REGULATION OF RESPIRATION

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The Respiratory system in human performs a critical task
That is to regulate & respond to $O_2$ demands
Maintaining a constant $O_2$ & $CO_2$ in the blood
Therefore, regulation of respiration is critically important for Homeostasis

Any physiological control system is composed of 3 interconnecting structures:
Integrator (centre), Sensor & Effector

The Respiratory Control System

Integrator (Centre) → neural network in brainstem
Sensors →
The main are chemosensors sensing changes in $CO_2$, $O_2$, & pH
Other contributors: in the lungs, cardiovascular, skeletal muscles, tendons of respiratory muscles,
Effector → respiratory muscles
Inspiration; diaphragm & external intercostals
Expiration; internal intercostals & abdominal recti

The Respiratory Centre

Present in brain stem
Medullary group of neurons (rhythmicty centre)
Pontine:
Apneustic
Pneumotaxic

Medullary Respiratory Neurons (Rhythmicty Centre)

2 distinct groups of neurons:
The Dorsal Respiratory Group (DRG)
The Ventral Respiratory Group (VRG)
The 2 groups are bilaterally paired
There is cross communication between them
responsible for initiation & regulation of breathing
Medullary Respiratory Neurons

Dorsal Respiratory Group (DRG)
- Inspiratory neurons that discharge during inspiration & stop discharging during expiration (Inspiratory Rhythm generator)
- They generate a Ramp Signal; they initiate inspiration with a weak burst of action potentials that gradually increase in amplitude, then ceases for the next 3 sec. until a new cycle begins
- This provides a gradual increase in lung volume during inspiration

Basic rhythmic breathing and Inspiratory Neuronal Activity
The basis of rhythmic breathing. During inspiration the activity of inspiratory neurons increases steadily (ramps up). At the end of inspiration, the activity shuts off abruptly and expiration occurs by virtue of elastic recoil of lungs.

Medullary Respiratory Neurons

Input to Dorsal Respiratory Group (DRG)
- The most important sensory comes from the adjacent central Chemoreceptors (chemosensitive area in medulla)
- Input from peripheral Chemoreceptors via afferent sensory of vagus (X) & glossopharyngeal (IX)
- Stimulatory input from Apneustic centre prolonging its activity
- Inhibitory input from Pneumotaxic centre terminating its activity

Medullary Respiratory Neurons

Output from Dorsal Inspiratory Group (DIG)
- Efferent nerves to spinal motoneurons supplying diaphragm (C3-5) & external intercostals (T1-T12).
- Stimulatory to Pneumotaxic centre

Inputs & output of DRG

Ventral Respiratory Neurons

Ventral Respiratory Group (VRG)
- Anterolateral to DRG
- Activated during heavy breathing; e.g. exercise
- During such conditions, the increased activity of inspiratory neurons activates the VRG
- In turn, the activated VRG discharge:
  - inhibiting inspiratory group
  - stimulating the muscles of expiration; internal intercostals (T6-L3), abdominal recti (T4-L3)
Rhythmicity Center
- I neurons located primarily in dorsal respiratory group (DRG):
  - Regulate activity of phrenic nerve.
- E neurons located in ventral respiratory group (VRG):
  - Passive process.
- Activity of E neurons inhibit I neurons.
  - Rhythmicity of I and E neurons may be due to pacemaker neurons.

Pontine Respiratory Centre
- 2 pontine centres that modify the rate & The Pattern of respiration:

**Apneustic centre:**
- In the lower 1/3 of pons, close to medullary groups
- sends stimulatory discharge to inspiratory neurons promoting inspiration
- Removal of its stimulatory effect → respiration becomes shallow & irregular

**Pneumotaxic centre**
- In upper 2/3 of pons
- Its major role is regulation of respiratory volume & rate
- Controlling cessation of inspiratory ramp signal from DRG:
  - Switch-off DRG & apneustic centre → expiration occurs
- Hypoactivation of this centre → prolonged deep inspiration
  - Hyperactivation → shallow inspiration

Thus, the pontine centres work in co-ordination to regulate rhythmic respiratory cycle; How
- Active inspiratory neurones → stimulation of ms. of inspiration & pneumotaxic centre
- Active pneumotaxic centre → inhibits apneustic & DRG → initiation of expiration
- Spontaneous activity of inspiratory neurons in DRG then starts another cycle
The co-ordinated work of neurons of respiratory centre

Overall Control of Activity of Respiratory Centre

- **A1. Involuntary (Automatic) Control:**
  - I- Chemoreceptor Reflexes
  - II- Neurogenic Reflexes
- **B1. Voluntary Control**

### 1- Central Chemoreceptors Pathway

#### Central chemosensitive area

- Lying just beneath ventral surface of medulla
- Relaying most important sensory input about changes in their close environment to respiratory centre in medulla & pons
- Most sensitive to change in PCO₂, H⁺ conc., but not to PO₂

#### Chemical regulation of activity of Respiratory centre which involves 2 pathways:

1. Central Chemoreceptor Pathway
2. Peripheral Chemoreceptor Pathway

- These chemoreceptors sense changes in PCO₂, PO₂ & pH

#### Under normal conditions, ~75-85% of respiratory drive is due to stimulation of central chemoreceptors by CO₂

- Central chemoreceptors are directly stimulated only by H⁺
- But H⁺ can not cross blood brain barrier while CO₂ can
- So, how central chemoreceptors are stimulated by an increase in arterial PCO₂?

Central chemoreceptors are stimulated by an INCREASE in H⁺ & PCO₂
Central (medullary) Chemoreceptors (mechanisms) the H⁺ (CO₂) sensors

Blood here

Cerebrospinal fluid here

Brain here

Respiratory control system

Ventilation

2- Peripheral Chemoreceptor Pathway

Peripheral Chemoreceptors

Peripheral chemoreceptors are the only sensors detecting a fall in PO2

Stimulation of Peripheral chemoreceptors

- The carotid & aortic bodies are sensitive to fall in PO₂, an increase in PCO₂ or H⁺ concentration
- They maximally stimulated when PO₂ decreases below 50-60mm Hg
- They detect changes in dissolved O₂ but not in the O₂ that is bound to Hb (e.g., in anaemia there is normal PO₂ but reduced content of O₂ bound to Hb)

The Oxygen Sensors (How do they work?)

What if Carotid bodies are removed?

- if there is decreased PO₂ (Hypoxia) with absence of peripheral chemoreceptors Hypoxia will inhibit respiration

Why?
- hypoxia depresses neuronal activity including that of respiratory centre
- Hypoxia → VD of cerebral vessels →→PCO₂ in CSF →→CO₂-mediated stimulation of central chemoreceptors →→ hypoventilation

A). Involuntary Automatic Control

II- Neurogenic Reflexes

- Hering-Breuer Inflation Reflex
- Hering-Breuer Deflation Reflex
- J-receptor Reflex
- Baroreceptors Reflex
- Cough & sneezing Reflexes
- Other influences (mediated via hypothalamus)
Neurogenic Reflexes

1- Hering-Breuer inflation reflex (inhibitory inspiratory reflex)

- Over-inflation of lungs → stimulation of slowly adapting stretch receptors in smooth muscles of large & small airways → afferent vagal signals → inhibitory to apneustic centre → termination of inspiration
- Pulmonary stretch receptors are present in the tracheobronchial tree and visceral pleura but not in lungs

2- Hering-Breuer deflation reflex (excitatory inspiratory reflex)

- Deep expiration → Deflation of the lungs → ↓ activity of previous stretch receptors or stimulate other proprioceptors in respiratory muscle → vagal afferent signals → inhibition of expiratory neurons

3- J-receptor Reflex

- Pulmonary emboli or oedema → juxta pulmonary-capillaries receptors stimulated due to increase in interstitial fluid volume which increase the pulmonary capillaries pressure → vagal afferent to respiratory centre → rapid shallow respiration
- These receptors are responsible for the sensation of air hunger (Dyspnea; shortness of breath)

4- Baroreceptor Reflex

- ↑ in ABP → stimulation of baroreceptors → afferent signals via X & IX → inhibitory to respiratory centre → decrease rate & depth of respiration → ↓ venous return → ↓ COP → ↓ ABP

5- Cough, Sneezing reflexes

- Dust, smoking, irritant substances → stimulation of irritant receptors in upper airways → afferent signals via vagus (Upper airways, [larynx, cough]) or trigeminal or olfactory (nose, sneezing) → respiratory centre → deep inspiration followed by forced expiration against closed glottis → opening of glottis → forceful outflow of air

Reflexes involved in Respiratory Control

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<th>Effector</th>
<th>Receptor</th>
<th>efferent output</th>
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<tbody>
<tr>
<td>Long inflation</td>
<td>Hering-Breuer inflation</td>
<td>Airway stretch receptors</td>
<td>Vagus</td>
</tr>
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<td>Pulmonary emboli</td>
<td>Hering-Breuer inflation</td>
<td>Airway stretch receptors</td>
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<tr>
<td>Retraction of lung</td>
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<td>Alveolar cough</td>
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<td>Inspiration of airway</td>
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<td>Systemic arterial</td>
<td>Baroreceptor reflex</td>
<td>Arterial &amp; venous bodies</td>
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<td>Blood pressure</td>
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Neurogenic Reflexes

Other Influences from higher centres

- **Temperature:** Increases respiratory rate
- **Pain:** Sudden pain decreases, prolonged pain increases rate
- **Alcohol:** Decreases rate

B). Voluntary Control of Breathing

Cortical Influence

- Through descending tracts from the cerebral cortex to motor neurons of the respiratory muscles (dorsolateral corticospinal tracts)
- This provides CNS the ability to override the automatic regulation of respiration for short time e.g., holding breath but the involuntary control will take over (↑ PCO₂, H⁺), or deliberate hyperventilation (↓ PCO₂)
Summary Of the Overall Control of Activity of Respiratory Centre

A Summary of Chemoreceptor Reflexes

Mark the following T or F

Respiratory chemoreceptors:

a). in the carotid and aortic bodies are most important in the ventilatory response to an elevated PCO2
b. in the carotid and aortic bodies are strongly stimulated by the low arterial O2 content in anaemic patients
c). in the medulla are responsive to changes in arterial PCO2
d. transducer a chemical changes into electric signals
e. may be sensitive to H+
Choose the best answer

Which of the following is the correct chain of events in the response to low Oxygen level?

a) peripheral chemoreceptors activated-impulses sent to respiratory centre- respiratory muscles stimulated
b) central chemoreceptors activated- impulses sent to respiratory centre- respiratory muscles stimulated
c) increased ventilation- impulses sent to respiratory centre- respiratory muscles stimulated
d) peripheral and central chemoreceptors activated- impulses sent to respiratory centre- respiratory muscles stimulated

What is the function of the Apneustic centre in the brain?

a) monitor changes in CO2, O2 & H+ ions
b) sends inhibitory signals to Inspiratory area in medulla
c) sends stimulatory signals to Inspiratory area in medulla
d) monitors changes in blood pressure

Peripheral chemoreceptors are sensitive to which of the following?

a). increased PO2
b). elevated arterial blood pressure
c). elevated pH
d). decreased PO2
e). decreased PCO2

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