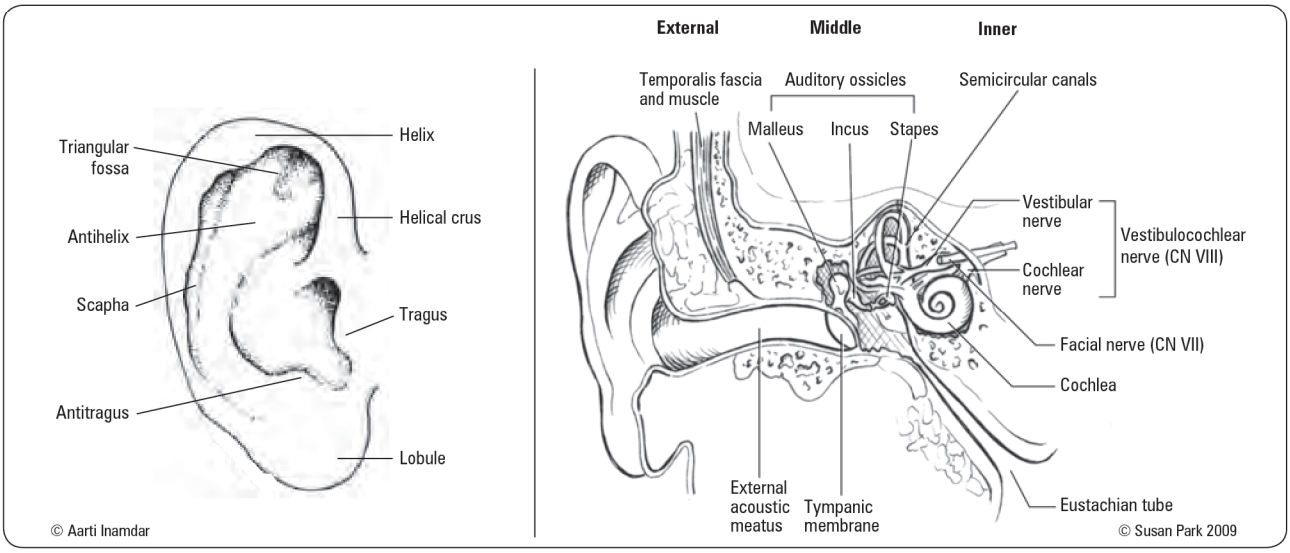


Figure 1. Surface anatomy of the external ear; anatomy of ear

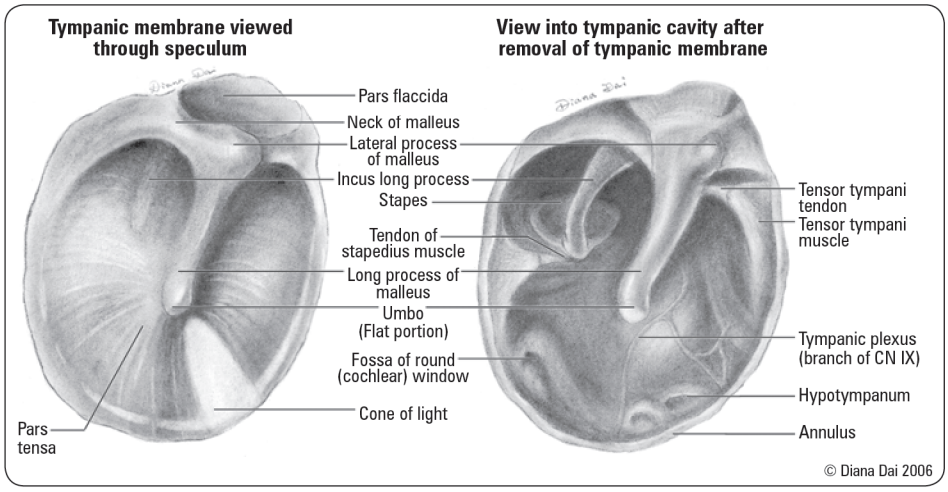


Figure 2. Normal appearance of right tympanic membrane on otoscopy

Nose

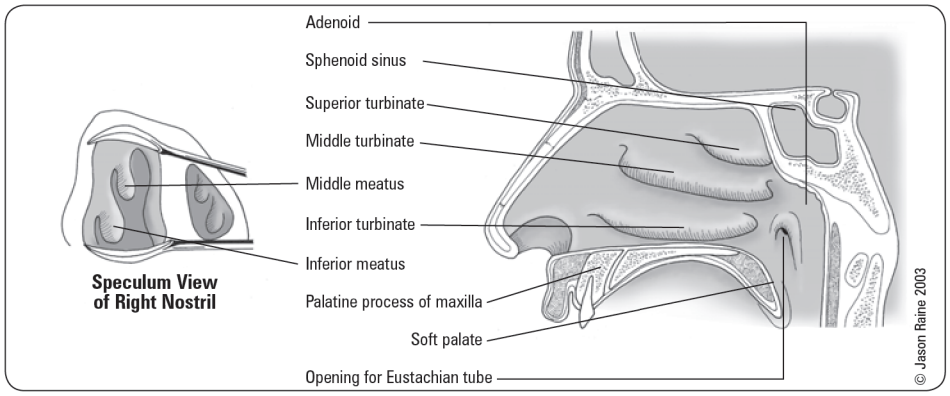


Figure 3. Nasal anatomy

Drainage into Nasal Cavity
- **Superior meatus**: sphenoid (via sphenoethmoidal recess), posterior ethmoid sinuses
- **Middle meatus**: frontal, maxillary, anterior ethmoid sinuses
- **Inferior meatus**: nasolacrimal duct

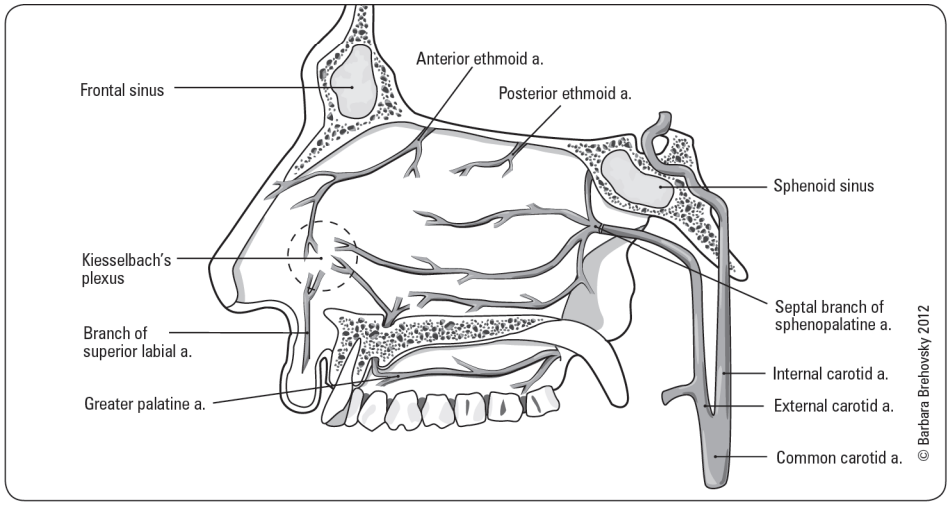
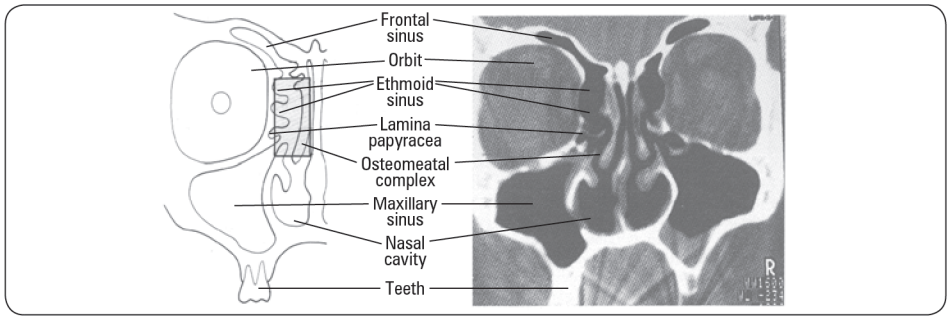


Figure 4. Nasal septum and its arterial supply (see *Epistaxis*, OT27 for detailed blood supply)



- **Nasopharynx**: skull base to soft palate
- **Oropharynx**: soft palate to hyoid bone
- **Laryngopharynx**: hyoid bone to inferior border cricoid cartilage

Figure 5. Anatomy of the four paranasal sinuses: maxillary, ethmoid, sphenoid, and frontal
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Throat

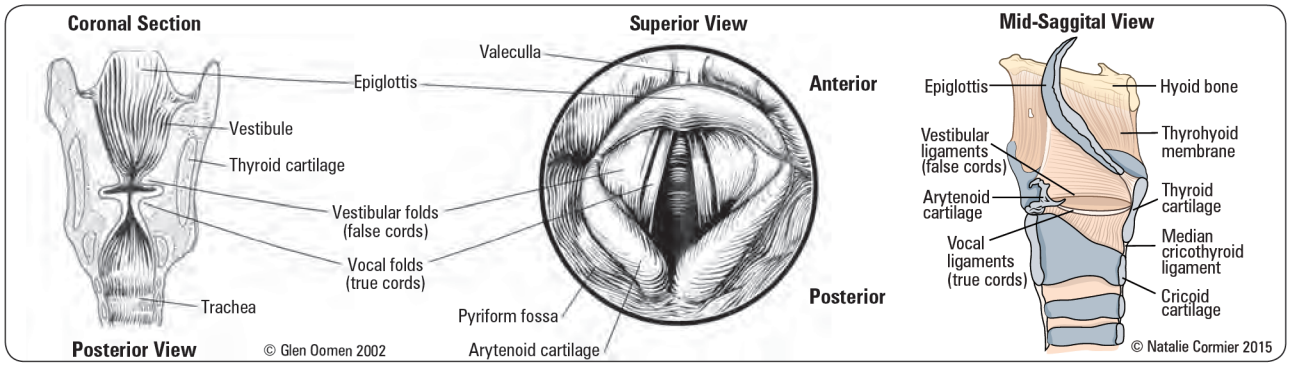


Figure 6. Anatomy of a normal larynx; superior view of larynx on indirect laryngoscopy

Head and Neck

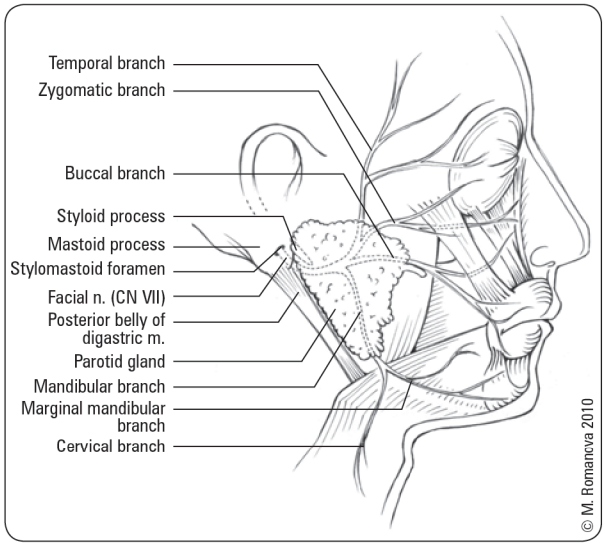


Figure 7. Extratemporal segment of facial nerve
Branches of facial nerve (in order from superior to inferior)
To **Z**anzibar **B**y **M**otor **C**ar

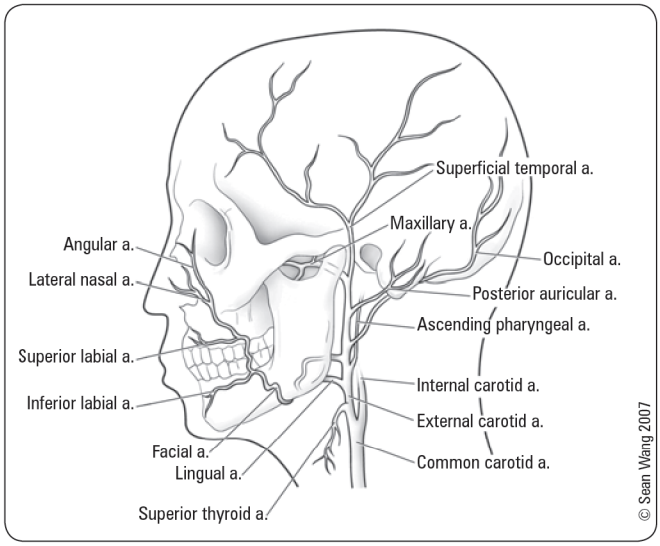


Figure 8. Blood supply to the face
Branches of the external carotid artery (in order from inferior to superior)
Some **A**ngry **L**ady **F**igured **O**ut **PMS**

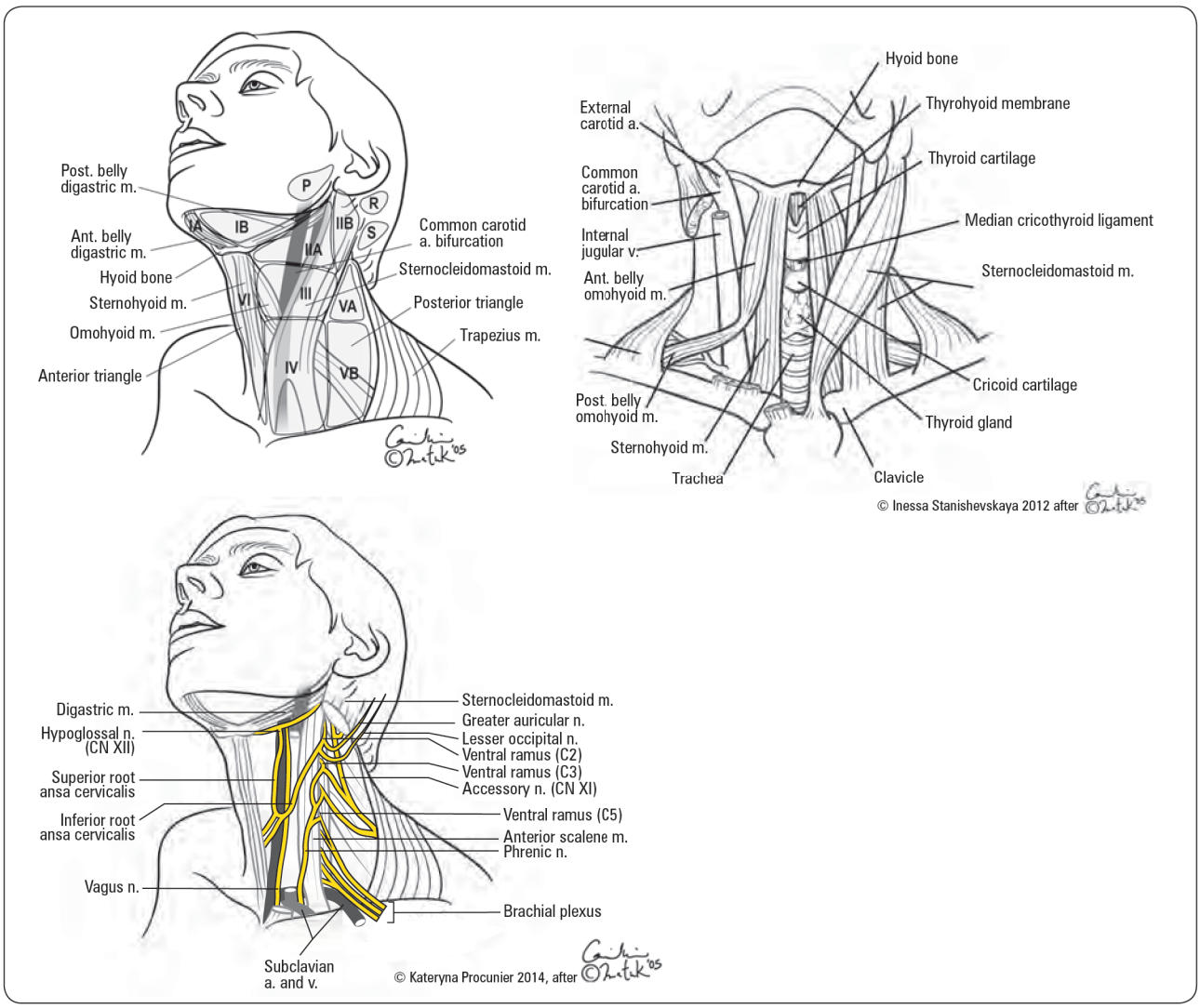


Figure 9. Anatomy of the neck

Anatomical Triangles of the Neck

Anterior triangle
- bounded by anterior border of SCM, midline of neck, and lower border of mandible
- divided into
  - **submental triangle:** bounded by both anterior bellies of digastric and hyoid bone
  - **digastric triangle:** bounded by anterior and posterior bellies of digastric and inferior border of mandible
  - **carotid triangle:** bounded by sternocleidomastoid, anterior belly of omohyoid, and posterior belly of digastric
    - contains: tail of parotid, submandibular gland, hypoglossal nerve, carotid bifurcation, and lymph nodes

Posterior triangle
- bounded by posterior border of sternocleidomastoid, anterior border of trapezius, and middle third of clavicle
- divided into
  - **occipital triangle:** superior to posterior belly of the omohyoid
  - **subclavian triangle:** inferior to posterior belly of omohyoid
- contains: spinal accessory nerve and lymph nodes

Table 1. Lymphatic Drainage of Nodal Groups and Anatomical Triangles of Neck

Nodal Group/Level	Location	Drainage
1. Suboccipital (S)	Base of skull, posterior	Posterior scalp
2. Retroauricular (R)	Superficial to mastoid process	Scalp, temporal region, external auditory meatus, posterior pinna
3. Parotid-preauricular (P)	Anterior to ear	External auditory meatus, anterior pinna, soft tissue of frontal and temporal regions, root of nose, eyelids, palpebral conjunctiva
4. Submental (Level IA)	Anterior bellies (midline) of digastric muscles, tip of mandible, and hyoid bone	Floor of mouth, anterior tongue, anterior mandibular alveolar ridge, lower lip
5. Submandibular (Level IB)	Anterior belly of digastric muscle, stylohyoid muscle, body of mandible	Oral cavity, anterior nasal cavity, soft tissues of the mid-face, submandibular gland
6. Upper jugular (Levels IIA and IIB)	Skull base to inferior border of hyoid bone along SCM muscle	Oral cavity, nasal cavity, naso/oro/hypopharynx, larynx, parotid glands
7. Middle jugular (Level III)	Inferior border of hyoid bone to inferior border of cricoid cartilage along SCM muscle	Oral cavity, naso/oro/hypopharynx, larynx
8. Lower jugular* (Level IV)	Inferior border of cricoid cartilage to clavicle along SCM muscle	Hypopharynx, thyroid, cervical esophagus, larynx
9. Posterior triangle** (Levels VA and VB)	Posterior border of SCM, anterior border of trapezius, from skull base to clavicle	Nasopharynx and oropharynx, cutaneous structures of the posterior scalp and neck
10. Anterior compartment*** (Level VI)	Hyoid bone (midline) to suprasternal notch between the common carotid arteries	Thyroid gland, glottic and subglottic larynx, apex of piriform sinus, cervical esophagus

*Virchow node: left lower jugular (level IV) supraclavicular node
**Includes some supraclavicular nodes
***Includes pretracheal, precricoid, paratracheal, and perithyroidal nodes

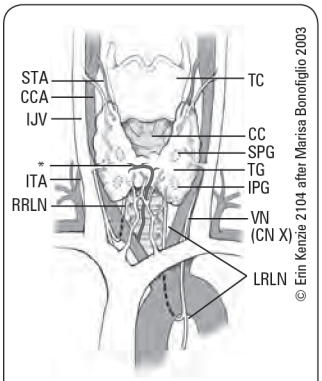
Paired Parasympathetic Ganglia of the Head and Neck
- **Ciliary:** pupillary constriction
- **Pterygopalatine:** lacrimal gland, nasal mucosa
- **Submandibular:** submandibular, sublingual glands
- **Otic:** parotid gland

Function of Facial Nerve

"Ears, Tears, Face, Taste"
Ears: stapedius muscle
Tears: lacrimation (lacrimal gland) and salivation (parotid)
Face: muscles of facial expression
Taste: sensory anterior 2/3 of tongue (via chorda tympani)

- **Left-sided** enlargement of a supraclavicular node (Virchow's node) may indicate an abdominal malignancy
- **Right-sided** enlargement may indicate malignancy of the mediastinum, lungs, or esophagus
- **Occipital and/or posterior auricular node** enlargement may indicate rubella

4 Strap Muscles of the Neck
- Thyrohyoid
- Omohyoid
- Sternohyoid
- Sternothyroid



STA	–	Superior thyroid artery
CCA	–	Common carotid artery
IJV	–	Internal jugular vein
ITA	–	Inferior thyroid artery
RRLN	–	Right recurrent laryngeal nerve
TC	–	Thyroid cartilage
CC	–	Cricoid cartilage
SPG	–	Superior parathyroid gland
TG	–	Thyroid gland
IPG	–	Inferior parathyroid gland
VN (CN X)	–	Vagus nerve (CN X)
LRLN	–	Left recurrent laryngeal nerve

*Thyroidea ima artery: present in 3% of population, arises from aortic arch or innominate artery

Figure 10. Anatomy of the thyroid gland

Differential Diagnoses of Common Presenting Problems

Dizziness

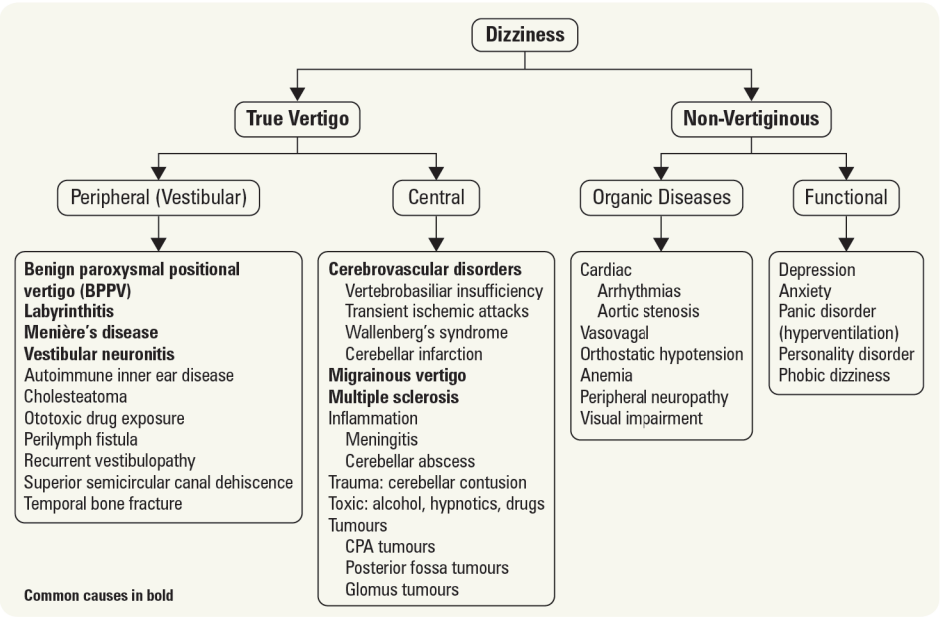


Figure 11. Differential diagnosis of dizziness

True nystagmus and vertigo caused by a peripheral lesion will never last longer than a couple of weeks because of compensation. Central lesions do not compensate, hence nystagmus and vertigo will persist

5 "D"s of Vertebrobasilar Insufficiency

Drop attacks
Diplopia
Dysarthria
Dizziness
Dysphagia

Otalgia

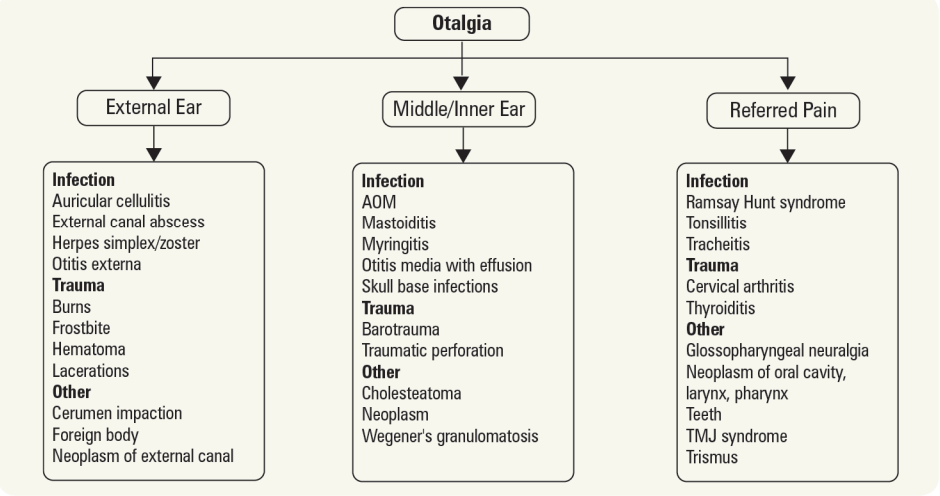


Figure 12. Differential diagnosis of otalgia

Hearing Loss

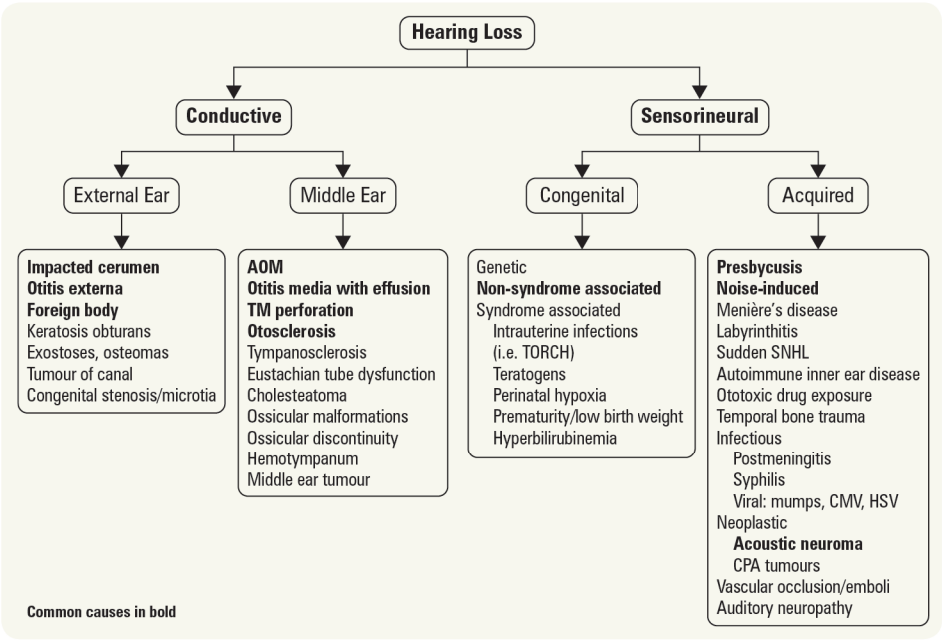


Figure 13. Differential diagnosis of hearing loss

Tinnitus

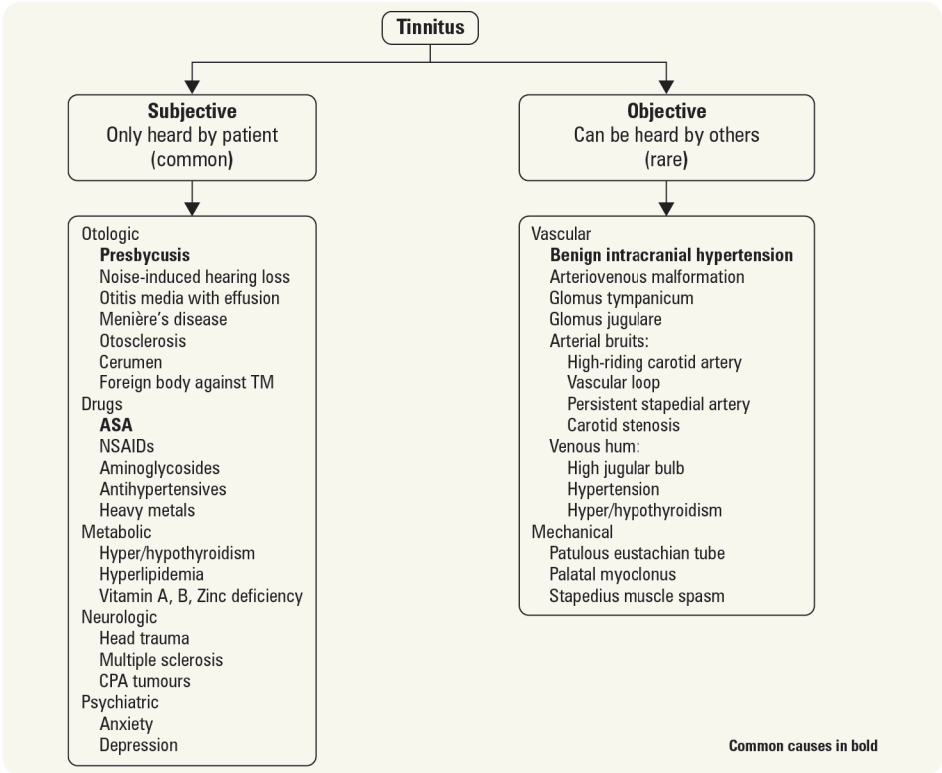


Figure 14. Differential diagnosis of tinnitus

Tinnitus is most commonly associated with SNHL

Glomus Tympanicum/Jugulare Tumour Signs and Symptoms

- Pulsatile tinnitus
- Hearing loss
- Blue mass behind TM
- Brown's sign (blanching of the TM with pneumatic otoscopy)

Nasal Obstruction

Table 2. Differential Diagnosis of Nasal Obstruction

Acquired	Congenital

Nasal Cavity
• Rhinitis
  • Acute/chronic
  • Vasomotor
  • Allergic
• Rhinosinusitis
• Foreign bodies
• Enlarged turbinates
• Tumour
  • Benign: polyps, inverting papilloma
  • Malignant
  • SCC
  • Esthesioneuroblastoma (olfactory neuroblastoma)
  • Adenocarcinoma
	Nasal Cavity
	• Nasal dermoid cyst
	• Encephalocele
	• Glioma
	• Choanal atresia

Nasal Septum • Septal deviation • Septal hematoma/abscess • Dislocated septum	**Nasal Septum** • Septal deviation • Septal hematoma/abscess • Dislocated septum

Nasopharynx
• Adenoid hypertrophy
• Tumour
  • Benign: juvenile nasopharyngeal angiofibroma (JNA), polyps
  • Malignant: nasopharyngeal carcinoma	

Systemic	
• Granulomatous diseases, diabetes, vasculitis	

Hoarseness

Table 3. Differential Diagnosis of Hoarseness

Infectious	• Acute/chronic laryngitis • Laryngotracheobronchitis (croup)	
Inflammatory	• GERD • Vocal cord polyps/nodules • Lifestyle: smoking, chronic EtOH use	
Trauma	• External laryngeal trauma • Endoscopy and endotracheal tube (e.g. intubation granuloma)	
Neoplasia	• Benign tumour • Papillomas (HPV infection) • Minor salivary gland tumours • Other	• Malignant tumours (e.g. thyroid) • SCC • Other
Cysts	• Retention cysts	
Systemic	• Endocrine • Hypothyroidism • Virilization	• Connective tissue disease • RA • SLE

Neurologic
(vocal cord paralysis due to superior ± recurrent laryngeal nerve injury)
	• Central lesions
	  • Cerebrovascular accident (CVA)
	  • Head injury
	  • Multiple sclerosis (MS)
	  • Skull base tumours
	  • Arnold-Chiari malformation
	• Peripheral lesions
	  • Unilateral
	  • Lung malignancy
		• Iatrogenic injury: thyroid, parathyroid surgery, carotid endarterectomy, patent ductus arteriosus (PDA) ligation
		• Bilateral
		  • Iatrogenic injury: bilateral thyroid surgery, forceps delivery
		• Neuromuscular
		  • Myasthenia gravis

Functional	• Psychogenic aphonia (hysterical aphonia)	
Congenital	• Laryngomalacia • Laryngeal web • Laryngeal atresia	

Lung malignancy is the most common cause of extralaryngeal vocal cord paralysis

Neck Mass

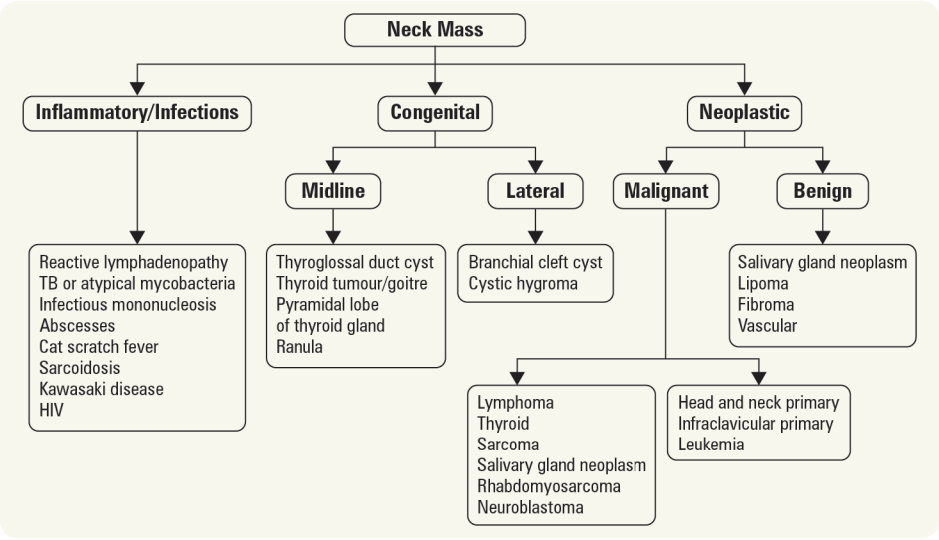


Figure 15. Differential diagnosis of a neck mass

Hearing

Normal Hearing Physiology

- **Conductive pathway (external auditory canal to cochlea):** air conduction of sound energy down the EAC → vibration of the tympanic membrane (area effect) → sequential vibration of the middle ear ossicles: malleus, incus, stapes (lever effect) → transmission of amplified vibrations from the stapes footplate in the middle ear to the oval window of the cochlea in the inner ear → pressure differential on cochlear fluid creates movement along the basilar membrane within the cochlea from base to apex
- **Neural pathway (nerve to brain):** basilar membrane vibration stimulates overlying hair cells in the organ of Corti → stimulation of bipolar neurons in the spiral ganglion of the cochlear division of CN VIII → cochlear nucleus → superior olivary nucleus → lateral lemniscus → inferior colliculus → Sylvian fissure of temporal lobe

Order of the Neural Pathway (with corresponding waves on ABR)

E COLI
Eighth cranial nerve (I – II)
Cochlear nucleus (III)
Superior **O**livary nucleus
Lateral leminiscus (IV – V)
Inferior colliculus

Types of Hearing Loss

1. Conductive Hearing Loss
- conduction of sound to the cochlea is impaired
- can be caused by external and middle ear disease

2. Sensorineural Hearing Loss
- due to a defect in the conversion of sound into neural signals or in the transmission of those signals to the cortex
- can be caused by disease of the inner ear (cochlea), acoustic nerve (CN VIII), brainstem, or cortex

3. Mixed Hearing Loss
- combination of conductive and sensorineural hearing loss

HL = Intensity x Duration

Auditory Acuity
- whispered-voice test: mask one ear and whisper into the other
- tuning fork tests (see Table 4; audiogram is of greater utility)
- sensitivity depends on which tuning fork used (256 Hz, 512 Hz, 1024 Hz; 512 Hz has the greatest sensitivity)
  - Rinne test
    - 512 Hz tuning fork is struck and held firmly on mastoid process to test BC; the tuning fork is then placed beside the pinna to test AC
    - If AC >BC → positive Rinne (normal)
  - Weber test
    - 512 Hz tuning fork is held on vertex of head and patient states whether it is heard centrally (Weber negative) or is lateralized to one side (Weber right, Weber left)
    - can place vibrating fork on patient's chin while they clench their teeth, or directly on teeth to elicit more reliable response
    - will only lateralize if difference in hearing loss between ears is >6 dB

Weber Test lateralization = ipsilateral conductive hearing loss or contralateral sensorineural hearing loss

The Weber test is more sensitive in detecting conductive hearing loss than the Rinne test

Table 4. The Interpretation of Tuning Fork Tests

Examples	Weber	Rinne
Normal or bilateral sensorineural hearing loss	Central	AC>BC (+) bilaterally
Right-sided conductive hearing loss, normal left ear	Lateralizes to right	BC>AC (–) right
Right-sided sensorineural hearing loss, normal left ear	Lateralizes to left	AC>BC (+) bilaterally
Right-sided severe sensorineural hearing loss or dead right ear, normal left ear	Lateralizes to left	BC>AC (–) right*

*A vibrating tuning fork on the mastoid stimulates the cochlea bilaterally, therefore in this case the left cochlea is stimulated by the Rinne test on the right (e.g. a false negative test). These tests are not valid if the ear canals are obstructed with cerumen (e.g. will create conductive loss)

Frequency of Tuning Fork (Hz)	Minimum Hearing Loss for Rinne to Reverse (BC>AC, NEGATIVE Rinne) (dB)
256	15
512	30
1024	45

Pure Tone Audiometry

- a threshold is the lowest intensity level at which a patient can hear the tone 50% of the time
- thresholds are obtained for each ear at frequencies of 250, 500, 1000, 2000, 4000, and 8000 Hz
- air conduction thresholds are obtained with headphones and measure outer, middle, inner ear, and auditory nerve function
- bone conduction thresholds are obtained with bone conduction oscillators which bypass the outer and middle ear

Range of Frequencies Audible to Human Ear
- 20 to 20000 Hz
- Most sensitive frequencies: 1000 to 4000 Hz
- Range of human speech: 500 to 2000 Hz

Degree of Hearing Loss

- determined on basis of the pure tone average (PTA) at 500, 1000, and 2000 Hz

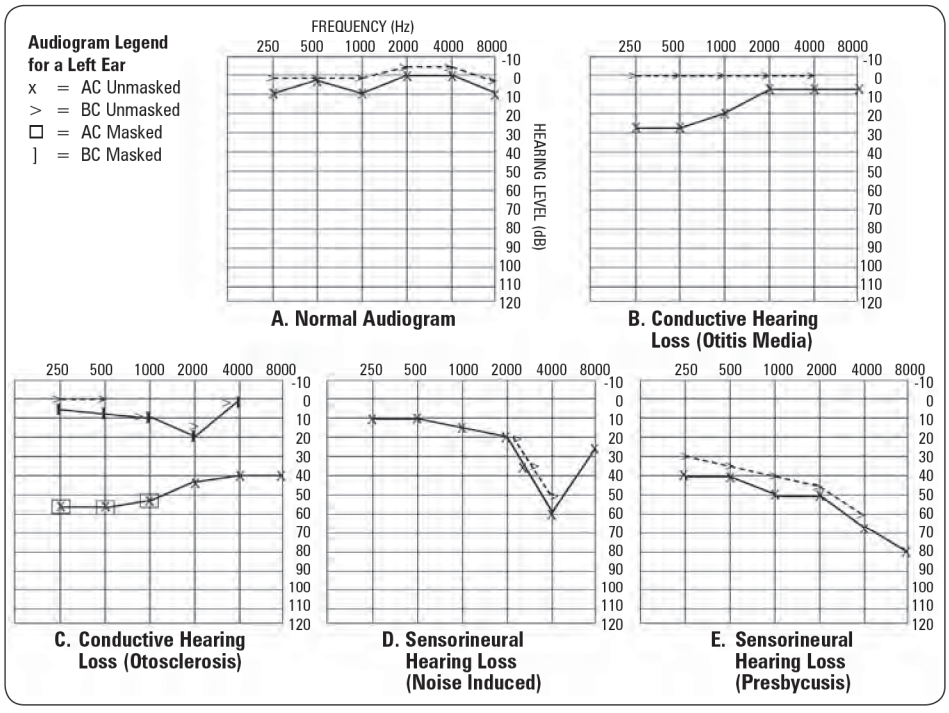


Figure 16. Types of hearing loss and associated audiograms of a left ear

Hearing loss most often occurs at higher frequencies. Noise-induced (occupational) HL is classically seen at 4000 Hz. HL associated with otosclerosis is seen at 2000 Hz (Carhart's notch)

PURE TONE PATTERNS

1. Conductive Hearing Loss (Figure 16B and 16C)
- BC in normal range
- AC outside of normal range
- gap between AC and BC thresholds >10 dB (an air-bone gap)

2. Sensorineural Hearing Loss (Figure 16D and 16E)
- both air and bone conduction thresholds below normal
- gap between AC and BC <10 dB (no air-bone gap)

3. Mixed Hearing Loss
- both air and bone conduction thresholds below normal
- gap between AC and BC thresholds >10 dB (an air-bone gap)

Speech Audiometry

Speech Reception Threshold
- lowest hearing level at which patient is able to repeat 50% of two syllable words which have equal emphasis on each syllable (spondee words)
- SRT and best pure tone threshold in the 500 to 2000 Hz range (frequency range of human speech) usually agree within 5 dB; if not, suspect a retrocochlear lesion or functional hearing loss
- used to assess the reliability of the pure tone audiometry

Speech Discrimination Test
- percentage of words the patient correctly repeats from a list of 50 monosyllabic words
- tested at 40 dB above the patient's SRT, therefore degree of hearing loss is taken into account
- patients with normal hearing or conductive hearing loss score >90%
- score depends on extent of SNHL
- rollover effect: a decrease in discrimination as sound intensity increases; typical of a retrocochlear lesion (e.g. acoustic neuroma)
- investigate further if scores differ more than 20% between ears as asymmetry may indicate a retrocochlear lesion
- used as best predictor of hearing aid response: a poor discrimination score indicates significant neural degeneration and hearing aids may not be the best option for the patient

Impedance Audiometry

Tympanogram
- the Eustachian tube equalizes the pressure between the external and middle ear
- tympanograms graph the compliance of the middle ear system against a pressure gradient ranging from to –400 to +200 mmH_2O
- tympanogram peak occurs at the point of maximum compliance: where the pressure in the external canal is equivalent to the pressure in the middle ear
- normal range: –100 to +50 mmH_2O

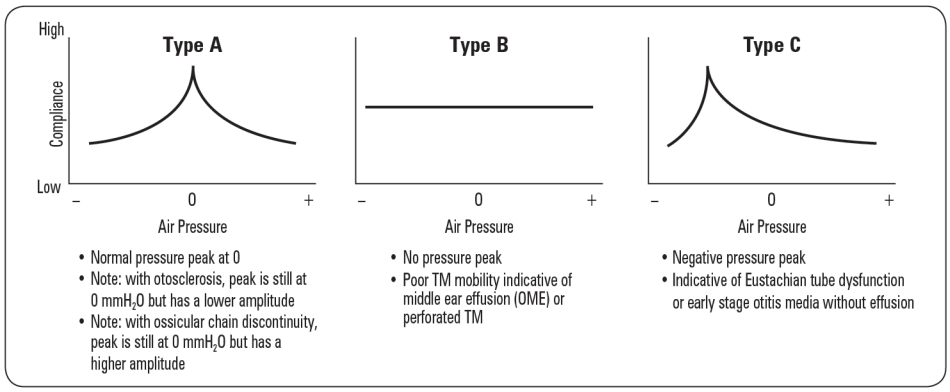


Figure 17. Tympanograms

Static Compliance
- volume measurement reflecting overall stiffness of the middle ear system
- normal range: 0.3-1.6 cc
- negative middle ear pressure and abnormal compliance indicate middle ear pathology
- in a type B curve, ear canal volumes of >2 cc in children and 2.5 cc in adults indicate TM perforation or presence of a patent ventilation tube

Acoustic Stapedial Reflexes
- stapedius muscle contracts in response to loud sound
- **acoustic reflex threshold** = 70-100 dB greater than hearing threshold; if hearing threshold >85 dB, reflex likely absent
- stimulating either ear causes bilateral and symmetrical reflexes
- for reflex to be present, CN VII must be intact and no conductive hearing loss in monitored ear
- if reflex is absent without conductive or severe sensorineural loss, suspect CN VII lesion
- **acoustic reflex decay test** = ability of stapedius muscle to sustain contraction for 10 s at 10 dB
- normally, little reflex decay occurs at 500 and 1000 Hz
- with cochlear hearing loss, acoustic reflex thresholds are 25-60 dB
- with retrocochlear hearing loss (acoustic neuroma), absent acoustic reflexes or marked reflex decay (>50%) within 5 s

Auditory Brainstem Response

- measures neuroelectric potentials (waves) in response to a stimulus in five different anatomic sites (see *Order of Neural Pathway* sidebar on OT9); this test can be used to determine the site of lesion
- delay in brainstem response suggests cochlear or retrocochlear abnormalities
- does not require volition or co-operation of patient (therefore of value in children and in malingerers)

Otoacoustic Emissions

- objective test of hearing where a series of clicks is presented to the ear and the cochlea generates an echo which can be measured
- often used in newborn screening
- can be used to uncover normal hearing in malingering patients
- absence of emissions can be due to hearing loss or fluid in the middle ear

Aural Rehabilitation

- dependent on degree of hearing loss, communicative requirements, motivation, expectations, and physical and mental abilities
- negative prognostic factors
  - poor speech discrimination
  - narrow dynamic range (recruitment)
  - unrealistic expectations
- types of hearing aids
  - BTE: behind-the-ear (with occlusive mould or open fit which allows natural sound to pass – for milder hearing losses)
  - ITE: in-the-ear, placed in concha
  - ITC: in-the-canal, placed entirely in ear canal
  - CIC: contained-in-canal, placed deeply in ear canal
  - bone conduction – bone-anchored hearing aid (BAHA): attached to the skull
  - contralateral routing of signals (CROS)
- assistive listening devices
  - direct/indirect audio output
  - infrared, FM radio, or induction loop systems
  - telephone, television, or alerting devices
- cochlear implants
  - electrode is inserted into the cochlea to allow direct stimulation of the auditory nerve
  - for profound bilateral sensorineural hearing loss not rehabilitated with conventional hearing aids
  - established indication: post-lingually deafened adults, pre- and post-lingually deaf children

Pre-lingually deaf infants are the best candidates for aural rehabilitation because they have maximal benefit from ongoing developmental plasticity

Bone Anchored Hearing Aids (BAHA)
BAHAs function based on bone conduction and are indicated primarily for patients with conductive hearing loss, unilateral hearing loss, and mixed hearing loss who cannot wear conventional hearing aids. BAHAs consist of a titanium implant, an external abutment, and a sound processor. The sound processor transmits vibrations through the external abutment to the titanium implant and then directly to the cochlea.

Pre-lingual deafness: deafness occurring before speech and language are acquired

Post-lingual deafness: deafness occurring after speech and language are acquired

Vertigo

Evaluation of the Dizzy Patient

- vertigo: illusion of rotational, linear, or tilting movement of self or environment
  - vertigo is produced by peripheral (inner ear) or central (brainstem-cerebellum) stimulation
- it is important to distinguish vertigo from other disease entities that may present with similar complaints of "dizziness" (e.g. cardiovascular, psychiatric, neurological, aging)

Table 5. Peripheral vs. Central Vertigo

Symptoms	Peripheral	Central
Imbalance	Moderate-severe	Mild-moderate
Nausea and Vomiting	Severe	Variable
Auditory Symptoms	Common	Rare
Neurologic Symptoms	Rare	Common
Compensation	Rapid	Slow
Nystagmus	Unidirectional Horizontal or rotatory	Bidirectional Horizontal or vertical

Table 6. Differential Diagnosis of Vertigo Based on History

Condition	Duration	Hearing Loss	Tinnitus	Aural Fullness	Other Features
Benign Paroxysmal Positional Vertigo (BPPV)	Seconds	–	–	–	
Menière's Disease	Minutes to hours Precedes attack	Uni/bilateral, fluctuating	+	Pressure/warmth	
Vestibular Neuronitis	Hours to days	–	–	–	
Labyrinthitis	Days	Unilateral	Whistling	–	Recent AOM
Acoustic Neuroma	Chronic	Progressive	+	–	Ataxia CN VII palsy

Table 7. Differential Diagnosis of Vertigo Based on Time Course

Time Course	Condition
Recurrent, lasting	BPPV
Single episode, lasting minutes to hours	Migraine, transient ischemia of the labyrinth or brainstem
Recurrent to hours	Menière's
Prolonged	Vestibular neuritis, MS, brainstem/cerebellum infarct
Acoustic neuroma	Chronic

Benign Paroxysmal Positional Vertigo

BPPV is the most common cause of episodic vertigo; patients often are symptomatic when rolling over in bed or moving their head to a position of extreme posterior extension such as looking up at a tall building or getting their hair washed at the hairdresser

Definition
- acute attacks of transient rotatory vertigo lasting **seconds to minutes** initiated by certain head positions, accompanied by torsional (i.e. rotatory) nystagmus (geotropic = fast phase towards the floor)
- most common form of positional vertigo (50% of patients with peripheral vestibular dysfunction)

Etiology
- due to canalithiasis (migration of free floating otoliths within the endolymph of the semicircular canal) or cupulolithiasis (otolith attached to the cupula of the semicircular canal)
  - can affect each of the 3 semicircular canals, although the posterior canal is affected in >90% of cases
  - causes: head injury, viral infection (URTI), degenerative disease, idiopathic
  - results in slightly different signals being received by the brain from the two balance organs resulting in sensation of movement

5 Signs of BPPV seen with Dix-Hallpike Maneuver
- Latency of ~20 s
- Crescendo/decrescendo vertigo lasting 20 s
- Geotropic rotatory nystagmus (nystagmus MUST be present for a positive test)
- Reversal of nystagmus upon sitting up

Diagnosis
- history (time course, provoking factors, associative symptoms)
- positive Dix-Hallpike maneuver (sensitivity 82%, specificity 71%)

Dix-Hallpike Positional Testing (see website for video and illustrations)
- the patient is rapidly moved from a sitting position to a supine position with the head hanging over the end of the table, turned to one side at 45° and neck extended 20° holding the position for 20 s
- onset of vertigo and rotary nystagmus indicate a positive test for the dependent side
- other diagnostic testing is not indicated in posterior canal BPPV

Treatment
- reassure patient that process resolves spontaneously
- particle repositioning maneuvers
  - Epley maneuver (performed by MD)
  - Brandt-Daroff exercises (performed by patient)
- surgery for refractory cases
- anti-emetics for N/V
- drugs to suppress the vestibular system delay eventual recovery and are therefore not used

Menière's Disease (Endolymphatic Hydrops)

Diagnostic Criteria for Menière's Disease (must have all three):
- Two spontaneous episodes of rotational vertigo ≥20 minutes
- Audiometric confirmation of SNHL (often low frequency)
- Tinnitus and/or aural fullness

Definition
- episodic attacks of tinnitus, hearing loss, aural fullness, and vertigo lasting **minutes to hours**

Proposed Etiology
- inadequate absorption of endolymph leads to endolymphatic hydrops (over accumulation) that distorts the membranous labyrinth

Epidemiology
- peak incidence 40-60 yr
- bilateral in 35% of cases

Clinical Features
- episodic vertigo, fluctuating low frequency SNHL, tinnitus, and aural fullness
- ± drop attacks (Tumarkin crisis), ± N/V
- vertigo disappears with time (min to h), but hearing loss remains
- early in the disease: fluctuating SNHL
- later stages: persistent tinnitus and progressive hearing loss
- attacks come in clusters and can be debilitating to the patient
- triggers: high salt intake, caffeine, stress, nicotine, and alcohol

Drop Attacks (Tumarkin's Otolithic Crisis) are sudden falls occurring without warning and without LOC

Treatment
- acute management may consist of bed rest, antiemetics, antivertiginous drugs (e.g. betahistine [Serc®]), and low molecular weight dextrans (not commonly used)
- long-term management may include
  - medical
    - low salt diet, diuretics (e.g. hydrochlorothiazide, triamterene, amiloride)
    - Serc® prophylactically to decrease intensity of attacks
    - local application of gentamicin to destroy vestibular end-organ, results in complete SNHL
  - surgical
    - selective vestibular neurectomy or transtympanic labyrinthectomy
    - vestibular implants have recently been introduced experimentally
- must monitor opposite ear as bilaterality occurs in 35% of cases

Before proceeding with gentamicin treatment, perform a gadolinium enhanced MRI to rule out CPA tumour as the cause of symptoms

Vestibular Neuronitis

Definition
- acute onset of disabling vertigo often accompanied by N/V and imbalance without hearing loss that resolves over **days** leaving a residual imbalance that lasts **days to weeks**

Etiology
- thought to be due to a viral infection (e.g. measles, mumps, herpes zoster)
- ~30% of cases have associated URTI symptoms
- other: microvascular events, diabetes, autoimmune process
- considered to be the vestibular equivalent of Bell's palsy, sudden hearing loss, and acute vocal cord palsy

Clinical Features
- acute phase
  - severe vertigo with N/V and imbalance lasting 1-5 d
  - irritative nystagmus (fast phase towards the offending ear)
  - patient tends to veer towards affected side
- convalescent phase
  - imbalance and motion sickness lasting days to weeks
  - spontaneous nystagmus away from affected side
  - gradual vestibular adaptation requires weeks to months
- incomplete recovery likely with the following risk factors: elderly, visual impairment, poor ambulation
- repeated attacks can occur

Treatment
- acute phase
  - bed rest, vestibular sedatives (Gravol®), diazepam
- convalescent phase
  - progressive ambulation especially in the elderly
  - vestibular exercises: involve eye and head movements, sitting, standing, and walking

Labyrinthitis

Definition
- acute infection of the inner ear resulting in vertigo and hearing loss

Etiology
- may be serous (viral) or purulent (bacterial)
- occurs as a complication of acute and chronic otitis media, bacterial meningitis, cholesteatoma, and temporal bone fractures
- bacterial: *S. pneumoniae, H, influenzae, M. catarrhalis, P. aeruginosa, P. mirabilis*
- viral: rubella, CMV, measles, mumps, varicella zoster

Clinical Features
- sudden onset of vertigo, N/V, tinnitus, and unilateral hearing loss with no associated fever or pain
- meningitis is a serious complication

Investigations
- CT head
- if meningitis is suspected: lumbar puncture, blood cultures

Treatment
- treat with IV antibiotics, drainage of middle ear ± mastoidectomy

Acoustic Neuroma (Vestibular Schwannoma)

Definition
- schwannoma of the vestibular portion of CN VIII

Pathogenesis
- starts in the internal auditory canal and expands into cerebellopontine angle (CPA), compressing cerebellum and brainstem
- when associated with type 2 neurofibromatosis (NF2): bilateral acoustic neuromas, café-au-lait skin lesions, and multiple intracranial lesions

Clinical Features
- usually presents with unilateral SNHL (chronic) or tinnitus
- dizziness and unsteadiness may be present, but true vertigo is rare as tumour growth occurs slowly and thus compensation occurs
- facial nerve palsy and trigeminal (V1) sensory deficit (corneal reflex) are late complications
- risk factors: exposure to loud noise, childhood exposure to low-dose radiation, history of parathyroid adenoma

Acoustic neuroma is the most common intracranial tumour causing SNHL and the most common cerebellopontine angle tumour

Diagnosis
- MRI with gadolinium contrast (gold standard)
- audiogram (to assess SNHL)
- poor speech discrimination relative to the hearing loss
- stapedial reflex absent or significant reflex decay
- ABR: increase in latency of the 5th wave
- vestibular tests: normal or asymmetric caloric weakness (an early sign)

In the elderly, unilateral tinnitus or SNHL is acoustic neuroma until proven otherwise

Treatment
- expectant management if tumour is very small, or in elderly
- definitive management is surgical excision
- other options: gamma knife, radiation

Tinnitus

Definition
- an auditory perception in the absence of an acoustic stimuli, likely related to loss of input to neurons in central auditory pathways and resulting in abnormal firing

History
- subjective vs. objective (see Figure 14, OT7)
- continuous vs. pulsatile (vascular in origin)
- unilateral vs. bilateral
- associated symptoms: hearing loss, vertigo, aural fullness, otalgia, otorrhea

Investigations
- audiology
- if unilateral
  - ABR, gadolinium enhanced MRI to exclude a retrocochlear lesion
  - CT to diagnose glomus tympanicum (rare)
  - MRI or angiogram to diagnose AVM
- if suspect metabolic abnormality: lipid profile, TSH

Treatment
- if a cause is found, treat the cause (e.g. drainage of middle ear effusion, embolization or excision of AVM)
- with no treatable cause: 50% will improve, 25% worsen, 25% remain the same
- avoid loud noise, ototoxic meds, caffeine, smoking
- tinnitus clinics

- identify situations where tinnitus is most bothersome (e.g. quiet times), mask tinnitus with soft music or "white noise"
- hearing aid if coexistent hearing loss
- tinnitus instrument: combines hearing aid with white noise masker
- trial of tocainamide

Diseases of the External Ear

Cerumen Impaction

Cerumen impaction is the most common cause of conductive hearing loss for those aged 15-50 yr

Etiology
- ear wax: a mixture of secretions from ceruminous and pilosebaceous glands, squames of epithelium, dust, and debris

Risk Factors
- hairy or narrow ear canals, in-the-ear hearing aids, cotton swab usage, osteomata

Clinical Features
- hearing loss (conductive)
- ± tinnitus, vertigo, otalgia, aural fullness

Treatment
- ceruminolytic drops (bicarbonate solution, olive oil, glycerine, Cerumenol®, Cerumenex®)
- syringing
- manual debridement (by MD)

Syringing

Indications
- Totally occlusive cerumen with pain, decreased hearing, or tinnitus

Contraindications
- Active infection
- Previous ear surgery
- Only hearing ear
- TM perforation

Complications
- Otitis externa
- TM perforation
- Trauma
- Pain
- Vertigo
- Tinnitus
- Otitis media

Method
- Establish that TM is intact
- Gently pull the pinna superiorly and posteriorly
- Using warm water, aim the syringe nozzle upwards and posteriorly to irrigate the ear canal

Exostoses

Definition
- bony protuberances in the external auditory canal composed of lamellar bone

Etiology
- possible association with swimming in cold water

Clinical Features
- usually an incidental finding
- if large, they can cause cerumen impaction or otitis externa

Treatment
- no treatment required unless symptomatic

Otitis Externa

Etiology
- bacteria (~90% of OE): *Pseudomonas aeruginosa, Pseudomonas vulgaris, E. coli, S. aureus*
- fungus: *Candida albicans, Aspergillus niger*

Risk Factors
- associated with swimming ("swimmer's ear")
- mechanical cleaning (Q-tips®), skin dermatitis, aggressive scratching
- devices that occlude the ear canal: hearing aids, headphones, etc.
- allergic contact dermatitis, dermatologic conditions (psoriasis, atopic dermatitis)

Clinical Features
- acute
  - pain aggravated by movement of auricle (traction of pinna or pressure over tragus)
  - otorrhea (sticky yellow purulent discharge)
  - conductive hearing loss ± aural fullness 2° to obstruction of external canal by swelling and purulent debris
  - posterior auricular lymphadenopathy
  - complicated OE exists if the pinna and/or the periauricular soft tissues are erythematous and swollen
- chronic
  - pruritus of external ear ± excoriation of ear canal
  - atrophic and scaly epidermal lining, ± otorrhea, ± hearing loss
  - wide meatus but no pain with movement of auricle
  - tympanic membrane appears normal

Pulling on the pinna is extremely painful in otitis externa, but is usually well tolerated in otitis media

Treatment
- clean ear under magnification with irrigation, suction, dry swabbing, and C&S
- bacterial etiology
  - antipseudomonal otic drops (e.g. ciprofloxacin) or a combination of antibiotic and steroid (e.g. Cipro HC®)
  - do not use aminoglycoside if the tympanic membrane (TM) is perforated because of the risk of ototoxicity
  - introduction of fine gauze wick (pope wick) if external canal edematous
  - ± 3% acetic acid solution to acidify ear canal (low pH is bacteriostatic)
  - systemic antibiotics if either cervical lymphadenopathy or cellulitis is present
- fungal etiology
  - repeated debridement and topical antifungals (gentian violet, Mycostatin® powder, boric acid, Locacorten®, Vioform® drops)
- ± analgesics
- chronic otitis externa (pruritus without obvious infection) → corticosteroid alone (e.g. diprosalic acid)

Malignant (Necrotizing) Otitis Externa (Skull Base Osteomyelitis)

Definition
- osteomyelitis of the temporal bone

Epidemiology
- occurs in elderly diabetics and immunocompromised patients

Etiology
- rare complication of otitis externa
- *Pseudomonas* infection in 99% of cases

Clinical Features
- otalgia and purulent otorrhea that is refractory to medical therapy
- granulation tissue on the floor of the auditory canal

Complications
- cranial nerve palsy (most commonly CN VII>CN X>CN XI)
- systemic infection, death

Management
- imaging: high resolution temporal bone CT scan, gadolinium enhanced MRI, technetium scan
- requires hospital admission, debridement, IV antibiotics, hyperbaric O_2
- may require OR for debridement of necrotic tissue/bone

Gallium and Technetium Scans
Gallium scans are used to show sites of active infection. Gallium is taken up by PMNs and therefore only lights up when active infection is present. It will not show the extent of osteomyelitis. Technetium scans provide information about osteoblastic activity and, as a result, are used to demonstrate sites of osteomyelitis. Technetium scans help with diagnosis whereas gallium scans are useful in follow-up

Diseases of the Middle Ear

Acute Otitis Media and Otitis Media with Effusion

- see *Pediatric Otolaryngology*, OT39

Chronic Otitis Media

Definition
- an ear with TM perforation in the setting of recurrent or chronic ear infections

Benign
- dry TM perforation without active infection

Chronic Serous Otitis Media
- continuous serous drainage (straw-coloured)

Chronic Suppurative Otitis Media
- persistent purulent drainage through a perforated TM

Cholesteatoma

Definition
- a cyst composed of keratinized desquamated epithelial cells occurring in the middle ear, mastoid, and temporal bone
- two types: congenital and acquired

Congenital
- presents as a "small white pearl" behind an intact tympanic membrane (anterior and medial to the malleus) or as a conductive hearing loss
- believed to be due to aberrant migration of external canal ectoderm during development
- not associated with otitis media/Eustachian tube dysfunction

Acquired (more common)
- primary cholesteatoma
  - frequently associated with retraction pockets in the pars flaccida (may lead to attic cholesteatomas which are difficult to visualize)
  - often has crusting or desquamated debris on lateral surface
- secondary cholesteatoma
  - pearly mass evident behind TM, frequently associated with marginal perforation
  - may appear as skin that have replaced the mucosa of the middle ear
- the associated chronic inflammatory process causes progressive destruction of surrounding bony structures

Mechanisms of Cholesteatoma Formation
- Epithelial migration through TM perforation (2° acquired)
- Invagination of TM (1° acquired)
- Metaplasia of middle ear epithelium or basal cell hyperplasia (congenital)

Clinical Features
- history of otitis media (especially if unilateral), ventilation tubes, ear surgery
- symptoms
  - progressive hearing loss (predominantly conductive although may get sensorineural hearing loss in late stage)
  - otalgia, aural fullness, fever
- signs
  - retraction pocket in TM, may contain keratin debris
  - TM perforation
  - granulation tissue, polyp visible on otoscopy
  - malodorous, unilateral otorrhea

Complications

Table 8. Complications of Cholesteatoma

Local	Intracranial
Ossicular erosion: conductive hearing loss	Meningitis
Inner ear erosion: SNHL, dizziness, and/or labyrinthitis	Sigmoid sinus thrombosis
Temporal bone infection: mastoiditis, petrositis	Intracranial abscess (subdural, epidural, cerebellar)
Facial paralysis	

Investigations
- audiogram and CT scan

Treatment
- there is no conservative therapy for cholesteatoma
- surgical: mastoidectomy ± tympanoplasty ± ossicular reconstruction

Mastoiditis

Definition
- infection (usually subperiosteal) of mastoid air cells, most commonly seen approximately two weeks after onset of untreated or inadequately treated acute suppurative otitis media
- more common in children than adults

Etiology
- acute mastoiditis caused by the same organisms as AOM: *S. pneumoniae, H. influenzae, M. catarrhalis, S. pyogenes, S. aureus, P. aeruginosa*

Clinical Features
- otorrhea
- tenderness to pressure over the mastoid
- retroauricular swelling with protruding ear
- fever, hearing loss, ± TM perforation (late)
- CT radiologic findings: opacification of mastoid air cells by fluid and interruption of normal trabeculations of cells (coalescence)

Classic Triad
- Otorrhea
- Tenderness to pressure over the mastoid
- Retroauricular swelling with protruding ear

Treatment
- IV antibiotics with myringotomy and ventilation tubes – usually all that is required acutely
- cortical mastoidectomy
  - debridement of infected tissue allowing aeration and drainage
- indications for surgery
  - failure of medical treatment after 48 h
  - symptoms of intracranial complications
  - aural discharge persisting for 4 wk and resistant to antibiotics

Complications of AOM are rare due to rapid and effective treatment of AOM with antibiotics

Otosclerosis

Definition
- fusion of stapes footplate to oval window so that it cannot vibrate

Otosclerosis is the 2nd most common cause of conductive hearing loss in 15-50 yr old (after cerumen impaction)

Etiology
- autosomal dominant, variable penetrance approximately 40%
- F>M, progresses during pregnancy (hormone responsive)

Clinical Features
- progressive conductive hearing loss first noticed in teens and 20s (may progress to sensorineural hearing loss if cochlea involved)
- ± pulsatile tinnitus
- tympanic membrane normal ± pink blush (Schwartz's sign) associated with the neovascularization of otosclerotic bone
- characteristic dip at 2000 Hz (Carhart's notch) on audiogram (see Figure 16C, OT10)

Treatment
- monitor with serial audiograms if coping with loss
- hearing aid (air conduction, bone conduction, BAHA)
- stapedectomy or stapedotomy (with laser or drill) with prosthesis is definitive treatment

Diseases of the Inner Ear

Congenital Sensorineural Hearing Loss

Hereditary Defects
- non-syndrome associated (70%)
  - often idiopathic, autosomal recessive
  - connexin 26 (GJB2) most common
- syndrome associated (30%)
  - Waardenburg: white forelock, heterochromia iridis (each eye different colour), wide nasal bridge and increased distance between medial canthi
  - Pendred: deafness associated with thyroid gland disorders, SLC26A4 gene, enlarged vestibular aqueducts
  - Treacher-Collins: first and second branchial cleft anomalies
  - Alport: hereditary nephritis

Prenatal TORCH Infections
- toxoplasmosis, others (e.g. HIV, syphilis), rubella, CMV, HSV

Perinatal
- Rh incompatibility
- anoxia
- hyperbilirubinemia
- birth trauma (hemorrhage into inner ear)

Postnatal
- meningitis, mumps, measles

High Risk Factors (for hearing loss in newborns)
- low birth weight/prematurity
- perinatal anoxia (low APGARs)
- kernicterus: bilirubin >25 mg/dL
- craniofacial abnormality
- family history of deafness in childhood
- 1st trimester illness: TORCH infections
- neonatal sepsis
- ototoxic drugs

- perinatal infection, including post-natal meningitis
- consanguinity
- 50-75% of newborns with SNHL have at least one of the above risk factors and 90% of these have spent time in the NICU
- presence of any risk factor: ABR study performed before leaving NICU and at 3 mo adjusted age
- early rehabilitation improves speech and school performance

Presbycusis

Presbycusis is the most common cause of SNHL

Definition
- SNHL associated with aging (starting in 5th and 6th decades)

Etiology
- hair cell degeneration
- age related degeneration of basilar membrane, possibly genetic etiology
- cochlear neuron damage
- ischemia of inner ear

Clinical Features
- progressive, bilateral hearing loss initially at high frequencies, then middle frequencies
- loss of discrimination of speech especially with background noise present – patients describe people as mumbling
- recruitment phenomenon: inability to tolerate loud sounds
- tinnitus

Treatment
- hearing aid if patient has difficulty functioning, hearing loss >30-35 dB, and good speech discrimination
- ± lip reading, auditory training, auditory aids (doorbell and phone lights)

Sudden Sensorineural Hearing Loss

Sudden SNHL may easily be confused with ischemic brain events. It is important to keep a high index of suspicion especially with elderly patients presenting with sudden SNHL as well as vertigo

Clinical Features
- presents as a sudden onset of significant SNHL (usually unilateral) ± tinnitus, aural fullness
- usually idiopathic, rule out other causes
  - autoimmune causes (e.g. ESR, rheumatoid factor, ANA)
  - MRI to rule out tumour and/or CT to rule out ischemic/hemorrhagic stroke if associated with any other focal neurological signs (e.g. vertigo, ataxia, abnormality of CN V or VII, weakness)

Treatment
- oral corticosteroids within 3 d of onset: prednisone 1 mg/kg/d for 10-14 d

Prognosis
- depends on degree of hearing loss
- 70% resolve within 10-14 d
- 20% experience partial resolution
- 10% experience permanent hearing loss

Autoimmune Inner Ear Disease

Etiology
- idiopathic
- may be associated with systemic autoimmune diseases (e.g. rheumatoid arthritis, SLE), vasculitides (e.g. GPA, polyarteritis nodosa), and allergies

Epidemiology
- most common between ages 20-50

Clinical Features
- rapidly progressive or fluctuating bilateral SNHL
- ± tinnitus, aural fullness, vestibular symptoms (e.g. ataxia, disequilibrium, vertigo)

Investigations
- autoimmune workup: CBC, ESR, ANA, rheumatoid factor

Treatment
- high-dose corticosteroids: treat early for at least 30 d
- consider cytotoxic medication for steroid non-responders

Drug Ototoxicity

Aminoglycosides
- streptomycin and gentamicin (vestibulotoxic), kanamycin, and tobramycin (cochleotoxic)
- toxic to hair cells by any route: oral, IV, and topical (if the TM is perforated)
- destroys sensory hair cells: outer first, inner second (therefore otoacoustic emissions are lost first)
- high frequency hearing loss develops earliest
- ototoxicity occurs days to weeks post-treatment
- must monitor with peak and trough levels when prescribed, especially if patient has neutropenia and/or history of ear or renal problems
- q24h dosing recommended (with amount determined by creatinine clearance)
- aminoglycoside toxicity displays saturable kinetics, therefore, once daily dosing presents less risk than divided daily doses
- duration of treatment is the most important predictor of ototoxicity
- treatment: immediately stop aminoglycosides

Salicylates
- hearing loss with tinnitus, reversible if discontinued

Antimalarials (Quinines)
- hearing loss with tinnitus
- reversible if discontinued but can lead to permanent loss

Others
- many antineoplastic agents are ototoxic (weigh risks vs. benefits)
- loop diuretics

Noise-Induced Sensorineural Hearing Loss

Pathogenesis
- 85-90 dB over months or years or single sound impulses >135 dB can cause cochlear damage
- bilateral SNHL initially and most prominently at 4000 Hz (resonant frequency of the temporal bone), known as "boilermaker's notch" on audiogram, extends to higher and lower frequencies with time (see Figure 16D, OT10)
- speech reception not altered until hearing loss >30 dB at speech frequency, therefore considerable damage may occur before patient complains of hearing loss
- difficulty with speech discrimination, especially in situations with competing noise

Phases of Hearing Loss
- dependent on: intensity of sound and duration of exposure
- temporary threshold shift
  - when exposed to loud sound, decreased sensitivity or increased threshold for sound
  - may have associated aural fullness and tinnitus
  - with removal of noise, hearing returns to normal
- permanent threshold shift
  - hearing does not return to previous state

Treatment
- hearing aid
- prevention
  - ear protectors: muffs, plugs
  - limit exposure to noise with frequent rest periods
  - regular audiologic follow-up

Temporal Bone Fractures

Table 9. Features of Temporal Bone Fractures

	Transverse (1)	Longitudinal (2)
Extension	Into bony labyrinth and internal auditory meatus	Into middle ear
Incidence	10-20%	70-90%
Etiology	Frontal/occipital trauma	Lateral skull trauma
CN Pathology	CN VII palsy (50%)	CN VII palsy (10-20%)
Hearing Loss	SNHL due to direct cochlear injury	CHL secondary to ossicular injury
Vestibular Symptoms	Sudden onset vestibular symptoms due to direct semicircular canal injury (vertigo, spontaneous nystagmus)	Rare
Other Features	Intact external auditory meatus, TM ± hemotympanum Spontaneous nystagmus CSF leak in Eustachian tube to nasopharynx ± rhinorrhea (risk of meningitis)	Torn TM or hemotympanum Bleeding from external auditory canal Step formation in external auditory canal CSF otorrhea Battle's sign = mastoid ecchymoses Raccoon eyes = periorbital ecchymoses

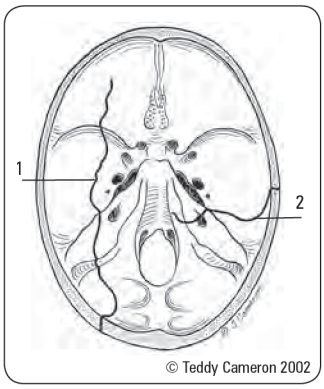


Figure 18. Types of temporal bone fractures

- characterized as longitudinal or transverse relative to the long axis of the petrous temporal bone
- temporal bone fractures are rarely purely transverse or longitudinal (often a mixed picture)

Hemotympanum can be indicative of temporal bone trauma

Diagnosis
- otoscopy
- do not syringe or manipulate external auditory meatus due to risk of inducing meningitis via TM perforation
- CT head
- audiology, facial nerve tests (for transverse fractures), Schirmer's test (of lacrimation), stapedial reflexes if CN VII palsy
- if suspecting CSF leak: look for halo sign, send fluid for β-2 transferrin

Signs of Basilar Skull Fracture

Battle's Sign: ecchymosis of the mastoid process of the temporal bone

Racoon Eyes

CSF Rhinorrhea/Otorrhea

Cranial Nerve Involvement: facial palsy → CN VII, nystagmus → CN VI, facial numbness → CN V

Treatment
- ABCs
- medical: expectant, prevent otogenic meningitis
- surgical: explore temporal bone, indications
  - CN VII palsy (immediate and complete)
  - gunshot wound
  - depressed fracture of external auditory meatus
  - early meningitis (mastoidectomy)
  - bleeding intracranially from sinus
  - CSF otorrhea (may resolve spontaneously)

Complications
- AOM ± labyrinthitis ± mastoiditis
- meningitis/epidural abscess/brain abscess
- post-traumatic cholesteatoma

Facial Nerve (CN VII) Paralysis

Etiology
- supranuclear and nuclear (MS, poliomyelitis, cerebral tumours)
- infranuclear

Treatment
- treat according to etiology plus provide corneal protection with artificial tears, nocturnal lid taping, tarsorrhaphy, gold weighting of upper lid
- facial paralysis that does not resolve with time or with medical treatment will often be referred for possible reanimation techniques to restore function
  - common reanimation techniques include
    - direct facial nerve anastomosis
    - interpositional grafts
    - anastomosis to other motor nerves
    - muscle transpositions

Table 10. Differential Diagnosis of Peripheral Facial Paralysis (PFP)

Etiology	Incidence	Findings	Investigations	Treatment, Follow-up, and Prognosis (Px)
Bell's Palsy Idiopathic, (HSV) infection of the facial nerve Diagnosis of exclusion	80-90% of PFP **Risk Factors:** DM Pregnancy Viral prodrome (50%)	**Hx** Acute onset Numbness of ear Schirmer's test Recurrence (12%) + FHx (14%) Hyperacusis (30%) **P/E** Paralysis or paresis of all muscle groups on one side of the face Absence of signs of CNS disease Absence of signs of ear or CPA diseases	Stapedial reflex absent Audiology normal (or baseline) EMG – best measure for prognosis Topognostic testing MRI with gadolinium – enhancement of CN VII and VIII High resolution CT	**Rx** Protect the eye to prevent exposure keratitis with patching or tarsorraphy Systemic steroids may lessen degeneration and hasten recovery Consider antiviral (acyclovir) **F/U** Spontaneous remission should begin within 3 wk of onset Delayed (3-6 mo) recovery portends at least some functional loss **Px** 90% recover spontaneously and completely overall; >90% recovery if paralysis was incomplete Poorer if hyperacusis, >60 yr, DM, HTN, severe pain
Ramsay Hunt Syndrome (Herpes Zoster Oticus) Varicella zoster infection of CN VII/VIII	4.5-9% of PFP **Risk Factors:** >60 yr Impaired immunity Cancer Radiotherapy Chemotherapy	**Hx** Hyperacusis SNHL Severe pain of pinna, mouth, or face **P/E** Vesicles on pinna, external canal (errupt 3-7 d after onset of pain) Associated herpes zoster ophthalmicus (uveitis, keratoconjunctivitis, optic neuritis, or glaucoma)	Stapedial reflex absent Audiology – SNHL Viral ELISA studies to confirm MRI with gadolinium (86% of facial nerves enhance)	**Rx** Avoid touching lesions to prevent spread of infection Systemic steroids can relieve pain, vertigo, avoid postherpetic neuralgia Acyclovir may lessen pain, aid healing of vesicles **F/U:** 2-4 wk **Px** Poorer prognosis than Bell's palsy; 22% recover completely, 66% incomplete paralysis, 10% complete paralysis
TEMPORAL BONE FRACTURE				
Longitudinal (90%)	20% have PFP	**Hx** Blow to side of head **P/E** Trauma to side of head Neuro findings consistent with epidural/subdural bleed	Skull x-rays CT head	**Px** Injury usually due to stretch or impingement; may recover with time
Transverse (10%)	40% have PFP	**Hx** Blow to frontal or occipital area **P/E** Trauma to front or back of head	Skull x-rays CT head	**Px** Nerve transection more likely
Iatrogenic		Variable (depending on level of injury)	Wait for lidocaine to wear off EMG	**Rx** Exploration if complete nerve paralysis No exploration if any movement present

Source: Paul Warrick, MD

Rhinitis

Definition

- inflammation of the lining (mucosa) of the nasal cavity

Table 11. Classification of Rhinitis

Inflammatory	Non-Inflammatory

• Perennial non-allergic
  • Asthma, ASA sensitivity
• Allergic
  • Seasonal
  • Perennial
• Atrophic
  • Primary: *Klebsiella ozena* (especially in elderly)
  • Acquired: post-surgery if too much mucosa or turbinate has been resected
• Infectious
  • Viral: e.g. rhinovirus, influenza, parainfluenza, etc.
  • Bacterial: e.g. *S. aureus*
  • Fungal
  • Granulomatous: TB, syphilis, leprosy
• Non-infectious
  • Sarcoidosis
  • GPA
• Irritant
  • Dust
  • Chemicals
  • Pollution
	• Rhinitis medicamentosa
	  • Topical decongestants
	• Hormonal
	  • Pregnancy
	  • Estrogens
	  • Thyroid
	• Idiopathic vasomotor

Rhinitis medicamentosa: rebound congestion due to the overuse of intranasal vasoconstrictors; for prevention, use of these medications for only 5-7 d is recommended

Table 12. Nasal Discharge: Character and Associated Conditions

Character	Associated Conditions
Watery/mucoid	Allergic, viral, vasomotor, CSF leak (halo sign)
Mucopurulent	Bacterial, foreign body
Serosanguinous	Neoplasia
Bloody	Trauma, neoplasia, bleeding disorder, hypertension/vascular disease

Allergic Rhinitis (Hay Fever)

Definition
- rhinitis characterized by an IgE-mediated hypersensitivity to foreign allergens
- acute-and-seasonal or chronic-and-perennial
- perennial allergic rhinitis often confused with recurrent colds

Etiology
- when allergens contact the respiratory mucosa, specific IgE antibody is produced in susceptible hosts
- concentration of allergen in the ambient air correlates directly with the rhinitis symptoms

Congestion reduces nasal airflow and allows the nose to repair itself (i.e. washes away the irritants)

Treatment should focus on the initial insult rather than target this defense mechanism

Epidemiology
- age at onset usually <20 yr
- more common in those with a personal or family history of allergies/atopy

Clinical Features
- nasal: obstruction with pruritus, sneezing
- clear rhinorrhea (containing increased eosinophils)
- itching of eyes with tearing
- frontal headache and pressure
- mucosa: swollen, pale, "boggy"
- seasonal (summer, spring, early autumn)
  - pollens from trees
  - lasts several weeks, disappears, and recurs following year at same time
- perennial
  - inhaled: house dust, wool, feathers, foods, tobacco, hair, mould
  - ingested: wheat, eggs, milk, nuts
  - occurs intermittently for years with no pattern or may be constantly present

Complications
- chronic sinusitis/polyps
- serous otitis media

Diagnosis
- history
- direct exam
- allergy testing

Treatment
- education: identification and avoidance of allergen
- nasal irrigation with saline
- antihistamines (e.g. diphenhydramine, fexofenadine)
- oral decongestants (e.g. pseudoephedrine, phenylpropanolamine)
- topical decongestant (may lead to rhinitis medicamentosa)
- other topicals: steroids (fluticasone), disodium cromoglycate, antihistamines, ipratropium bromide
- oral steroids if severe
- desensitization by allergen immunotherapy

Vasomotor Rhinitis

- neurovascular disorder of nasal parasympathetic system (vidian nerve) affecting mucosal blood vessels
- nonspecific reflex hypersensitivity of nasal mucosa
- caused by
  - temperature change
  - alcohol, dust, smoke
  - stress, anxiety, neurosis
  - endocrine: hypothyroidism, pregnancy, menopause
  - parasympathomimetic drugs
  - beware of rhinitis medicamentosa: reactive vasodilation due to prolonged use (>5 d) of nasal drops and sprays (Dristan®, Otrivin®)

Clinical Features
- chronic intermittent nasal obstruction, varies from side to side
- rhinorrhea: thin, watery
- mucosa and turbinates: swollen
- nasal allergy must be ruled out

Treatment
- elimination of irritant factors
- parasympathetic blocker (Atrovent® nasal spray)
- steroids (e.g. beclomethasone, fluticasone)
- surgery (often of limited lasting benefit): electrocautery, cryosurgery, laser treatment, or removal of inferior or middle turbinates
- vidian neurectomy (rarely done)
- symptomatic relief with exercise (increased sympathetic tone)

Rhinosinusitis

Pathogenesis of Rhinosinusitis
- ostial obstruction or dysfunctional cilia permit stagnant mucous and, consequently, infection
- all sinuses drain to a common prechamber under the middle meatus called the osteomeatal complex

Definition
- inflammation of the mucosal lining of the sinuses and nasal passages

Classification
- acute: <4 wk
- subacute: 4-8 wk
- chronic: >8-12 wk

Table 13. Etiologies of Rhinosinusitis

Ostial Obstruction	Inflammation	• URTI • Allergy
	Mechanical	• Septal deviation • Turbinate hypertrophy • Polyps • Tumours • Adenoid hypertrophy • Foreign body • Congenital abnormalities (e.g. cleft palate)
	Immune	• GPA • Lymphoma, leukemia • Immunosuppressed patients (e.g. neutropenics, diabetics, HIV)
Systemic		• Cystic fibrosis • Immotile cilia (e.g. Kartagener's)
Direct Extension	Dental	• Infection
	Trauma	• Facial fractures

Acute Bacterial Rhinosinusitis

Definition
- bacterial infection of the paranasal sinuses and nasal passages lasting >7 d
- clinical diagnosis requiring ≥2 major symptoms, at least one of the symptoms is either nasal obstruction or purulent/discoloured nasal discharge
  - **major symptoms**
    - facial pain/pressure/fullness
    - nasal obstruction
    - purulent/discoloured nasal discharge
    - hyposmia/anosmia
  - **minor symptoms**
    - headache
    - halitosis
    - fatigue
    - dental pain
    - cough
    - ear pain/fullness

Etiology
- bacteria: *S. pneumoniae* (35%), *H. influenzae* (35%), *M. catarrhalis, S. aureus*, anaerobes (dental)
- children are more prone to a bacterial etiology, but viral is still more common
- maxillary sinus most commonly affected
- must rule out fungal causes (mucormycosis) in immunocompromised hosts (especially if painless, black or pale mucosa on examination)

Clinical Features
- sudden onset of
  - nasal blockage/congestion and/or purulent nasal discharge/posterior nasal drip
  - ± facial pain or pressure, hyposmia, sore throat
- persistent/worsening symptoms >5-7 d or presence of purulence for 3-4 d with high fever
- speculum exam: erythematous mucosa, mucopurulent discharge, pus originating from the middle meatus
- predisposing factors: viral URTI, allergy, dental disease, anatomical defects
- differentiate from acute viral rhinosinusitis (course: <10 d, peaks by 3 d)

Management
- depends on symptom severity (i.e. intensity/duration of symptoms, impact on quality of life)
- mild-moderate: INCS
  - if no response within 72 h, add antibiotics
- severe: INCS + antibiotics
- antibiotics
  - 1st line: amoxicillin x 10 d (TMP-SMX or macrolide if penicillin allergy)
- if no response to 1st line antibiotics within 72 h, switch to 2nd line
  - 2nd line: fluoroquinolones or amoxicillin-clavulanic acid inhibitors
- adjuvant therapy (saline irrigation, analgesics, oral/topical decongestant) may provide symptomatic relief
- CT indicated only if complications are suspected

Acute Rhinosinusitis Complications
Consider hospitalization if any of the following are suspected
- Orbital (Chandler's classification)
  - Periorbital cellulitis
  - Orbital cellulitis
  - Subperiosteal abscess
  - Orbital abscess
  - Cavernous sinus thrombosis
- Intracranial
  - Meningitis
  - Abscess
- Bony
  - Subperiosteal frontal bone abscess ("Pott's Puffy tumour")
  - Osteomyelitis
- Neurologic
  - Superior orbital fissure syndrome (CN III/IV/VI palsy, immobile globe, dilated pupils, ptosis, V1 hypoesthesia)
  - Orbital apex syndrome (as above, plus neuritis, papilledema, decreased visual acuity)

Chronic Rhinosinusitis

Definition
- inflammation of the mucosa of paranasal sinuses and nasal passages >8-12 wk
- diagnosis requiring ≥2 major symptoms for >8-12 wk and ≥1 objective finding of inflammation of the paranasal sinuses (CT/endoscopy)

Etiology
- unclear etiology but the following may contribute or predispose
  - inadequate treatment of acute rhinosinusitis
  - bacterial colonization/biofilms
    - *S. aureus*, enterobacteriaceae, *Pseudomonas, S. pneumoniae, H. influenzae*, β-hemolytic *streptococci*
  - fungal infection (e.g. *Aspergillus, Zygomycetes, Candida*)
  - anatomic abnormality (e.g. lost ostia patency, deviated septum – predisposing factors)
  - allergy/allergic rhinitis
  - ciliary disorder (e.g. cystic fibrosis, Kartagener syndrome)
  - chronic inflammatory disorder (e.g. GPA)
  - untreated dental disease

Clinical Features (similar to acute, but less severe)
- chronic nasal obstruction
- purulent anterior/posterior nasal discharge
- facial congestion/fullness
- facial pain/pressure
- hyposmia/anosmia
- halitosis
- chronic cough
- maxillary dental pain

Management
- identify and address contributing or predisposing factors
- obtain CT or perform endoscopy
- if polyps present: INCS, oral steroids ± antibiotics (if signs of infection), refer to otolaryngologist/H&N surgeon
- if polyps absent: INCS, antibiotics, saline irrigation, oral steroids (severe cases)
- antibiotics for 3-6 wk
  - amoxillin-clavulanic acid inhibitors, fluoroquinolone (moxifloxacin), macrolide (clarithromycin), clindamycin, Flagyl® (metronidazole)
- surgery if medical therapy fails or fungal sinusitis: FESS, balloon sinoplasty

Allergic fungal rhinosinusitis is a chronic sinusitis affecting mostly young, immunocompetent, atopic individuals

Treatment options include FESS ± intranasal topical steroids, antifungals, and immunotherapy

FESS = Functional Endoscopic Sinus Surgery
Opening of the entire osteomeatal complex in order to facilitate drainage while sparing the sinus mucosa

Complications
- same as acute sinusitis, mucocele

Epistaxis

Blood Supply to the Nasal Septum (see Figure 4, OT3)
1. Superior posterior septum
   - internal carotid → ophthalmic → anterior/posterior ethmoidal
2. Posterior septum
   - external carotid → internal maxillary → sphenopalatine artery → nasopalatine
3. Lower anterior septum
   - external carotid → facial artery → superior labial artery → nasal branch
   - external carotid → internal maxillary → descending palatine → greater palatine
- these arteries all anastomose to form Kiesselbach's plexus, located at Little's area (anterior-inferior portion of the cartilaginous septum)
- bleeding from above middle turbinate is internal carotid, and from below is external carotid

90% of nose bleeds occur in Little's area

Table 14. Etiology of Epistaxis

Type	Causes	
Local	Trauma (most common) • Fractures: facial, nasal • Self-induced: digital, foreign body	Tumours • Benign: polyps, inverting papilloma, angiofibroma • Malignant: SCC, esthesioneuroblastoma (olfactory neuroblastoma)
	Iatrogenic: nasal, sinus, orbit surgery	Inflammation • Rhinitis: allergic, non-allergic • Infections: bacterial, viral, fungal
	Barometric changes	
	Nasal dryness: dry air ± septal deformities	Idiopathic
	Septal perforation	
	Chemical: cocaine, nasal sprays, ammonia, etc.	
Systemic	Coagulopathies • Meds: anticoagulants, NSAIDs • Hemophilias, von Willebrand's • Hematological malignancies • Liver failure, uremia	
	Vascular: HTN, atherosclerosis, Osler-Weber-Rendu (hereditary hemorrhagic telangectasia)	
	Others: GPA, SLE	

Special Cases
- Adolescent male with unilateral recurrent epistaxis - consider juvenile nasopharyngeal angiofibroma (JNA); this is the most common benign tumour of the nasopharynx
- Thrombocytopenic patients: use resorbable packs to avoid risk of re-bleeding caused by pulling out the removable pack

Investigations
- CBC, PT/PTT (if indicated)
- x-ray, CT as needed

Treatment
- locate bleeding and achieve hemostasis

1. ABCs
- lean patient forward to minimize swallowing blood and avoid airway obstruction
- apply constant firm pressure for 20 min on cartilaginous part of nose (not bony pyramid)
- if significant bleeding, assess vitals for signs of hemorrhagic shock ± IV NS, cross-match blood

2. Determine Site of Bleeding
- anterior/posterior hemorrhage defined by location in relationship to bony septum
- visualize nasal cavity with speculum
- use cotton pledget with topical lidocaine ± topical decongestant (i.e. Otrivin®) to help identify area of bleeding (often anterior septum)
- if suspicious bleeding disorder, coagulation workup (platelet number and platelet function assay)

3. Control the Bleeding
- first line topical vasoconstrictors (Otrivin®)
- if first line fails and bleeding adequately visualized, cauterize with silver nitrate
- **do not cauterize both sides of the septum** at one time due to risk of septal perforation from loss of septal blood supply

A. Anterior hemorrhage treatment
- if failure to achieve hemostasis with cauterization
  - place anterior pack* with half inch Vaseline®-soaked ribbon gauze strips layered from nasal floor toward nasal roof extending to posterior choanae or lubricated absorbable packing (i.e. Gelfoam wrapped in Surgicel®) for 2-3 d
  - can also attempt packing with Merocel® or nasal tampons of different shapes
  - can also apply Floseal® (hemostatic matrix consisting of topical human thrombin and cross-linked gelatin) if other methods fail

B. Posterior hemorrhage treatment
- if unable to visualize bleeding source, then usually posterior source
  - place posterior pack* using a Foley catheter, gauze pack, or Epistat® balloon
  - subsequently, layer anterior packing bilaterally
  - admit to hospital with packs in for 3-5 d
  - watch for complications: hypoxemia (naso-pulmonic reflex), toxic shock syndrome (Rx: remove packs immediately), pharyngeal fibrosis/stenosis, alar/septal necrosis, aspiration

C. If anterior/posterior packs fail to control epistaxis
- ligation or embolization of culprit arterial supply by interventional radiology
- ± septoplasty

* antibiotics for any posterior pack or any pack left for >48 h because of risk of toxic shock syndrome

4. Prevention
- prevent drying of nasal mucosa with humidifiers, saline spray, or topical ointments
- avoidance of irritants
- medical management of HTN and coagulopathies

Hoarseness

Definitions
- hoarseness: change in voice quality, ranging from voice harshness to voice weakness; reflects abnormalities anywhere along the vocal tract from oral cavity to lungs
- dysphonia: a general alteration in voice quality
- aphonia: no sound emanates from vocal folds

If hoarseness present for >2 wk in a smoker, laryngoscopy must be done to rule out malignancy

Acute Laryngitis

Definition
- <2 wk inflammatory changes in laryngeal mucosa

Etiology
- viral: influenza, adenovirus
- bacterial: Group A *Streptococcus*
- mechanical acute voice strain → submucosal hemorrhage → vocal cord edema → hoarseness
- environmental: toxic fume inhalation

Clinical Features
- URTI symptoms, hoarseness, aphonia, cough attacks, ± dyspnea
- true vocal cords erythematous/edematous with vascular injection and normal mobility

Treatment
- usually self-limited, resolves within ~1 wk
- voice rest
- humidification
- hydration

Vocal Cord Paralysis

Unilateral: affected cord lies in the parmedian position, inadequate glottic closure during phonation → weak, breathy voice. Usually medializes with time whereby phonation and aspiration improve. Treatment options include voice therapy, injection laryngoplasty (Radiesse), medialization using silastic block

Bilateral: cords rest in midline therefore voice remains good but respiratory function is compromised and may present as stridor. If no respiratory issues, may monitor closely and wait for improvement. If respiratory issues, intubate and will likely require a tracheotomy

- avoid irritants (e.g. smoking)
- treat with antibiotics if there is evidence of coexistent bacterial pharyngitis

Chronic Laryngitis

Definition
- >2 wk inflammatory changes in laryngeal mucosa

Etiology
- repeated attacks of acute laryngitis
- chronic irritants (dust, smoke, chemical fumes)
- chronic voice strain
- chronic rhinosinusitis with postnasal drip
- chronic EtOH use
- esophageal disorders: GERD, Zenker's diverticulum, hiatus hernia
- systemic: allergy, hypothyroidism, Addison's disease

Clinical Features
- chronic dysphonia: rule out malignancy
- cough, globus sensation, frequent throat clearing 2° to GERD
- laryngoscopy: cords erythematous, thickened with ulceration/granuloma formation, and normal mobility

Treatment
- remove offending irritants
- treat related disorders (e.g. antisecretory therapy for GERD)
- speech therapy with voice rest
- ± antibiotics ± steroids to decrease inflammation
- laryngoscopy to rule out malignancy

Vocal Cord Polyps

Definition
- structural manifestation of vocal cord irritation
- acutely, polyp forms 2° to capillary damage in the subepithelial space during extreme voice exertion

Etiology
- most common benign tumour of vocal cords
- voice strain (muscle tension dysphonia)
- laryngeal irritants (GERD, allergies, tobacco)

Epidemiology
- 30-50 yr of age
- M>F

Clinical Features
- hoarseness, aphonia, cough attacks ± dyspnea
- pedicled or sessile polyp on free edge of vocal cord
- typically polyp asymmetrical, soft, and smooth
- more common on the anterior 1/3 of the vocal cord
- intermittent respiratory distress with large polyps

Treatment
- avoid irritants
- endoscopic laryngeal microsurgical removal if persistent or if high risk of malignancy

Vocal Cords: Polyps vs. Nodules

Polyps	Nodule
Unilateral, asymmetric	Bilateral
Acute onset	Gradual onset
May resolve spontaneously	Often follow a chronic course
Subepithelial capillary breakage	Acute: submucosal hemorrhage or edema Chronic: hyalinization within submucosal lesion
Soft, smooth, fusiform, pedunculated mass	Acute: small, discrete nodules Chronic: hard, white, thickened fibrosed nodules
Proton pump inhibitor	Voice rest but no whispering, hydration, speech therapy if refractory to therapy
Surgical excision if persistent or in presence of risk factors for laryngeal cancer	Surgical excision as last resort

Vocal Cord Nodules

Definition
- vocal cord callus
- i.e. "screamer's or singer's nodules"

Etiology
- early nodules occur 2° to submucosal hemorrhage
- mature nodules result from hyalinization which occurs with long-term voice abuse
- chronic voice strain
- frequent URTI, smoke, EtOH

Epidemiology
- frequently in singers, children, bartenders, and school teachers
- F>M

Clinical Features
- hoarseness worst at end of day
- on laryngoscopy
  - often bilateral
  - at the junction of the anterior 1/3 and posterior 2/3 of the vocal cords – point of maximal cord vibration
- chronic nodules may become fibrotic, hard, and white

Treatment
- voice rest
- hydration
- speech therapy
- avoid irritants
- surgery rarely indicated for refractory nodules

Benign Laryngeal Papillomas

Etiology
- HPV types 6, 11
- possible hormonal influence, possibly acquired during delivery

Epidemiology
- biphasic distribution: 1) birth to puberty (most common laryngeal tumour) and 2) adulthood

Clinical Features
- hoarseness and airway obstruction
- can seed into tracheobronchial tree
- highly resistant to complete removal
- some juvenile papillomas resolve spontaneously at puberty
- may undergo malignant transformation
- laryngoscopy shows wart-like lesions in supraglottic larynx and trachea

Treatment
- microdebridement or CO_2 laser
- adjuvants under investigation: interferon, cidofovir, acyclovir
- HPV vaccine may prevent/decrease the incidence but more research is needed

Laryngeal Carcinoma

- see *Neoplasms of the Head and Neck*, OT35

Salivary Glands

Sialadenitis

Definition
- inflammation of salivary glands

Etiology
- viral most common (mumps)
- bacterial causes: *S. aureus, S. pneumoniae, H. influenzae*
- obstructive vs. non-obstructive
- obstructive infection involves salivary stasis and bacterial retrograde flow

Predisposing Factors
- HIV
- anorexia/bulimia
- Sjögren's syndrome
- Cushing's, hypothyroidism, DM
- hepatic/renal failure
- meds that increase stasis: diuretics, TCAs, β-blockers, anticholinergics, antibiotics
- sialolithiasis (can cause chronic sialadenitis)

Bilateral enlargement of the parotid glands may be a manifestation of a systemic disease, such as Sjögren's or an eating disorder (i.e. anorexia, bulimia)

Clinical Features
- acute onset of pain and edema of parotid or submandibular gland that may lead to marked swelling
- ± fever
- ± leukocytosis
- ± suppurative drainage from punctum of the gland

Mumps usually presents with bilateral parotid enlargement ± SNHL ± orchitis

Investigations
- U/S imaging to differentiate obstructive vs. non-obstructive sialadenitis

Treatment
- bacterial: treat with cloxacillin ± abscess drainage, sialogogues
- viral: no treatment

Sialolithiasis

Definition
- ductal stone (mainly hydroxyapatite) in adults, sand/sludge in children, leading to chronic sialadenitis
- 80% in submandibular gland, <20% in parotid gland, ~1% in sublingual gland

Risk Factors
- any condition causing duct stenosis or a change in salivary secretions (e.g. dehydration, diabetes, EtOH, hypercalcemia, psychiatric medication)

Clinical Features
- pain and tenderness over involved gland
- intermittent swelling related to meals
- digital palpation reveals presence of calculus

Investigations
- U/S ± sialogram

Treatment
- may resolve spontaneously
- encourage salivation to clear calculus
- massage, analgesia, antibiotics, sialogogues (e.g. lemon wedges, sour lemon candies), warm compresses
- remove calculi endoscopically, by dilating duct or orifice, or by excision through floor of the mouth
- if calculus is within the gland parenchyma, the whole gland must be excised

Salivary Gland Neoplasms

Etiology
- anatomic distribution
  - parotid gland: 70-85%
  - submandibular gland: 8-15%
  - sublingual gland: 1%
  - minor salivary glands, most concentrated in hard palate: 5-8%
- malignant (see Table 15, OT32 and Table 16, OT36)
- benign
  - benign mixed (pleomorphic adenoma): 80%
  - Warthin's tumour (5-10% bilateral, M>F): 10%
  - cysts, lymph nodes and adenomas: 10%
  - oncocytoma: <1%

Epidemiology
- 3-6% of all head and neck neoplasms in adults
- mean age at presentation: 55-65
- M=F

Parotid Gland Neoplasms

Clinical Features
- 80% benign (pleomorphic adenoma: most common), 20% malignant (mucoepidermoid: most common)
- if bilateral, suggests benign process (Warthin's tumour, Sjögren's, bulimia, mumps) or possible lymphoma
- facial nerve involvement (i.e. facial paralysis): increases risk of malignancy

Investigations
- FNA biopsy
- CT, U/S, or MRI to determine extent of tumour

Treatment
- treatment of choice is surgery for all salivary gland neoplasms – benign and malignant
- pleomorphic adenomas are excised due to risk of malignant transformation (5% risk over prolonged period of time)
- superficial tumour
  - superficial parotidectomy above plane of CN VII ± radiation
  - incisional biopsy contraindicated
- deep lesion
  - near-total parotidectomy sparing as much of CN VII as possible
  - if CN VII involved then it is removed and cable grafted
- complications of parotid surgery
  - hematoma, infection, salivary fistula, temporary facial paresis, Frey's syndrome (gustatory sweating)

Prognosis
- benign: excellent, <5% of pleomorphic adenomas may recur
- malignant: dependent on stage and type of malignancy (see Table 16, OT36)

A mass sitting above an imaginary line drawn between the mastoid process and angle of the mandible is a parotid neoplasm until proven otherwise

DDx Parotid Tumour

Benign
- Pleomorphic adenoma
- Warthin's tumour (more common in men)
- Benign lymphoepithelial cysts (viral eitiology e.g. HIV)
- Oncocytoma

Malignant
- Mucoepidermoid carcinoma
- Adenoid cystic carcinoma
- Acinic cell carcinoma

Frey's syndrome is a post-operative complication characterized by gustatory sweating. It is due to aberrant innervation of cutaneous sweat glands by parasympathetic nerve fibres that are divided during surgery

Neck Masses

Approach to a Neck Mass

- ensure that the neck mass is not a normal neck structure (hyoid, transverse process of C1 vertebra, prominent carotid bulb)
- any neck mass persisting for >2 wk should be investigated for possible neoplastic causes

Table 15. Acquired Causes of Neck Lumps According to Age

Age (yr)	Possible Causes of Neck Lump		
<20	1. Congenital	2. Inflammatory/Infectious	3. Neoplastic
20-40	1. Inflammatory	2. Congenital	3. Neoplastic
>40	1. Neoplastic	2. Inflammatory	3. Congenital

Differential Diagnosis
- congenital
  - lateral (branchial cleft cyst, lymphatic/venous/venolymphatic malformation)
  - midline (thyroglossal duct cyst, dermoid cyst, laryngocele)
- infectious/inflammatory
  - reactive lymphadenopathy (2º to tonsillitis, pharyngitis)
  - infectious mononucleosis
  - Kawasaki, Kikuchi, Kimura, Cat Scratch, Castleman's
  - HIV
  - salivary gland calculi, sialadenitis
  - thyroiditis
- granulomatous disease
  - mycobacterial infections
  - sarcoidosis
- neoplastic
  - lymphoma
  - salivary gland tumours
  - thyroid tumours
  - metastatic malignancy ("unknown primary")

Inflammatory vs. Malignant Neck Masses

	Inflammatory	Neoplastic
History		
Painful	Y	N
H&N infection	Y	N
Fever	Y	N
Weight loss	N	Y
CA risk factors	N	Y
Age	Younger	Older
Physical		
Tender	Y	N
Rubbery	Y	Occ.
Rock hard	N	Y
Mobile	Y	± fixed

Evaluation

Investigations
- history and physical (including nasopharynx and larynx)
- all other investigations and imaging are dependent upon clinical suspicion following history and physical
- laboratory investigations
  - WBC: infection vs. lymphoma
  - Mantoux TB test
  - thyroid function tests and scan
- imaging
  - neck U/S
  - CT scan
  - angiography: vascularity and blood supply to mass
- biopsy: for histologic examination
  - FNA: least invasive
  - needle biopsy
  - open biopsy: for lymphoma
- identification of possible primary tumour (rule out a metastatic lymph node from an "unknown primary")
  - panendoscopy: nasopharyngoscopy, laryngoscopy, esophagoscopy, bronchoscopy with washings, and biopsy of suspicious lesions
  - biopsy of normal tissue of nasopharynx, tonsils, base of tongue, and hypopharynx
  - primary identified 95% of time → stage and treat
  - primary occult 5% of time: excisional biopsy of node for histologic diagnosis → manage with radiotherapy and/or neck dissection (squamous cell carcinoma)

Congenital Neck Masses

Branchial Cleft Cysts/Fistula

Embryology
- at the 6th wk of development, the 2nd branchial arch grows over the 3rd and 4th arches and fuses with the neighbouring caudal pre-cardial swelling forming the cervical sinus
- 3 types of malformations
  1. branchial fistula: persistent communication between skin and GI tract
  2. branchial sinus: blind-ended tract opening to skin
  3. branchial cyst: persistent cervical sinus with no external opening

Clinical Features
- 2nd branchial cleft malformations most common
  - sinuses and fistulae present in infancy as a small opening anterior to the sternocleidomastoid muscle
  - cysts present as a smooth, painless, slowly enlarging lateral neck mass, often following a URTI
- 1st branchial cleft malformations present as sinus/fistula or cyst in preauricular area or on face over angle of mandible
- 3rd branchial cleft malformations present as recurrent thyroiditis or thyroid abscess and have a tract leading usually to the left pyriform sinus
- there is controversy whether or not 4th branchial cleft anomalies exist, as they may be remnants of the thyrothymic axis

Treatment
- surgical removal of cyst or fistula tract
- if infected: allow infection to settle before removal (antibiotics may be required)

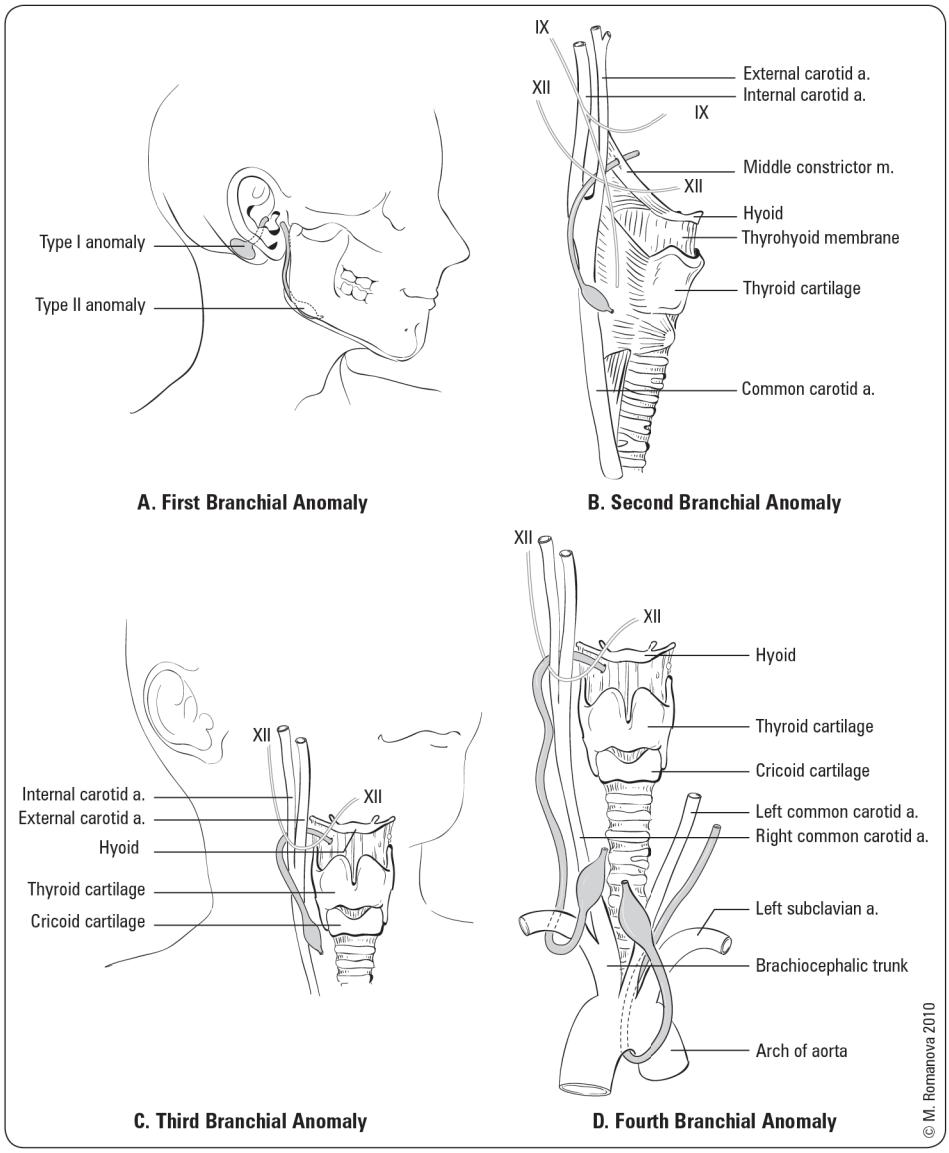


Figure 19. Branchial cleft cysts

Thyroglossal Duct Cysts

Embryology

- thyroid originates as ventral midline diverticulum at base of tongue caudal to junction of 3rd and 4th branchial arches (foramen cecum) and migrates down to inferior aspect of neck
- thyroglossal duct cysts are vestigial remnants of tract

Clinical Features

- usually presents in childhood or during 20-40s as a midline cyst that enlarges with URTI and elevates with swallowing and tongue protrusion

Treatment

- pre-operative antibiotics to reduce inflammation (infection before surgery is a well described cause of recurrence)
- small potential for neoplastic transformation so complete excision of cyst and tissue around tract up to foramen cecum at base of tongue with removal of central portion of hyoid bone (Sistrunk procedure) recommended

Lymphatic Malformation

Definition
- lymphatic malformation arising from vestigial lymph channels of neck

Clinical Features
- usually present by age 2
- can be macrocystic (composed of large thin-walled cysts, usually below level of mylohyoid muscle) or microcystic (composed of minute cysts, usually above level of mylohyoid muscle)
- usually painless, soft, compressible
- infection causes a sudden increase in size

Treatment
- can regress spontaneously after bacterial infection, therefore do not plan surgical intervention until several months after infection
- macrocystic lesions can be treated by sclerotherapy or surgical excision
- microcystic lesions are difficult to treat, but can be debulked

Neoplasms of the Head and Neck

Pre-Malignant Disease
- **leukoplakia**
  - hyperkeratosis of oral mucosa
  - risk of malignant transformation 5-20%
- **erythroplakia**
  - red superficial patches adjacent to normal mucosa
  - commonly associated with epithelial dysplasia
  - associated with carcinoma *in situ* or invasive tumour in 40% of cases
- **dysplasia**
  - histopathologic presence of mitoses and prominent nucleoli
  - involvement of entire mucosal thickness = carcinoma *in situ*
  - associated progression to invasive cancer in 15-30% of cases

All patients presenting with a head and neck mass should be asked if they are experiencing the following obstructive, referred, or local symptoms:
- Dyspnea or stridor (positional vs. non-positional)
- Hoarseness or dysphonia
- Otalgia
- Non-healing oral ulcer
- Dysphagia
- Hemoptysis, hematemesis

Investigations
- initial metastatic screen includes CXR
- scans of liver, brain, and bone only if clinically indicated
- CT scan is superior to MRI for the detection of pathologic nodal disease and bone cortex invasion
- MRI is superior to discriminate tumour from mucus and to detect bone marrow invasion
- ± PET scans

Detection of cervical lymph nodes on physical exam:
False negative rate: 15-30%
False positive rate: 30-40%

Treatment
- treatment depends on
  - histologic grade of tumour
  - stage
  - physical and psychological health of patient
  - facilities available
  - expertise and experience of the medical and surgical oncology team
- in general
  - 1° surgery for malignant oral cavity tumours with radiotherapy reserved for salvage or poor prognostic indicators
  - 1° radiotherapy for nasopharynx, oropharynx, hypopharynx, larynx malignancies with surgery reserved for salvage
  - palliative chemotherapy for metastatic or incurable disease
  - concomitant chemotherapy increases survival in advanced disease
  - chemotherapy has a role as induction therapy prior to surgery and radiation
  - panendoscopy to detect primary disease when lymph node metastasis is identified
  - anti-EGFR treatment (cetuximab, panitumumab) has a role as concurrent therapy with radiation for SCC of the head and neck (for advanced local and regional disease)

Pathological lymphadenopathy defined radiographically as:
- A jugulodigastric node >1.5 cm in diameter, or a retropharyngeal node >1 cm in diameter
- A node of any size which contains central necrosis

Prognosis
- synchronous tumours occur in 9-15% of patients
- late development of 2nd primary most common cause of post-treatment failure after 36 mo

Common sites of distant metastases for head and neck neoplasms:
lungs > liver > bones

Table 16. Quick Look-Up Summary of Head and Neck Malignancies – Etiology and Epidemiology

Etiology	Epidemiology	Risk Factors
Oral Cavity		
95% SCC others: sarcoma, melanoma, minor salivary gland tumour	Mean age: 50-60 yr M>F Most common site of H&N cancers 50% on anterior 2/3 of tongue	Smoking/EtOH Poor oral hygiene Leukoplakia, erythroplakia Lichen planus, chronic inflammation Sun exposure – lip HPV infection
Nose and Paranasal Sinus		
75-80% SCC Adenocarcinoma (2nd most common) and mucoepidermoid 99% in maxillary/ethmoid sinus 10% arise from minor salivary glands	Mean age: 50-70 yr Rare tumours ↓ incidence in last 5-10 yr	Wood/shoe/textile industry Hardwood dust (nasal/ethmoid sinus) Nickel, chromium (maxillary sinus) Air pollution Chronic rhinosinusitis
Carcinoma of the Pharynx – Subtypes (Nasopharynx, Oropharynx, Hypopharynx, and Larynx)		
Nasopharynx		
90% SCC ~10% lymphoma	Mean age: 50-59 yr M:F= 2.4:1 Incidence 0.8 per 100,000 100x increased incidence in Southern Chinese	Epstein-Barr virus (EBV) Salted fish Nickel exposure Poor oral hygiene Genetic – Southern Chinese
Oropharynx		
95% SCC – poorly differentiated Up to 70% of oropharnyngeal cancer (OPC) attributable to HPV	Mean age: 50-70 yr Patients with HPV+ OPC are approximately 10 yrs younger Prevalence of HPV+ OPC has increased by 225% from 1988 to 2004. M:F = 4:1	Smoking/EtOH HPV 16 infection: increased sexual encounters, specifically oral sex
Hypopharynx		
95% SCC 3 sites 1. pyriform sinus (60%) 2. post-cricoid (30%) 3. post pharyngeal wall (10%)	Mean age: 50-70 yr M>F 8-10% of all H&N cancer	Smoking/EtOH
Larynx		
SCC most common 3 sites 1. supraglottic (30-35%) 2. glottic (60-65%) 3. subglottic (1%)	Mean age: 45-75 yr M:F = 10:1 45% of all H&N cancer	Smoking/EtOH HPV 16 infection strongly associated with the risk of laryngeal squamous cell cancers
Salivary Gland		
40% mucoepidermoid 30% adenoid cystic 5% acinic cell 5% malignant mixed 5% lymphoma	Mean age: 55-65 yr M=F 3-6% of all H&N cancer Rate of malignancy: Parotid 15-25% Submandibular 37-43% Minor salivary >80%	
Thyroid (90% benign – 10% malignant)		
>80% papillary 5-15% follicular 5% medullary <5% anaplastic 1-5% hürthle cell 1-2% metastatic	Children Adults <30 or >60 yr Nodules more common in females Malignancy more common in males	Radiation exposure Family history – papillary CA or multiple endocrine neoplasia – MEN II Older age Male Papillary – Gardner's, Cowden's, familial adenomatous polyposis (FAP)
Parathyroid	Mean age: 44-55 yr Rare tumour	

Risk Factors for Head and Neck Cancer include
- Smoking
- EtOH (synergistic with smoking)
- Radiation
- Occupational/environmental exposures
- Oral HPV infection (independent of smoking and EtOH exposure)

The smaller the salivary gland, the greater the likelihood that a mass in the gland is malignant

Table 17. Quick Look-Up Summary of Head and Neck Malignancies – Diagnosis and Treatment

Clinical Features	Investigations	Treatment	Prognosis
Oral Cavity			
Asymptomatic neck mass (30%) Non-healing ulcer ± bleeding Dysphagia, sialorrhea, dysphonia Oral fetor, otalgia, leukoplakia, or erythroplakia (pre-malignant changes or CIS)	Biopsy CT	1° surgery local resection ± neck dissection ± reconstruction 2° radiation	5 yr survival T1/T2: 75% T3/T4: 30-35% Poor prognostic indicators Depth of invasion, close surgical margins location (tongue worse than floor of mouth) Cervical nodes, extra-capsular spread
Nose and Paranasal Sinus			
Early symptoms: Unilateral nasal obstruction Epistaxis, rhinorrhea **Late symptoms:** 2° to invasion of nose, orbit, nerves, oral cavity, skin, skull base, cribriform plate	CT/MRI Biopsy	Surgery and radiation Chemoradiotherapy	5 yr survival: 30-60% Poor prognosis 2° to late presentation
Nasopharynx			
Cervical nodes (60-90%) Nasal obstruction, epistaxis Unilateral otitis media ± hearing loss CN III to VI, IX to XII (25%) Proptosis, voice change, dysphagia	Nasopharyngoscopy Biopsy CT/MRI	1° radiation, chemoradiation Surgery for limited or recurrent disease	5 yr survival T1: 79% T2: 72% T3: 50-60% T4: 36-42%
Oropharynx			
Odynophagia, otalgia Ulcerated/enlarged tonsil Fixed tongue/trismus/dysarthria Oral fetor, bloody sputum HPV+ OPC predominantly arises at base of tongue or tonsillar region Cervical lymphadenopathy (60%) Distant mets: lung/bone/liver (7%)	Biopsy Determine HPV status via RT=PCR: positive if presence of HPV DNA and p16 overexpression CT	1° radiation 2° surgery local resection ±neck dissection ±reconstruction	5 year overall survival Stratified by TMN stage (I, II, III, IV) HPV negative OPC (70%, 58%, 50%, 30%) HPV positive OPC (88%, 78%, 71%, 74%) HPV positive OPC further stratified by stage, age and smoking pack years (PY) group I (T1-3N0-N2c, ≤20 PY): 89% group II (T1-3N0-N2c, >20 PY): 64% group III (T4 or N3, age ≤70): 57% group IVA (T4 or N3, age >70): 40%
Hypopharynx			
Dysphagia, odynophagia Otalgia, hoarseness Cervical lymphadenopathy	Pharyngoscopy Biopsy CT	1° radiation 2° surgery	5 yr survival T1: 53% T2/T3: 36-39% T4: 24%
Larynx			
Dysphagia, odynophagia, globus Otalgia, hoarseness Dyspnea/stridor Cough/hemoptysis Cervical nodes (rare with glottic CA)	Laryngoscopy CT/MRI	1° radiation 2° surgery 1° surgery for bulky T4 disease	5 yr survival T4: >40% (surgery with radiation) Control rate early lesions >90% (radiation) 10 to 12% of small lesions fail radiotherapy
Salivary Gland			
Painless mass (occ. pain is possible) CN VII palsy Cervical lymphadenopathy Rapid growth Invasion of skin Constitutional signs/symptoms	FNA MRI/CT/U/S	1° surgery ± neck dissection Post-operative radiotherapy Chemotherapy if unresectable	Parotid 10 yr survival: 85, 69, 43, and 14% for stages T1 to T4 Submandibular 2 yr survival: 82%, 5 yr: 69% Minor salivary gland 10 yr survival: 83, 52, 25, 23% for stages T1 to T4
Thyroid			
Thyroid mass, cervical nodes Vocal cord paralysis Hyper/hypothyroidism Dysphagia	FNA U/S	1° surgery I^{131} for intermediate and high risk well differentiated thyroid cancer	Recurrences occur within 5 yr Need long-term follow-up: clinical exam, thyroglobulin
Parathyroid			
Increased serum Ca^{2+} Neck mass Bone disease, renal disease Pancreatitis	Sestamibi	Wide surgical excision Post-operative monitoring of serum Ca^{2+}	Recurrence rates 1 yr: 27% 5 yr: 82% 10 yr: 91% Mean survival: 6-7 yr

Thyroid Carcinoma

Table 18. Bethesda Classification of Thyroid Cytology

Category	Risk of Malignancy
Non-diagnostic or unsatisfactory	Unknown
Benign	0-3%
Follicular lesion of undetermined significance/ Atypia of undetermined significance	5-15%
Follicular/hürthle cell neoplasms	15-30%
Suspicious for malignancy	60-75%
Malignant	97-99%

Table 19. Thyroid Carcinoma

	Papillary	Follicular	Medullary	Anaplastic	Lymphoma
Incidence (% of all thyroid cancers)	70-75%	10%	3 to 5% (10% familial 90% sporadic)	<5%	<1%
Route of Spread	Lymphatic	Hematogenous	Lymphatic and hematogenous		
Histology	Orphan Annie nuclei Psammoma bodies Papillary architecture	Capsular/vascular invasion Invasion influences prognosis	Amyloid May secrete calcitonin, prostaglandins, ACTH, serotonin, kallikrein, or bradykinin	Giant cells Spindle cells	
Other	**P**s – **P**apillary cancer **P**opular (most common) **P**alpable lymph nodes **P**ositive I^{131} uptake **P**ositive prognosis **P**ost-operative I^{131} scan to guide treatments	**F**s – **F**ollicular cancer **F**ar away mets **F**emale (3:1) NOT **F**NA (cannot be diagnosed by FNA) **F**avourable prognosis	**M**s – **M**edullary cancer **M**ultiple endocrine neoplasia (**M**EN IIa or IIb) a**M**yloid **M**edian node dissection	More common in elderly 70% in women 20-30% have Hx of differentiated thyroid Ca (mostly papillary) or nodular goitre mass Rapidly enlarging neck Rule out lymphoma	Usually non-Hodgkin's lymphoma Rapidly enlarging thyroid mass Hx of Hashimoto's thyroiditis increases risk 60x 4:1 female predominance dysphagia, dyspnea, stridor, hoarseness, neck pain, facial edema, accompanied by "B" symptoms*
Prognosis	98% at 10 yr	92% at 10 yr	50% at 10 yr 20% at 10 yr if detected when clinically palpable	20-35% at 1 yr 13% at 10 yr	5 yr survival Stage IE 55%-80% Stage IIE 20%-50% Stage IIE/IV 15%-35%
Treatment	Small tumours: Near total thyroidectomy or lobectomy Diffuse/bilateral: Total thyroidectomy ± post-operative I^{131} treatment	Small tumours: Near total thyroidectomy/lobectomy/ isthmectomy Large/diffuse tumours: Total thyroidectomy	Total thyroidectomy Median lymph node dissection if lateral cervical nodes +ve Modified neck dissection Post-operative thyroxine Tracheostomy Screen asymptomatic relatives	Radiation and chemotherapy Small tumours: Total thyroidectomy ± external beam	Non-surgical Combined radiation Chemotherapy (CHOP**)

*B symptoms = fever, night sweats, chills, weight loss >10% in 6 mo ** CHOP = cyclophosphamide, adriamycin, vincristine, prednisone

Approach to Thyroid Nodule

- all patients with thyroid nodules require evaluation of serum TSH and ultrasound
- any nodule >5 mm with suspicious sonographic features (particularly microcalcifications) should undergo FNA
- any nodule >1 cm should undergo FNA
- when performing repeat FNA on initially non-diagnostic nodules, U/S-guided FNA should be employed
- nuclear scanning has minimal value in the investigation of the thyroid nodule

Table 20. Management of the Thyroid Nodule

Treatment	Indications
Radioiodine therapy	For the treatment of hyperthyroidism or as adjuvant treatment after surgery in the treatment of papillary or follicular carcinoma
Chemotherapy and/or radiotherapy	Anaplastic CA or thyroid lymphoma
Surgical excision	Mass that is "suspicious" on FNA Malignancy other than anaplastic CA or thyroid lymphoma Mass that on FNA is benign but increasing in size on serial imaging and/or >3-4 cm in size Hyperthyroidism not amenable to medical therapy

***U/S findings:** cystic: risk of malignancy <1%; solid: risk of malignancy ~10%; solid with cystic components: risk of malignancy same as if solid

Indications for Post-Operative Radioactive Iodine Ablation – I^{131}
Adjuvant therapy: decrease recurrent disease
RAI therapy: treat persistent cancer

Pediatric Otolaryngology

Acute Otitis Media

Definition
- all of: presence of middle ear effusion (MEE); presence of middle ear inflammation (MEI); acute onset of symptoms of MEE and MEI

Epidemiology
- most frequent diagnosis in sick children visiting clinicians' offices and most common reason for antibiotic administration
- peak incidence between 6-15 mo; ~85% of children have >1 episode by 3 yr old
- seasonal variability: peaks in winter

Etiology
- primary defect causing AOM: Eustachian tube dysfunction/obstruction → stasis/colonization by pathogens
- bacterial: *S. pneumoniae*, non-typable *H. influenzae, M. catarrhalis*, Group A *Streptococcus, S. aureus*
- viral: RSV, influenza, parainfluenza, adenovirus
- commonly due to bacterial/viral co-infection

Predisposing Factors
- Eustachian tube dysfunction/obstruction
  - swelling of tubal mucosa
    - upper respiratory tract infection (URTI)
    - allergic rhinitis
    - chronic rhinosinusitis
  - obstruction/infiltration of Eustachian tube ostium
    - tumour: nasopharyngeal carcinoma (adults)
    - adenoid hypertrophy (not due to obstruction but by maintaining a source of infection)
    - barotrauma (sudden changes in air pressure)
  - inadequate tensor palati function: cleft palate (even after repair)
  - abnormal Eustachian tube
    - Down syndrome (horizontal position of Eustachian tube), Crouzon syndrome, cleft palate, and Apert syndrome
- disruption of action of
  - cilia of Eustachian tube: Kartagener's syndrome
  - mucus secreting cells
  - capillary network that provides humoral factors, PMNs, phagocytic cells
- immunosuppression/deficiency due to chemotherapy, steroids, DM, hypogammaglobulinemia, cystic fibrosis

Risk Factors
- non-modifiable: young age, family history of OM, prematurity, orofacial abnormalities, immunodeficiencies, Down syndrome, race, and ethnicity
- modifiable: lack of breastfeeding, day care attendance, household crowding, exposure to cigarette smoke and air pollution, pacifier use

Pathogenesis
- obstruction of Eustachian tube → air absorbed in middle ear → negative pressure (an irritant to middle ear mucosa) → edema of mucosa with exudate/effusion → infection of exudate from nasopharyngeal secretions

Clinical Features
- triad of otalgia, fever (especially in younger children), and conductive hearing loss
- rarely tinnitus, vertigo, and/or facial nerve paralysis
- otorrhea if tympanic membrane perforated
- infants/toddlers
  - ear-tugging (this alone is not a good indicator of pathology)
  - hearing loss, balance disturbances (rare)
  - irritable, poor sleeping
  - vomiting and diarrhea
  - anorexia
- otoscopy of TM
  - hyperemia
  - bulging, pus may be seen behind TM
  - loss of landmarks: handle and long process of malleus not visible

Clinical Assessment of AOM in Pediatrics
JAMA 2010;304:2161-2169

In assessment of AOM in pediatrics, ear pain is the most useful symptom with a likelihood ratio (LR) between 3.0-7.3. Useful otoscopic signs include erythematous (LR 8.4, 95% CI 7-11), cloudy (LR 34, 95% CI 28-42), bulging (LR 51, 95% CI 36-73), and immobile tympanic membrane (LR 31, 95% CI 26-37) on pneumatic otoscopy.

Diagnosis
- history
  - acute onset of otalgia or ear tugging in a preverbal child, otorrhea, decreased hearing
  - unexplained irritability, fever, upper respiratory symptoms, poor sleeping, anorexia, N/V, and diarrhea
- physical
  - febrile
  - MEE on otoscopy: immobile tympanic membrane, acute otorrhea, loss of bony landmarks, opacification of TM, air-fluid level behind TM
  - MEI on otoscopy: bulging TM with marked discolouration (hemorrhagic, red, grey, or yellow)

Management
- observation for 48-72 h without antimicrobials may be appropriate since >80% of AOM in children resolve spontaneously
- criteria for watchful waiting approach
  - child is >6 mo old
  - child does not have immunodeficiency, chronic cardiac or pulmonary disease, anatomical abnormalities of the head or neck, a history of complicated otitis media (suppurative complications of chronic perforation) or Down syndrome
  - the illness is not severe – otalgia appears to be mild and fever is <39°C in the absence of antipyretics
  - parents are capable of recognizing signs of worsening illness and can readily access medical care if the child does not improve
- antimicrobials are indicated if child does not meet the criteria for watchful waiting or does not improve/worsens during observation
- maintain hydration
- symptomatic relief: acetaminophen, ibuprofen
- referral to otolaryngology for myringotomy and tympanostomy tubes may be warranted for recurrent infections

Treatment
- **antimicrobial agents for AOM**
  - 1st line treatment (no penicillin allergy)
    - amoxicillin: 75 mg/kg/d to 90 mg/kg/d divided 3x/d
  - 2nd line treatment
    - cefprozil: 30 mg/kg/d divided 2x/d
    - cefuroxime axetil: 30 mg/kg/d divided 2x/d
    - ceftriaxone: 50 mg/kg intramuscularly (or intravenously) x 1 dose
    - azithromycin: 10 mg/kg OD x 1 dose, then 5 mg/kg OD x 4 doses
    - clarithromycin: 15 mg/kg/d divided 2x/d
  - if initial therapy fails (i.e. no symptomatic improvement after 2-3 d)
    - amoxicillin-clavulanate: 90 mg/kg/d amoxicillin, 6.4 mg/kg/d clavulanate divided 2x/d for 10 d
  - if AOM-related symptoms do not resolve with amoxicillin/clavulanate, a course of ceftriaxone 50 mg/kg/d intramuscularly (or intravenously) 1/d x 3 doses could be considered

Antibiotics for Acute Otitis Media in Children
Cochrane DB Syst Rev 2013;1:CD000219
Study: Meta-analysis of Randomized Controlled Trials (RCTs) on children (1-15 mo) with acute otitis media comparing any antibiotic regime to placebo and expectant observation.
Data Sources: Cochrane Central Register of Controlled Trials (2012 issue 10), MEDLINE (1966 to October 2012), OLDMEDLINE (1958 to 1965), EMBASE (January 1990 to November 2012), Current Contents (1966 to November 2012), CINAHL (2008 to November 2012) and LILACS (2008 to November 2012) without language restrictions.
Main Outcomes: 1) Pain at 24 h, 2-3 d, and 4-7 d; 2) Abnormal tympanometry findings; 3) TM perforation; 4) Contralateral otitis; 5) AOM recurrences; 6) Serious complications from AOM; 7) Adverse effects from antibiotics.
Results: Treatment with antibiotics had no significant impact on pain at 24 h. However, pain at 2-3 d and 4-7 d was lower in the antibiotic groups with a NNT of 20. Antibiotics had no significant effect on tympanometry findings, number of AOM recurrences, or severity of complications. Antibiotic treatment led to a significant reduction in TM perforations (NNT 33) and halved contralateral AOM (NNT 11). Adverse events (vomiting, diarrhea, or rash) occurred more often in children taking antibiotics.
Conclusion: The role of antibiotics is largely restricted to pain control at 2-7 d, but most (82%) settle without antibiotics. This can also be achieved by analgesics. However, antibiotic treatment can reduce risk of TM perforation and contralateral AOM episodes. These benefits must be weighed against risks of adverse events from antibiotics.

Complications
- extracranial
  - hearing loss and speech delay (secondary to persistent MEE), TM perforation, extension of suppurative process to adjacent structures (mastoiditis, petrositis, labyrinthitis), cholesteatoma, facial nerve palsy, middle ear atelectasis, ossicular necrosis, vestibular dysfunction, persistent effusion (often leading to hearing loss)
- intracranial
  - meningitis, epidural and brain abscess, subdural empyema, lateral and cavernous sinus thrombosis, carotid artery thrombosis, facial nerve paralysis
- other
  - mastoiditis, labyrinthitis, sigmoid sinus thrombophlebitis

Otitis Media with Effusion

Definition
- presence of fluid in the middle ear without signs or symptoms of ear infection

Epidemiology
- most common cause of pediatric hearing loss
- not exclusively a pediatric disease
- follows AOM frequently in children
- middle ear effusions have been shown to persist following an episode of AOM for 1 mo in 40% of children, 2 mo in 20%, and >3 mo in 10%

Risk Factors
- same as AOM

Clinical Features
- conductive hearing loss ± tinnitus
  - confirm with audiogram and tympanogram (flat) (see Figure 16B, OT10 and Figure 17B, OT11)
- fullness – blocked ear
- ± pain, low grade fever
- otoscopy of tympanic membrane
  - discolouration – amber or dull grey with "glue" ear
  - meniscus fluid level behind TM
  - air bubbles
  - retraction pockets/TM atelectasis
  - most reliable finding with pneumotoscopy is immobility

Treatment
- expectant: 90% resolve by 3 mo
- document hearing loss with audiogram
- no clinical evidence that antihistamines, decongestants, or antibiotics clear disease faster
- surgery: myringotomy ± ventilation tubes ± adenoidectomy (if enlarged or on insertion of second set of tubes after first set falls out)
- ventilation tubes to equalize pressure and drain ear

Indications for Myringotomy and Tympanostomy Tubes in Recurrent AOM (RAOM) and OME
- Chronic bilateral OME and documented hearing difficultues >3 mo
- Unilateral of bilateral OME >3 mo and symptoms likely attributable to OME (e.g. balance problems, poor school performance, ear discomfort, etc.)
- At-risk children (permanent hearing loss, speech/language delay, autism-spectrum disorder, syndromes/craniofacial disorders, blindness, cleft palate, developmental delay) with unilateral or bilateral OME with type B tympanogram or persistent effusion > 3 mo
- RAOM (>3 episodes in 6 mo or >4 in 12 mo) with unilateral or bilateral middle ear effusion

Clinical practice guidelines: Tympanostomy tubes in children. *Otolaryng Head Neck* 2013;149:S1-S35

Complications of Otitis Media with Effusion
- hearing loss, speech delay, learning problems in young children
- chronic mastoiditis
- ossicular erosion
- cholesteatoma especially when retraction pockets involve pars flaccida
- retraction of tympanic membrane, atelectasis, ossicular fixation

Adenoid Hypertrophy
- size peaks at age 5 and resolves by age 12
- increase in size with repeated URTI and allergies

Clinical Features
- nasal obstruction
  - adenoid facies (open mouth, high arched palate, narrow midface, malocclusion)
  - history of hypernasal voice and snoring
  - long-term mouth breather; minimal air escape through nose
- choanal obstruction
  - chronic rhinosinusitis/rhinitis
  - obstructive sleep apnea
- chronic inflammation
  - nasal discharge, post-nasal drip, and cough
  - cervical lymphadenopathy

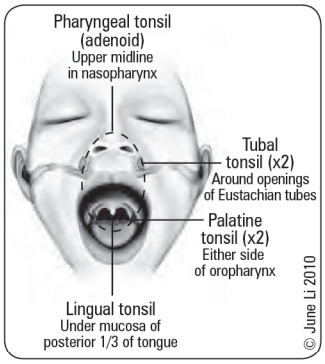


Figure 20. Waldeyer's ring
An interrupted circle of protective lymphoid tissue at the upper ends of the respiratory and alimentary tracts

Diagnosis
- enlarged adenoids on nasopharyngeal exam (usually with flexible nasopharyngoscope)
- enlarged adenoid shadow on lateral soft tissue x-ray

Complications
- Eustachian tube obstruction leading to serous otitis media
- interference with nasal breathing, necessitating mouth-breathing
- malocclusion
- sleep apnea/respiratory disturbance
- orofacial developmental abnormalities

Adenoidectomy

Indications for Adenoidectomy
- chronic upper airway obstruction with sleep disturbance/apnea ± cor pulmonale
- chronic nasopharyngitis resistant to medical treatment
- chronic serous otitis media and chronic suppurative otitis media (with 2nd set of tubes)
- recurrent acute otitis media resistant to antibiotics
- suspicion of nasopharyngeal malignancy
- persistent rhinorrhea secondary to nasal obstruction

Contraindications
- uncontrollable coagulopathy
- recent pharyngeal infection
- conditions that predispose to velopharyngeal insufficiency (cleft palate, impaired palatal function, or enlarged pharynx)

Complications
- bleeding, infection
- velopharyngeal insufficiency (hypernasal voice or nasal regurgitation)
- scarring of Eustachian tube orifice

Sleep-Disordered Breathing in Children

Definition
- spectrum of sleep-related breathing abnormalities ranging from snoring to OSA

Epidemiology
- peak incidence between 2-8 yr when tonsils and adenoids are the largest relative to the pharyngeal airway

Etiology
- due to a combination of anatomic and neuromuscular factors
  - adenotonsillar hypertrophy
  - craniofacial abnormalities
  - neuromuscular hypotonia (i.e. cerebral palsy, Down syndrome)
  - obesity

Clinical Features
- heavy snoring, mouth breathing, pauses or apnea, enuresis, excessive daytime sleepiness, behavioural/learning problems, diagnosis of ADHD, morning headache, failure to thrive

Investigations
- flexible nasopharyngoscopy for assessment of nasopharynx and adenoids
- polysomnography (apnea-hypopnea index >1/h considered abnormal)

Treatment
- surgical: bilateral tonsillectomy and adenoidectomy
- nonsurgical: CPAP, BiPAP, sleep hygiene

Acute Tonsillitis

- see Pediatrics, P58

Peritonsillar Abscess (Quinsy)

Definition
- cellulitis of space behind tonsillar capsule extending onto soft palate leading to abscess

Etiology
- bacterial: Group A strep (GAS) (50% of cases), *S. pyogenes, S. aureus, H. influenzae,* and anaerobes

Epidemiology
- can develop from acute tonsillitis with infection spreading into plane of tonsillar bed
- unilateral
- most common in 15-30 yr age group

Clinical Features
- fever and dehydration
- sore throat, dysphagia, and odynophagia
- extensive peritonsillar swelling but tonsil may appear normal
- edema of soft palate
- uvular deviation
- trismus (due to irritation and reflex spasm of the medial pterygoid)
- dysphonia (edema → failure to elevate palate) 2° to CN X involvement
- unilateral referred otalgia
- cervical lymphadenitis

Quinsy Triad
- Trismus
- Uvular deviation
- Dysphonia ("hot potato voice")

Complications
- aspiration pneumonia 2° to spontaneous rupture of abscess
- airway obstruction
- lateral dissection into parapharyngeal and/or carotid space
- bacteremia
- retropharyngeal abscess

Treatment
- secure airway
- surgical drainage (incision or needle aspiration) with C&S
- warm saline irrigation
- IV penicillin G x 10 d if cultures positive for GAS
- add PO/IV metronidazole or clindamycin x 10 d if culture positive for *Bacteroides*
- consider tonsillectomy after second episode

Other Sources of Parapharyngeal Space Infections
- pharyngitis
- acute suppurative parotitis (see *Salivary Glands*, OT30)
- AOM
- mastoiditis (Bezold's abscess)
- odontogenic infection

Tonsillectomy

Absolute Indications
- most common indication: sleep-disordered breathing
- 2nd most common indication: recurrent throat infections
- tonsillar hypertrophy causing upper airway obstruction, obstructive sleep apnea, severe dysphagia, or cardiopulmonary complications such as cor pulmonale
- suspicion of malignancy (e.g. lymphoma, squamous cell carcinoma)
- orofacial/dental deformity
- hemorrhagic tonsillitis

Relative Indications (To Reduce Disease Burden)
- recurrent throat infection with a frequency of at least 7 episodes in the past year, at least 5 episodes per year for 2 yr, or at least 3 episodes per year for 3 yr, with documentation in the medical record for each episode of sore throat and 1 or more of the following: temperature >38.3°C, cervical adenopathy, tonsillar exudate, or positive test for Group A β-hemolytic *streptococcus* (Paradise Criteria)
- chronic tonsillitis with halitosis (bad breath) or sore throat ± tonsilloliths (clusters of calcified material that form in the crevices of the tonsils)
- complications of tonsillitis: quinsy/peritonsillar abscess, parapharyngeal abscess, retropharyngeal abscess
- failure to thrive

Relative Contraindications
- velopharyngeal insufficiency: overt or submucous/covert cleft of palate, impaired palatal function due to neurological or neuro-muscular abnormalities
- hematologic: coagulopathy, anemia
- infectious: active local infection without urgent obstructive symptoms

Complications
- hemorrhage: early (within 24 h); delayed (within 7-10 d)
- odynophagia and/or otalgia; dehydration 2° to odynophagia
- infection
- atlantoaxial subluxation (Grisel's syndrome) - rare

Airway Problems in Children

DIFFERENTIAL DIAGNOSIS BY AGE GROUP

Neonates (Obligate Nose Breathers)
- extralaryngeal
  - choanal atresia (e.g. CHARGE syndrome)
  - nasopharyngeal dermoid, glioma, encephalocele
  - glossoptosis: Pierre-Robin sequence, Down syndrome, lymphatic malformation, hemangioma
- laryngeal
  - laryngomalacia: most common cause of stridor in children
  - laryngocele

  - vocal cord palsy (due to trauma or Arnold-Chiari malformation)
  - glottic web
  - subglottic stenosis
  - laryngeal cleft
- tracheal
  - tracheoesophageal fistula
  - tracheomalacia
  - vascular rings

2-3 Months
- congenital
  - laryngomalacia
  - vascular: subglottic hemangioma (more common), innominate artery compression, double aortic arch
  - laryngeal papilloma
- acquired
  - subglottic stenosis: post-intubation
  - tracheal granulation: post-intubation
  - tracheomalacia: post-tracheotomy and TEF repair

Infants – Sudden Onset
- foreign body aspiration
- croup
- bacterial tracheitis
- caustic ingestion
- epiglottitis

Children and Adults
- infection
  - Ludwig's angina
  - peritonsillar/parapharyngeal abscess
  - retropharyngeal abscess
- neoplastic
  - squamous cell carcinoma (SCC) (adults): larynx, hypopharynx
  - retropharyngeal: lymphoma, neuroblastoma
  - nasopharyngeal: carcinoma, rhabdomyosarcoma
- allergic
  - angioneurotic edema
  - polyps (suspect cystic fibrosis in children)
- trauma
  - laryngeal fracture, facial fracture
  - burns and lacerations
  - post-intubation
  - caustic ingestion
- congenital
  - lingual thyroid/tonsil

Signs of Airway Obstruction

Stridor
- note quality, timing (inspiratory or expiratory)
- body position important
  - lying prone: subglottic hemangioma, double aortic arch
  - lying supine: laryngomalacia, glossoptosis
- site of stenosis
  - vocal cords or above: inspiratory stridor
  - subglottis and extrathoracic trachea: biphasic stridor
  - distal tracheobronchial tree: expiratory stridor

Respiratory Distress
- nasal flaring
- supraclavicular and intercostal indrawing
- sternal retractions
- use of accessory muscles of respiration
- tachypnea
- cyanosis
- altered LOC

Feeding Difficulty and Aspiration
- supraglottic lesion
- laryngomalacia
- vocal cord paralysis
- laryngeal cleft → aspiration pneumonia
- TEF

Acute Laryngotracheobronchitis (Croup)

- inflammation of tissues in subglottic space ± tracheobronchial tree
- swelling of mucosal lining and associated with thick, viscous, mucopurulent exudate which compromises upper airway (subglottic space narrowest portion of upper airway)
- normal function of ciliated mucous membrane impaired

Etiology
- viral: parainfluenzae I (most common), II, III, influenza A and B, RSV

Clinical Features
- age: 4 mo-5 yr
- preceded by URTI symptoms
- generally occurs at night
- biphasic stridor and croupy cough (loud, sea-lion bark)
- appear less toxic than epiglottitis
- supraglottic area normal
- rule out foreign body and subglottic stenosis
- "steeple-sign" on AP x-ray of neck
- if recurrent croup, think subglottic stenosis

Signs of Croup

The 3 Ss
Stridor
Subglottic swelling
Seal bark cough

Treatment
- racemic epinephrine via MDI q1-2h, prn (only if in respiratory distress)
- systemic corticosteroids (e.g. dexamethasone, prednisone)
- adequate hydration
- close observation for 3-4 h
- intubation if severe
- hospitalize if poor response to steroids after 4 h and persistent stridor at rest
- consider alternate diagnosis if poor response to therapy (e.g. bacterial tracheitis)
- if recurrent episodes of croup-like symptoms, consider bronchoscopy several weeks after acute episode settles to rule out underlying subglottic stenosis

Acute Epiglottitis

- acute inflammation causing swelling of supraglottic structures of the larynx without involvement of vocal cords

Acute epiglottitis is a medical emergency

Etiology
- *H. influenzae* type b
- relatively uncommon condition due to Hib vaccine

Clinical Features
- any age, most commonly 1-4 yr
- rapid onset
- toxic-looking, fever, anorexia, restlessness
- cyanotic/pale, inspiratory stridor, slow breathing, lungs clear with decreased air entry
- prefers sitting up ("tripod" posture), open mouth, drooling, tongue protruding, sore throat, dysphagia

When managing epiglottitis, it is important not to agitate the child, as this may precipitate complete obstruction

Investigations and Management
- investigations and physical exam may lead to complete obstruction, thus preparations for intubation or tracheotomy must be made prior to any manipulation
- stat ENT/anesthesia consult(s)
- WBC (elevated), blood and pharyngeal cultures after intubation
- lateral neck radiograph (only done if patient stable)

Thumb sign: cherry-shaped epiglottic swelling seen on lateral neck radiograph

Treatment
- secure airway
- IV access with hydration
- antibiotics: IV cefuroxime, cefotaxime, or ceftriaxone
- moist air
- extubate when leak around tube occurs and afebrile
- watch for meningitis

Subglottic Stenosis

Congenital
- diameter of subglottis <4 mm in neonate (due to thickening of soft tissue of subglottic space or maldevelopment of cricoid cartilage)

Acquired
- following prolonged, repeated, or traumatic intubation
  - most commonly due to endotracheal intubation; nasal intubation is less traumatic and preferred in long-term intubation as it puts less pressure on the subglottis (tube sits at different orientation) and there is less movement
  - subglottic stenosis is related to duration of intubation and pressure of the endotracheal tube cuff
- can also be due to foreign body, infection (e.g. TB, diphtheria, syphilis), or chemical irritation

Clinical Features
- biphasic stridor
- respiratory distress
- recurrent/prolonged croup

Diagnosis
- rigid laryngoscopy and bronchoscopy

Treatment
- if soft stenosis: divide tissue with knife or laser, dilate with balloon ± steroids
- if firm stenosis: laryngotracheoplasty

Laryngomalacia

- short aryepiglottic folds, omega-shaped epiglottis, pendulous mucosa
- caused by indrawing of supraglottis on inspiration leading to laryngopharyngeal reflux of acid

Clinical Features
- high-pitched inspiratory stridor at 1-2 wk
- constant or intermittent and more pronounced supine and following URTI
- usually mild but when severe can be associated with cyanosis or feeding difficulties, leading to failure to thrive

Treatment
- observation is usually sufficient as symptoms spontaneously subside by 12-18 mo in >90% of cases
- if severe, division of the aryepiglottic folds (supraglottoplasty) provides relief

Laryngomalacia is the most common cause of stridor in infants

Foreign Body

Ingested
- usually stuck at cricopharyngeus
- coins, toys, batteries (emergency)
- presents with drooling, dysphagia, stridor if very large

Aspirated
- usually stuck at right mainstem bronchus
- peanuts, carrot, apple core, popcorn, balloons
- presentation
  - stridor if lodged in trachea
  - unilateral "asthma" if bronchial, therefore often misdiagnosed as asthma
  - if totally occludes airway: cough, lobar pneumonia, atelectasis, mediastinal shift, pneumothorax, death

Diagnosis and Treatment
- any patient with suspected foreign body should be kept NPO immediately
- inspiration-expiration chest x-ray (if patient is stable)
- bronchoscopy or esophagoscopy with removal
- rapid onset, not necessarily febrile or elevated WBC

Foreign body inhalation is the most common cause of accidental death in children

Batteries MUST be ruled out as a foreign body (vs. coins) as they are lethal and can erode through the esophagus. Batteries have a halo sign around the rim on AP x-ray and a step deformity on lateral x-ray

Deep Neck Space Infection

- most commonly arise from an infection of the mandibular teeth, tonsils, parotid gland, deep cervical lymph nodes, middle ear, or the sinuses
- often a rapid onset and may progress to fatal complications

Etiology
- usually mixed aerobes and anaerobes that represent the flora of the oral cavity, upper respiratory tract, and certain parts of the ears and eyes

Clinical Features
- sore throat or pain and trismus
- dysphagia and odynophagia
- stridor and dyspnea
- late findings may include dysphonia and hoarseness
- swelling of the face and neck, erythema
- asymmetry of the oropharynx with purulent oral discharge
- lymphadenopathy

Diagnosis
- lateral cervical view plain radiograph
- CT
- MRI

Treatment
- secure the airway
- surgical drainage
- maximum doses of IV systemic antimicrobials regimens according to the site of infection

These investigations should be obtained carefully and the surgeon should consider accompanying the patient as the worst place to lose an airway is during imaging

Ludwig's angina is the prototypical infection of the submandibular and sublingual space

Common Medications

Table 21. Antibiotics

Generic Name (Brand Name)	Dose	Indications	Notes
amoxicillin (Amoxil®, Amoxi ®, Amox®)	Adult: 500 mg PO tid Children: 75-90 mg/kg/d in 2 divided doses	*Streptococcus, Pneumococcus, H. influenzae, Proteus* coverage	May cause rash in patients with infectious mononucleosis
piperacillin with tazobactam (Zosyn®)	3 g PO q6h	Gram-positive and negative aerobes and anaerobes plus *Pseudomonas* coverage	May cause pseudomembranous colitis
ciprofloxacin (Cipro®, Ciloxan®)	500 mg PO bid	*Pseudomonas, Streptococci*, MRSA, and most Gram-negative; no anaerobic coverage	Do not give systemic quinolones to children
erythromycin (Erythrocin®, EryPed®, Staticin®, T-Stat®, Erybid®, Novorythro Encap®)	500 mg PO qid	Alternative to penicillin	Ototoxic

Table 22. Otic Drops

Generic Name (Brand Name)	Dose	Indications	Notes
ciprofloxacin (Ciprodex®)	4 gtt in affected ear bid	For otitis externa and complications of otitis media *Pseudomonas, Streptococci*, MRSA, and most Gram-negative; no anaerobic coverage	
neomycin, polymyxin B sulfate, and hydrocortisone (Cortisporin Otic®)	5 gtt in affected ear tid	For otitis externa Used for inflammatory conditions which are currently infected or at risk of bacterial infections	May cause hearing loss if placed in inner ear
hydrocortisone and acetic acid (VoSol HC®)	5-10 gtt in affected ear tid	For otitis media	Bactericidal by lowering pH
tobramycin and dexamethasone (TobraDex®)	5-10 gtt in affected ear bid	For chronic suppurative otitis media	Risk of vestibular or cochlear toxicity

Table 23. Nasal Sprays

Generic Name (Brand Name)	Indications	Notes
Steroid		
flunisolide (Rhinalar®) budesonide (Rhinocort®) triamcinolonoe (Nasacort®) beclomethasone (Beconase®) mometasone furoate, monohydrate (Nasonex®) fluticasone furoate (Avamys®)	Allergic rhinitis Chronic sinusitis	Requires up to 4 wk of consistent use to have effect Long-term use Dries nasal mucosa; may cause minor bleeding Patient should stop if epistaxis May sting Flonase® and Nasonex® not absorbed systemically
Antihistamine		
levocarbastine (Livostin®)	Allergic rhinitis	Immediate effect If no effect by 3 d then discontinue Use during allergy season
Decongestant		
xylometazoline (Otrivin®) oxymetazoline (Dristan®) phenylephrine (Neosynephrine®)	Acute sinusitis Rhinitis	Careful if patient has hypertension Short-term use (<5 d) If long-term use, can cause decongestant addiction (i.e. rhinitis medicamentosa)
Antibiotic/Decongestant		
framycetin, gramicidin, phenylephrine (Soframycin®)	Acute sinusitis	
Anticholinergic		
ipratropium bromide (Atrovent®)	Vasomotor rhinitis	Careful not to spray into eyes as can cause burning or precipitation of narrow angle glaucoma Increased rate of epistaxis when combined with topical nasal steroids
Lubricants		
saline, NeilMed®, Rhinaris®, Secaris®, Polysporin®, Vaseline®	Dry nasal mucosa	Use prn Rhinaris® and Secaris® may cause stinging

Source: Dr. MM Carr

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