Section Four – Control of Respiration

Lecture 7:
- Central control.
- Chemical control.

Objectives:

i. To describe the medullary and pontine respiratory control centers and explain how the ventilatory pattern is generated and controlled.

ii. To describe the chemical control of breathing via central and peripheral chemoreceptors, and indicate how this is altered in abnormal clinical states.

iii. To describe the effects of different body organs on respiration.
Respiratory Areas in Brainstem

- **Medullary respiratory center**
  - Dorsal groups stimulate the diaphragm
  - Ventral groups stimulate the intercostal and abdominal muscles

- **Pontine (pneumotaxic) respiratory group**
  - Involved with switching between inspiration and expiration (respiratory ramp).

- **Pontine (apneuostic center)** prevents the switch off of the respiratory ramp.
Respiratory Structures in Brainstem
Dorsal group (located in the medulla) receive from the vagus (peripheral chemoreceptors, baroreceptors and lung receptors). They are responsible for the rhythm (unknown cause). Normal inspiration.

Ventral group: Located at the medulla, they remain inactive during quite breathing but increase on need, signals from the dorsal to ventral → contribution of ventral to respiration. They cause inspiration and expiration. Active expiration.

Pneumotaxic center: Located at the upper one-third of the pons, it sends signals to the inspiratory center to switch off inspiratory ramp. When the pneumotaxic signal is strong, inspiration is terminated in 0.5 seconds, but when weak, then termination occurs after 5 seconds. So this center can affect the rate of respiration.

Apneuostic center: Located at the lower two-thirds of the pons, may send signals to the dorsal to prevent or retard the switch off of the respiratory ramp → lung filled with air.
Rhythmic Ventilation

- **Starting inspiration**
  - Medullary respiratory center neurons are continuously active
  - Center receives stimulation from receptors and simulation from parts of brain concerned with voluntary respiratory movements and emotion
  - Combined input from all sources causes action potentials to stimulate respiratory muscles

- **Increasing inspiration**
  - More and more neurons are activated

- **Stopping inspiration**
  - Neurons stimulating also responsible for stopping inspiration and receive input from pontine group and stretch receptors in lungs. Inhibitory neurons activated and relaxation of respiratory muscles results in expiration.
INHALATION (2 seconds)

- Inspiratory muscles contract
- Inspiration occurs
  
- Dorsal respiratory group active

QUIET BREATHING

- Passive expiration occurs
- Inspiratory muscles relax

EXHALATION (3 seconds)

- Dorsal respiratory group inhibited
Modification of Ventilation

- **Cerebral and limbic system**
  - Respiration can be voluntarily controlled and modified by emotions

- **Chemical control**
  - **Carbon dioxide is major regulator**
    - Increase or decrease in pH can stimulate chemosensitive area, causing a greater rate and depth of respiration
  - Oxygen levels in blood affect respiration when a 50% or greater decrease from normal levels exists
The chemoreceptors are specialized cells capable of detecting changes in the concentration of physically dissolved O2, CO2, or hydrogen ion (H+) in the extracellular fluid immediately surrounding them. These chemosensitive cells are divided functionally, anatomically and geographically into the **peripheral** and **central chemoreceptors**. They function to regulate ventilation so CO2 is maintained nearly constant and at a level consistent with CO2 production and O2 consumption by the tissues of the body.

**In the central chemoreceptors, CO2 and H+ effect**: H+ are the most potent stimulator, but they do not cross the blood brain barrier, but when CO2 increases, it passes the BBB and so it forms H+ to stimulate the chemosensitive area in the medulla near the respiratory center. It has a very acute effect (in hours), but after 1-2 days, it decreases because of renal HCO3 formation.
The peripheral chemoreceptors are located in discrete structures known as the **carotid** and **aortic bodies**. O2 has no direct effect but through peripheral chemoreceptors (aortic and carotid bodies). They have little effect compared to CO2 and H+. The carotid send impulses through Hering's nerve → glossopharangeal nerve to dorsal group. Aortic → vagus → dorsal group. These receptors (aortic and carotid bodies) are sensitive to O2 (30-60mmHg). They are also sensitive to CO2 and H+ but the effect of CO2 and H+ on the respiratory center is stronger than on the chemoreceptors.
Modifying Respiration

Higher centers of the brain (speech, emotions, voluntary control of breathing, and action potentials in motor pathways)

- Carotid body
- Aortic body
- Medullary chemoreceptors: \( \downarrow \text{pH}, \uparrow \text{CO}_2 \)
- Carotid and aortic body chemoreceptors: \( \downarrow \text{O}_2 \)
- Hering-Breuer reflex (stretch receptors in lungs)
- Proprioceptors in muscles and joints
- Receptors for touch, temperature, and pain stimuli

Input to respiratory centers in the medulla oblongata and pons modifies respiration
Regulation of Blood pH and Gases

- Decreased stimulation of the respiratory centers results.
- An increase in blood pH (often caused by a decrease in blood CO₂) is detected by the medullary chemoreceptors.
- A decrease in blood pH is caused by the increase in blood CO₂.
- A decrease in blood pH is caused by the decrease in blood CO₂.
- Blood O₂ increases.
- Increased stimulation of the respiratory centers results.
- Increased stimulation of the respiratory muscles by the respiratory centers results in increased ventilation, which increases gas exchange.
Herring-Breuer Reflex

- Limits the degree of inspiration and prevents overinflation of the lungs
  - **Infants**
    - Reflex plays a role in regulating basic rhythm of breathing and preventing overinflation of lungs
  - **Adults**
    - Reflex important only when tidal volume large as in exercise
Other factors affecting respiration as:

- **Voluntary control**: For short periods of time, respiration can be controlled voluntarily.

- **Irritant receptors of airways**: The epithelium of the trachea, bronchi, and bronchioles is supplied with sensory nerve endings called pulmonary irritant receptors that are stimulated by many incidents.

- **Lung “J” receptors**: They are stimulated especially when the pulmonary capillaries become engorged with blood or when pulmonary edema occurs in such conditions as congestive heart failure → dyspnea.

- **Brain edema**: The activity of the respiratory center may be depressed or even inactivated by acute brain edema resulting from brain concussion.

- **Anesthesia**: The most prevalent cause of respiratory depression and respiratory arrest is overdosage with anesthetics or narcotics.
- **Periodic breathing**: deep and shallow, for example:

  **Chyne-Stokes breathing**: on fast breathing, CO2 is decreased and O2 is increased → respiratory depression and after few seconds, it recurs. It is found in all normal subjects but damped by the fluids of blood, and the brain contains dissolved CO2 and O2 to minimize the effect but it can occur in:

  1. Severe heart failure, where slow blood circulation to the brain
  2. Brain damage → reverse feed-back
Lecture 8:

- Effect of exercise, age, sleep apnea on respiration.
- Respiratory investigations.
- Hypoxia.

Objectives:

i. To list the ventilatory changes accompanying the process of ageing.

ii. To explain the ventilatory changes accompanying the process of exercise.

iii. To define sleep apnea.

iv. To distinguish between obstructive and restrictive lung disorders.

v. To evaluate the different types of hypoxia.

vi. Define hypercapnia, cyanosis and dyspnea.
Ventilation in Exercise

- **Ventilation increases abruptly**

- **At onset of exercise:** The brain (motor cortex & other higher centers) transmit impulses into brain stem to excite the respiratory center and so an increase in ventilation.

- **Movement of limbs has strong influence:** increase pulmonary ventilation by exciting joint and muscle proprioceptors that send excitatory impulses to the respiratory center.

- **Conditioned (learned) response:** mediated by neural input to the respiratory center probably from cerebral cortex.

- **Ventilation increases gradually**
  - After immediate increase, gradual increase occurs (4-6 minutes)
  - Anaerobic threshold is highest level of exercise without causing significant change in blood pH
    - If exceeded, lactic acid produced by skeletal muscles
Effects of Aging

- Vital capacity and maximum minute ventilation decrease
- Residual volume and dead space increase
- Ability to remove mucus from respiratory passageways decreases
- Gas exchange across respiratory membrane is reduced
Sleep apnea

- Loss of spontaneous breathing
- May last for > 10 seconds
- May recur 300-500 per night sleep
  - May be due to obstruction of pharynx
  - May be due to impaired CNS respiratory drive
Respiratory investigations

- Blood pH
- Blood gas determination (blood $O_2$ & $CO_2$)
- Respiratory function tests:
  - Maximum expiratory flow (400ml/min) (Peak Expiratory Flow Meter).
  - FVC (Force vital capacity).
  - FEV1 (Forced expiratory volume in the first second).
  - FEV1/FVC ratio
Types of respiratory abnormalities

- **Restrictive**

- **Obstructive**
**Restrictive Disorders or Diseases**

- limited lung expansion.
- reduced lung volumes.
- decreased expiratory flow rates from predicted values.
- the ratio of the actual FEV1.0 to the FVC of the subject is normal (i.e, FEV1.0/FVC> 80%).
- The loss of lung volume with restrictive disorders is reflected by reductions in other lung volumes (RV, FRC) and a reduced FEF25-75% from predicted values.
- Some restrictive diseases include pulmonary fibrosis, tuberculosis, pleural effusion, spinal cord injury that affects innervation to the respiratory muscles.
**Obstructive Disorders or Diseases**

- increased airway resistance causing reduced expiratory airflow rates.
- associated with airway dysfunction.

The actual (recorded) FEV1.0/FVC is less than 80% and the FEV1.0 and FEF\textsubscript{25-75} are 75% or less of the predicted values.

- Examples of obstructive diseases include asthma, chronic bronchitis, and emphysema.
- For example, with mild asthma, the FVC may be normal but the FEV\textsubscript{1.0} and FEF\textsubscript{25-75} reduced from normal.
- During the early stages of emphysema, the VC and FVC may be within normal limits, but with advanced emphysema the FVC is reduced.
Pulmonary emphysema
Infection, obstruction, alveolar damage, decrease diffusing capacity, very low VA/Q (shunt) and very high VA/Q (dead space).

Pneumonia
- Infection, filling of areas with fluid and consolidation, reduction of VA/Q leading to hypoxia and hypercapnia.

Asthma: Spastic contraction to bronchioles leading to hypoxia.
Hypoxia

- Hypoxia is a general term which mean inadequate oxygenation; of the air, the blood or the cells.

- *Effects of Hypoxia:*

Hypoxia affects nervous system first. The person first has a feeling of well-being. Ultimately, there is loss of coordination, fade up of vision and memory, then unconsciousness and death if hypoxia is not relieved.
Types:

- **Circulatory hypoxia:** blood flow to the tissues is too low that adequate O\(_2\) is not delivered to it despite a normal PO\(_2\) & Hb concentration. It may result from cardiovascular diseases like in case of heart failure, shock.

- **Histotoxic hypoxia:** the cell is unable to utilize the O\(_2\) because a toxic agent like cyanide has interfered with the cell’s essential metabolic process and the cells suffer from hypoxia despite that the amount of O\(_2\) reaching the cells is normal.

- **Anemic hypoxia:** the arterial PO\(_2\) is normal but the total O\(_2\) content of the blood is reduced because of reduced numbers of RBCs, reduced Hb concentration or abnormal Hb.

- **Hypoxic hypoxia:** it means decreased O\(_2\) saturation of the blood. It may result from: pneumonia, inadequate ventilation (respiratory muscles paralysis), drowning. The net result of hypoxemia is tissue hypoxia i.e., inadequate supply of the tissues with O\(_2\).
**Hypercapnia:**
It means excess $\text{CO}_2$ in the body fluids.
Not necessary hypercapnia associated with hypoxia except only when hypoxia is caused by hypoventilation or circulatory deficiency.

if hypercapnia does begin to occur, this immediately stimulates pulmonary ventilation which corrects the hypercapnia.

**Outcome of hypercapnia:**
* When alveolar PCO$_2$ rises between 60-75 mmHg, the person feels dyspneic (breathing about as rapidly and deeply as he can (air hunger)).
* Between 80-100 mmHg PCO$_2$, the person becomes lethargic and sometimes even semicomatose.
* When PCO$_2$ rises to 120-150mmHg, anesthia and death can result.
Cyanosis (blueness):
Cyanosis means bluish discoloration of the skin and mucous membranes. It is caused by excessive amount of deoxygenated hemoglobin (reduced hemoglobin; not combined with \(O_2\)) in the skin capillaries. This reduced Hb has an intense dark-blue-purple color that is shown through the skin and mucous membrane. definite cyanosis appears whenever the arterial blood contains more than 5gm/100ml of deoxygenated hemoglobin.

**Types of cyanosis:**
1-Peripheral cyanosis: It affects the skin and the lips but spares the mucous membrane of the palate. It is caused by cutaneous vasoconstriction which slows the flow and increases \(O_2\) extraction in the skin. Physiological during exposure to cold but is also an important manifestation of heart failure.

2-Central cyanosis: It is caused by reduced arterial \(O_2\) saturation (less than 85%, at the lung where it is 97% saturation of Hb with \(O_2\)) and affects the skin and mucous membrane of the mouth. It is seen in cardiac and chest diseases
Dyspnea (air hunger):
It is the sense of breathlessness that limits the ability to ventilate enough to satisfy the demand of air. It is some sort of difficulty in breathing i.e., it is a subjective feeling during which a patient may report being breathless. Another name is air hunger.