Regulation of Respiration

By

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Objectives

• By the end of the lecture students should be able to
  – Summarize nervous control of respiration
  – Explain the location and function of various respiratory centers
  – Explain Hering breuer reflex
  – Summarize the role of Chemical control in regulation of respiration.
Control of Respiration

• Nervous control
  – Respiratory centers/group of neurons
  – Their functions
  – Hering breuer reflex

• Chemical control
  – Central chemoreceptors
  – Peripheral chemoreceptors
Control Of Respiration

- Central controller
  - Brain stem (Pons, Medulla)
  - Cortex
  - Other parts of brain

1. Sensors
   - Chemoreceptors:
     - Central
     - Peripheral
   - Pulmonary receptors
   - Other receptors

2. Central controller

3. Effectors
   - Resp. Muscles
     - Diaphragm
     - Abd. Muscles
     - Accessory Muscles
Some stimulus disrupts homeostasis by increasing:

**Arterial blood P_{CO_2}** (or decreasing pH or P_{O_2})

**Receptors**

- **Central chemoreceptors in medulla**
- **Peripheral chemoreceptors in aortic and carotid bodies**

**Control center**

Inspiratory area in medulla oblongata

**Output**

Nerve impulses

**Effectors**

Diaphragm and other muscles of respiration contract more forcefully and more frequently (hyperventilation)

Return to homeostasis when response brings arterial blood P_{CO_2}, pH, and P_{O_2} back to normal.
Nervous Control

• Three major group of neurons
  – Medullary group
    • Dorsal respiratory group
    • Ventral respiratory group
  Both the above group are bilaterally paired and communicate with each other
  – Pontine group
    • Pneumotaxic center
    • Apneustic center
Dorsal Respiratory Group

• Located in
  – Nucleus of tractus solitarius (sensory termination of 9\textsuperscript{th} and 10\textsuperscript{th} cranial nerves)
  – Reticular formation

• Also known as inspiratory center

• Receives signal from peripheral chemoreceptors, baroreceptors and special lung receptors
Dorsal Respiratory Group

• Inspiratory neurons—discharge during inspiration & stop discharging during expiration (Respiratory Rhythm generator)

• Generate a Ramp Signal

• Initiate inspiration with a weak burst of action potentials—gradually increase in amplitude, & ceases for the next 3 sec until a new cycle begins

• Provides a gradual increase in lung volume during inspiration
Inspiratory Ramp

Two characteristics of inspiratory ramp

1. Control of the rate of increase of the ramp signal
   • During heavy respiration, the ramp increases rapidly and therefore fills the lungs rapidly

2. Control of the limiting point at which the ramp suddenly ceases
   • Limits the rate of respiration
Ventral Respiratory Group Of Neurons

- Situated in medulla oblongata anterior and lateral to the inspiratory center
- Formed by neurons of nucleus ambiguous and nucleus retro ambiguous
- Expiratory center
Ventral Respiratory Group Of Neurons

Function:
• Center is inactive during quiet breathing
• During forced breathing or when the inspiratory center is inhibited it becomes active
• Forced breathing signals are spilled to ventral group
Pneumotaxic center

• Situated in upper Pons
• Formed by nucleus parabrachialis

Function
• Controls medullary respiratory centers
• Switch-off the inspiratory center
• Limits the duration of inspiration
• Also increases the rate of breathing by shorten expiration as well (secondary)
Medullary Respiratory Neurons

Input & Output of DRG

Central chemoreceptors

Apneustic centre

Pneumotaxic centre

Peripheral chemoreceptors

Spinal motoneurons

Cervical (3,4,5) & Thoracic (1-12)
Apneustic center

• Situated in lower Pons
• Lower 1/3 close to medullary groups

Function:
• Center increases depth of inspiration by acting directly on the inspiratory center.
• Sends stimulatory discharge to inspiratory neurons promoting inspiration
• Removal of its stimulatory effect → respiration becomes shallow & irregular
How Pontine Respiratory Centres work to regulate rhythmic respiratory cycle?

- Active dorsal medullary inspiratory neurons → stimulatory discharge to muscles of inspiration
- Pneumotaxic centre → activated → inhibits apneustic & DRG → initiation of expiration
- Then, the spontaneous activity of inspiratory neurons starts another cycle
Hering Breuer reflex

- **Stimulus:** overstretching
- **Receptors:** stretch receptors
- **Afferents:** Vagii
- **Center:** Dorsal respiratory group
- **Efferents:** Vagii
- **Effectors:** muscles of expiration
- **Response:** limit the inspiration
  - Operates when tidal volume becomes 1.5L
Chemical Control of Respiration

Objective:
• To maintain proper concentration of O₂, CO₂ & H⁺ in the tissues.

Chemoreceptors:
• Central chemoreceptors (chemo sensitive area)
  – Direct chemical control of Resp. center activity
• Peripheral Chemoreceptors
  – Indirect chemical control of Resp. center activity
• Stimuli
Stimuli Affecting the Respiratory Center

Chemical control
• CO2 (via CSF and brain interstitial fluid H+ concentration)
• O2 (via carotid and aortic bodies)
• H+

Nonchemical control
• Vagal afferents from receptors in the airways and lungs
• Afferents from the pons, hypothalamus, and limbic system
• Afferents from proprioceptors
• Afferents from baroreceptors: arterial, atrial, ventricular, pulmonary
Chemosensitive Area of Resp. Centre

- Located bilaterally less than 0.2mm beneath the ventral surface of medulla.
- Highly sensitive to changes in blood PCO2 or H+ conc.
Stimulation of Chemosensitive Area

1. H+ ions:
   • Primary stimulus/direct stimulus for neurons of chemo sensitive area
   • Changes in H+ conc. In blood have less effect than changes in PCO2
   • H+--cannot cross blood Brain Barrier
   • Normal pH of CSF is 7.32 less buffering
   • Changes in pH of CSF for given change in PCO2 is greater than that in blood
Stimulation of Chemosensitive Area

2. CO₂:
Acute Effect:-

• stimulates chemo sensitive neurons indirectly
• Little direct effect
• CO₂ is lipid soluble cross BBB
• PCO₂ in blood immediately leads to increase PCO₂ in CSF & brain tissue
• CO₂ + H₂O → H₂CO₃ → H⁺ + HCO₃⁻
• H⁺ conc. promptly rises in CSF
Stimulation of Chemosensitive Area

Chronic Effect :

• Initial effect is massive
• Decreased stimulatory effect of CO2 after 1-2 days, due to :
  i. Renal adjustment of H+
  ii. Diffusion of HCO3 in brain
Stimulation of Chemosensitive Area

3. O₂

- Changes in oxygen concentration have no *direct* effect
- O₂Hb dissociation curve shows normal oxygen delivery between 60-500mmHg
- Peripheral chemoreceptors are activated when PO₂ falls below 70mmHg
Peripheral Chemoreceptors

**Location:** outside the brain;
1. In carotid bodies – Largest number
2. In aortic bodies – Sizable number
3. In other arteries of thorax
4. Few in abdominal region

Afferents via 9th & 10th CN to DRG
Peripheral Chemoreceptors

**Sensitivity:** Respond to:
- Decrease in arterial PO₂ (most responsive)
- Decrease in arterial pH
- Increase in arterial PCO₂

- Acts through carotid bodies
- Always exposed to high PO₂ due to high blood flow 20 times normal
- Decrease PO₂ causes rapid firing of impulses from carotid bodies
Peripheral Chemoreceptors

• $\uparrow$CO$_2$ and H+ ions excites chemoreceptors & indirectly increases respiratory activity
• Central effect of both these factors is more potent
• Peripheral effect is 5times more rapid
• Important in increasing the rapidity of response to carbon dioxide at the onset of exercise
Peripheral Chemoreceptors

Role of Art. PCO2/pH

• Indirect effect is less important i.e. increase PCO2 & decrease H+ conc.

• Stimulate central chemoreceptors directly.

• Direct effect is 7 times more powerful.

• Indirect effect is 5 times rapid.

• *In human carotid but not aortic bodies respond to fall in Art. pH.*
**Stimulation of Peripheral Chemoreceptors**

- Highly glandular cells—glomus cells directly synapse with nerve endings
- Glomus cells work as peripheral chemoreceptors
- Stimulate nerve endings
- O2 sensitive K+ channels inactivated when PO2 is less
- Cells depolarize
- Open calcium channels
- Intracellular Ca rises & stimulate neurotransmitter release
- Afferents send signals to CNS and stimulate respiration
Mechanism of Neurotransmitter Release by Glomus Cells

1. Low PO₂
2. K⁺ channels close
3. Cell depolarizes
4. Voltage-gated Ca²⁺ channel opens
5. Ca²⁺ entry
6. Exocytosis of dopamine-containing vesicles
7. Signal to medullary centers to increase ventilation
Effect of $O_2$ on Alveolar Ventilation

- Decrease in $O_2$ content of alveolar air increases respiratory minute volume
- Increase is slight when the pO$_2$ >60 mm Hg
- Marked increase when pO$_2$ <60 mm Hg
‘J’ Receptors of Lungs

- Located in juxtacapillary receptors present in wall of the alveoli
- Close contact with the pulmonary capillaries.
- Stimulated during conditions like pulmonary edema, pulmonary congestion, pneumonia, exposure of exogenous and endogenous chemicals like histamine, serotonin.
- Stimulation produces apnea.
Irritant Receptors Of Lungs

• Situated on the wall of bronchi and bronchioles of lungs
• Stimulated by harmful chemicals like ammonia & sulfur dioxide.
• Stimulation produces reflex hyperventilation & bronchospasm that prevents entry of harmful chemicals into the alveoli.
Brain Edema

- Respiratory center activity—depressed or inactivated by acute brain edema
- Reason: Brain concussion
- Head injury leads to swelling of damaged brain tissues—compress cerebral arteries blocks cerebral blood supply.
- Respiratory depression due to brain edema
- Relieved temporarily by i/v hypertonic solutions like mannitol
  - These solutions osmotically remove fluids of the brain, decreases intracranial pressure restores respiration
Anesthetics

• Most likely cause of respiratory depression & arrest is over dosage with anesthetics or narcotics
• Anesthetic agents causing respiratory depression
  – Sodium pentobarbital
  – Halothane
  – Morphine
CHYNE STOKES BREATHING

• Abnormality of respiration--periodic breathing
• Person breathes deeply for a short interval and then breathes slightly or not at all for an additional interval, in repeated cycle
• Cheyne-stokes breathing-- slowly waxing and waning respiration occurring every 40 to 60 seconds
Cause of Cheyne-Stokes Breathing

• When a person over breathes, too much carbon dioxide is blown off and increased oxygen in the pulmonary blood, as pulmonary blood reach the brain, inhibits the excess ventilation

• When over ventilated blood reaches the respiratory center, becomes depressed to an excessive amount

• Cessation of respiration leads to opposite effect i.e. carbon dioxide increases and oxygen decreases in the alveoli and stimulates the respiratory center

• Under normal condition this mechanism is damped

• In cardiac failure blood flow is slow transport of gases to brain is delayed, cheyne stokes breathing takes place.
CHEYNE – STOKES Breathing (*Periodic Breathing*)

Slowly waxing & waning respiration occurring over and over again approximately every 40 - 60 seconds.

Over Breathing $\rightarrow \downarrow$ PCO$_2$ & $\uparrow$ PO$_2$ (In Pul. Blood)

$\downarrow$ Inhibition of Brainstem

$\downarrow$ Slowing of Breathing

$\downarrow$ APNEA

$\downarrow$ PO$_2$ & $\uparrow$ CO$_2$

Cycle begins Again

![Diagram showing the depth of respiration and PCO$_2$ of respiratory neurons compared to PCO$_2$ of lung blood with the respiratory center excited or inhibited, illustrating the periodic breathing pattern.](image-url)
Sleep apnea

• Cessation of breathing during sleep
• Restless sleep and day drowsiness
• Loud snoring, apnea period, increased heart rate, pulmonary and systemic hypertension
• Two types
  1. Central Sleep apnea
  2. Obstructive sleep apnea
Central sleep apnea

• Causes
  – Central respiratory center damage
  – Respiratory muscle disorders
  – Stroke
  – Abnormalities of neuromuscular apparatus

• Treatment
  – Sedatives are helpful
  – Respiratory center stimulation
  – CPAP(continuous positive airway pressure)
Obstructive Sleep apnea

• Absence of spontaneous breathing

• Causes
  – Relaxation of respiratory muscles
  – Blockage of upper airway

• Loud snoring → followed by ↓PO2 & ↑PCO2 due to apnea → respiratory center stimulated → regain breathing
Obstructive Sleep apnea

• Common in obese individuals
  – Deposition of fat in soft tissue of pharynx and compress it

• Treatment
  – Remove the cause
  – CPAP(*continuous positive airway pressure*)
THANK YOU