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 Inferior-Anteriorly
  - **Internal Intercostal Muscle:**
    - Transitions into the Posterior Intercostal Membrane
  - **Innermost Intercostal Muscle:**
    - Oriented Diagonally Inferior-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 Antero-Posterior 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
    - $\text{O}_2$ in $\text{CO}_2$ 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 \(\rightarrow\) 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:**
  o At a constant temperature, the pressure of a gas is *inversely proportional* to its volume.
  o I.e. Gases move from High Pressure → Low Pressure

- **Dalton’s Law (of partial pressures):**
  o 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}
  o Also, the proportion (%age) of a gas in a mixture =
    ▪ The %age of the total pressure that it contributes =
      • Its partial pressure.
  o Simply: *Each gas in a solution exerts a pressure exactly proportional to its abundance.*

- **Henry’s Law (of dissolved gases):**
  o ‘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)**
  o 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:**
  o **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)
  o **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
  - **Intra Pleural Pressure:**
    - Becomes more subatmospheric (more negative)
  - **Intra Pulmonary 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
  - **Intra Pleural Pressure:**
    - Becomes less subatmospheric (more positive)
  - **Intra Pulmonary Pressure:**
    - Becomes positive. (relative to \( P_{atm} \))
  - **Air:**
    - Flows Out

**Respiratory Rates:**

- **Respiratory Rate:** (f)
  - Breathing Frequency
- **Respiratory Minute Volume (Minute Ventilation Rate):** (\( V_e \))
  - Amount of air moved via Tidal Ventilation Each Minute.
  - \( V_e = V_T \times f \)
    - Minute Ventilation Rate = Tidal Volume x Respiratory Rate
- **Alveolar Ventilation:** (\( V_A \))
  - Amount of air reaching the Alveoli each minute
  - \( V_A = (V_T - V_D) \times f \)
    - Alveolar Ventilation = (Tidal Volume – Dead Space) x Frequency
Respiratory Volumes:
- **Tidal Volume** ($V_T$)
  - 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
  - $$TLC = RV + ERV + V_T + IRV$$
Haemoglobin (Hb):

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

- **Role in O₂ Transport:**
  - Each *Heme Unit* can carry *1xOxygen Molecule* (*O₂*)
  - Therefore 1xHaemoglobin can carry *4xOxygen Molecules*.

- **Factors Altering Hb Affinity for O₂:**
  - **Things Changing its Shape/Functional Properties:**
    - Hb Saturation: % of Heme units containing bound *O₂*
      - Therefore also *Pₒ₂*
    - *Pₒ₂*
    - Blood pH
    - Temperature
    - 2,3-BisPhosphoGlycerate (or DPG – disphosphoglycerate) (By-product of Glycolysis.)

- **The Physics Behind Hb’s Function:**
  - 1. *Greatly Increases O₂-Carrying Capacity of Blood:*
    - By binding *O₂*, Hb effectively removes the dissolved *O₂* from solution.
      - Acts as an *O₂* buffer.
      - → More of the Alveolar *O₂* can diffuse into the blood (→ & Haemoglobin) before the *Partial Pressure Gradient* is equalized.
    - Hence, *Blood-O₂ Content = Dissolved O₂ + Hb-Bound O₂*
  - 2. *Binds O₂ Co-Operatively:*
    - The more *O₂* 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 *O₂*-Hb Saturation
          - Low affinity for *O₂*
        - **R-State (Relaxed):**
          - High *O₂*-Hb Saturation
          - High affinity for *O₂*
  - 3. *O₂-Hb-Dissociation Curve:*
    - **Plateau Region (O₂ Loading Zone):**
      - In the lungs (*Pₒ₂ = high*)
      - NB: Normal *Pₒ₂* 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 (O₂ Un-Loading Zone):**
      - In Systemic Capillary Beds (*Pₒ₂ = low*)
      - The *Pₒ₂* Range where Capillary beds *Unload* their *O₂* → Tissue cells.
      - NB: As soon as *Pₒ₂* drops below ≈ 60mmHg, Hb begins to ‘Dump’ its *O₂*.  

![O₂-Hb-Dissociation Curve](www.MedStudentNotes.com)
Shifting The Curve:

- **Right Shift:**
  - Favours Unloading of O\(_2\) to Tissues
  - Reduces Hb’s Affinity for O\(_2\) \(\Rightarrow\) Stabilises ‘T-Conformation’.
  - **Causes:**
    - ↑ Temperature (eg. exercising muscles)
    - ↑ DPG (from Glycolysis)
    - ↑ P\(_{CO2}\) (causes ↑Carbonic Acid \(\Rightarrow\) ↓ affinity for O\(_2\)) \(\Rightarrow\) Bohr Effect
    - ↑ Acid (H\(^+\)) \(\Rightarrow\) Root Effect

- **Left Shift:**
  - Favours Loading of O\(_2\) to Tissues
  - Increases Hb’s Affinity for O\(_2\) \(\Rightarrow\) Stabilises ‘R-Conformation’.
  - **Causes:**
    - Opposites of Above

**Mechanisms of CO\(_2\) Transport**

- **3 Routes To The Lungs:**
  - **1. Dissolved In Plasma:**
    - Tissue CO\(_2\) \(\Rightarrow\) Dissolved Plasma CO\(_2\) \(\Rightarrow\) Pulmonary Capillaries \(\Rightarrow\) Diffusion to Alveoli
  - **2. Bound to Hb:**
    - Tissue CO\(_2\) \(\Rightarrow\) Dissolved RBC CO\(_2\) \(\Rightarrow\) CO\(_2\) + Hb \(\Rightarrow\) HbCO\(_2\) \(\Rightarrow\) Pulmonary Capillaries (P\(_{CO2}\) ↓ as dissolved CO\(_2\) diffuses to Alveoli) \(\Rightarrow\) Dissolved RBC CO\(_2\) \(\Rightarrow\) Diffusion to Alveoli
  - **3. In Bicarbonate-Ion Form:**
    - Tissue CO\(_2\) \(\Rightarrow\) Dissolved RBC CO\(_2\) \(\Rightarrow\) H\(_2\)CO\(_3\) \(\Rightarrow\) HCO\(_3^-\) \(\Rightarrow\) Exits RBC to Plasma \(\Rightarrow\) Pulmonary Capillaries \(\Rightarrow\) Re-Enters RBC from Plasma \(\Rightarrow\) Dissolved RBC CO\(_2\) \(\Rightarrow\) Diffusion to Alveoli
    - Converted to Bicarb by *Carbonic Anhydrase*:
      - CO\(_2\) + H\(_2\)O \(\leftrightarrow\) H\(_2\)CO\(_3\) \(\leftrightarrow\) H\(^+\) + HCO\(_3^-\)

**Ventilation vs. Perfusion**

- **Regional Pulmonary Blood Flow:**
  - **Ventilation-Perfusion Matching:**
    - Not All Alveoli are Perfused or Ventilated equally.
    - **Ventilation-Perfusion Ratios:**
      - \( V_\text{A}/Q \) (Alveolar Ventilation Rate / Blood Flow Rate)
    - **Zone 1:**
      - Capillary Pressure never exceeds Alveolar Air Pressure.
      - No Blood Flow at all.
      - V/Q Ratio \(\Rightarrow\) 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 \(\Rightarrow\) 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 $\rightarrow$ Lymphatics

- **Lymphatic Vessels:**
  - Actively pump Interstitial Fluid $\rightarrow$ Blood Vessels

- **Oedema Safety Factor:**
  - For oedema to occur, Pul.Cap-Pressure must rise above Colloid Osmotic Pressure.
    - Pul.Cap-Pressure $\approx$ 7mmHg
    - C.Osmotic Pressure $\approx$ -28mmHg
  - Therefore a +21mmHg rise in Pul.Cap-Pressure is needed.

![Image of Lung with interstitial fluid accumulation](image)

**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.

![Image of Pulmonary Embolism](image)
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 \approx 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 HCO₃⁻ (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 \( \text{pK} = \log_{10} \left( \frac{[\text{Products}]}{[\text{Reactants}] \right) \)
    - 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.
      - 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

![Acid-Base Balance Regulation](www.MedStudentNotes.com)
-1st Line Of Defence: Chemical Buffer Systems:

  - #1. Carbonic-Acid-Bicarbonate Buffer System:
    o The most important Body Buffer System
    o Occurs within the Red Blood Cell
      ▪ Carbonic Anhydrase (in RBC) catalyses: \((\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3)\)
      ▪ Operates in conjunction with the respiratory system.
        ▪ Ie. Blowing off CO\(_2\) shifts eq. To the left \(\Rightarrow\) Less \([\text{H}^+]\) \(\Rightarrow\) pH increases.
    o Clinical Assessment of Acid/Base:
      ▪ 3 Factors Required:
        • 1. Blood pH
        • 2. Blood \(P_{\text{CO}_2}\)
        • 3. Plasma Bicarbonate
    o When the ratio of \([\text{HCO}_3^-]/[\text{H}_2\text{CO}_3]\) = 20:1, The blood pH will be normal = pH 7.4
      ▪ Ie. The \([\text{Bicarbonate}]\) : \([\text{Carbonic Acid}]\) = 20:1
      ▪ Ie. The \([\text{Bicarbonate}]\) : \([\text{Carbon Dioxide}]\) = 20:1
    ▪ Changing this ratio – Changes Blood pH:
      • \(\text{pH} \uparrow\) When:
        o [Bicarbonate]\(\uparrow\) (Pushes Equation to the Left)
        o [Carbon Dioxide]\(\downarrow\) (Pushes Equation to the Left)
      • \(\text{pH} \downarrow\) When:
        o [Bicarbonate]\(\downarrow\) (Pushes Equation to the Right)
        o [Carbon Dioxide]\(\uparrow\) (Pushes Equation to the Right)

![Chemical Buffer System Diagram](image)

\[\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^-\]  
Carbon Dioxide ↔ Carbonic Acid ↔ Bicarbonate Ion  

**Simplified Equation**

\[\text{Net CO}_2 \text{ (dissolved)} + \text{H}_2\text{O} \leftrightarrow \text{H}^+ + \text{HCO}_3^- \text{ (pK 6.11)}\]

- #2. Phosphate Buffer System:
  o Second most important Body Buffer System
  o Operates in the internal fluid of all cells.
  \[\text{H}_2\text{PO}_4^- (aq) \rightleftharpoons \text{H}^+ (aq) + \text{HPO}_4^{2-} (aq)\]

- #3. Protein Buffers (in RBCs & Intracellular Buffers)
  o Both intracellular and extracellular proteins have negative charges and can serve as \(\text{H}^+\) buffers.
  o 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 \(\text{H}^+\).
    ▪ Forms a weak acid + carbon dioxide (CO\(_2\)).
    ▪ After \(O_2\) is released (in the peripheral tissues), Hb binds CO\(_2\) and \(\text{H}^+\) ions.
    ▪ As blood reaches the lungs these actions reverse themselves \(\Rightarrow\) Hb binds \(O_2\), releasing the \(\text{CO}_2\) and \(\text{H}^+\) ions.
    ▪ The \(\text{H}^+\) combines with bicarbonate (\(\text{HCO}_3^-\)) \(\Rightarrow\) carbonic acid (\(\text{H}_2\text{CO}_3\)). The \(\text{H}_2\text{CO}_3\) breaks down to form water (H\(_2\)O) and carbon dioxide (CO\(_2\)) which are excreted via expiration through the lungs. Therefore respirations help maintain pH.
- Respiratory System – Short Term:
  - (CO₂ Excretion)
  - CO₂ constantly produced during Metabolic Processes
  - Eliminated by lungs.
  - If not eliminated from body, pH would quickly become Acidic (Bicarb-Buffer Eqn. Shifts to Right)
  - CO₂: The Controller Of Ventilation:
    - CO₂ 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:
    - HCO₃⁻ Filtered → Renal Tubules → Combined with H⁺ → Carbonic Acid → H₂O + CO₂ → Blood
    - H⁺ Filtered → Renal Tubules → Combines with HCO₃⁻ → Carbonic Acid → H₂O + CO₂ → Blood
      → Combines with HPO₄^{2⁻} or NH₃ → Excreted in Urine.
  - In Short:
    - Carbonic Acid is recovered → CO₂ & H₂O → Blood
    - Ammonium & Hydrogen Phosphate → Excreted in Urine.
Metabolic Vs. Respiratory pH Disturbances:

- **Metabolic** –
  - **Acidosis:**
    - Due to ↓[HCO₃⁻]
    - (Due to inability of the body to form bicarbonate (HCO₃⁻) in the kidney)
    - (Or, Due to Lactic/Keto Acid build-up)
  - **Alkalosis:**
    - Due to ↑[HCO₃⁻]
    - (Due to Loss of H⁺ in Urine or Vomiting)
    - (Or, Due to Retention of Bicarbonate (HCO₃⁻))

- **Respiratory** –
  - **Acidosis:**
    - Due to ↑Pₐ₉₂ (Due to decreased ventilation of the pulmonary alveoli, → elevated Pₐ₉₂).
  - **Alkalosis:**
    - Due to ↓Pₐ₉₂ (Due to increased alveolar respiration (hyperventilation) → decreased plasma [CO₂])

- **Compensatory Mechanisms:**
  - 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 (vice versa)
  - NB: Regulation of breathing – normally via Pₐ₉₂ (because H⁺ can’t cross Blood-Brain Barrier). However, in Metabolic Acidosis, the Pₐ₉₂ 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 O₂ Consumption)
- **During Light-Moderate Exercise:** – Linear Relationship between O₂ Demand & Ventilation.
- **During Severe Exercise:** - O₂ 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 PCO₂:
    - **Central Chemoreceptors – (Chemosensitive Area of Medulla):**
      - ↑Arterial PCO₂ \( \xrightarrow{} \) ↑CSF-[H⁺] (Cerebro-Spinal Fluid)
      - ↑CSF-[H⁺] Stimulates Respiratory Centre
    - **Peripheral Chemoreceptors – (Aortic & Carotid Bodies):**
      - ↑Arterial PCO₂ \( \xrightarrow{} \) ↑Arterial-[H⁺]
      - ↑Arterial-CO₂ \( \xrightarrow{} \) HCO₃⁻ + Arterial-H⁺ ... Via the Bicarbonate-Buffer System.
      - ↑H⁺ Stimulates Ventilation
      - ↓H⁺ Depresses Ventilation
  - **Arterial Non-CO₂[H⁺]:**
    - Peripheral Chemoreceptors – (Aortic & Carotid Bodies):
      - ↑Non-CO₂-Generated [H⁺] \( \xrightarrow{} \) ↑Arterial-[H⁺]
      - NB: Non-CO₂-Generated [H⁺] = Lactic-Acid/Keto-Acids/Etc.
      - ↑H⁺ Stimulates Ventilation
      - ↓H⁺ Depresses Ventilation
  - **↓Arterial O₂:**
    - Peripheral Chemoreceptors – (Aortic & Carotid Bodies):
      - ↓Arterial-O₂ (to below ≈100mmHg) \( \xrightarrow{} \) Strong Respiratory Stimulation
        - Increased Breathing Rate
        - Increased Breathing Depth
    - NB: Acclimatization:
      - In Low O₂ environments (mountain climbing), the Central Respiratory Centres lose sensitivity for CO₂. Therefore, Low-O₂ 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)
    - ↓VC (Vital Capacity) - Because They Can’t Expel All the Gas in their Lungs
    - ↓FEV₁ (Forced Expiratory Volume in 1 Sec) – Because of Dynamic Airway Compression
  - Key Diagnostic Feature:
    - If their FEV₁ is Less Than 80% of FVC
      - (FEV₁ = 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”

  ![Diagram of Equal Pressure Point](image)

  - **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.