Objectives

- Identify where the structures that regulate breathing are located.

- Describe how the inspiratory and expiratory neurons in the medulla establish the basic pattern of breathing.

- Describe the effect impulses from the pneumotaxic and apneustic centers in the pons have on the medullary centers of breathing.

- Identify the effect of various reflexes on breathing.
Objectives (cont.)

- Describe how the central and peripheral chemoreceptors differ in the way they regulate breathing.

- State how the central chemoreceptors respond differently to respiratory and nonrespiratory acid-base disorders.

- Describe how the regulation of breathing in individuals with chronic hypercapnia differs from the regulation of breathing in healthy persons.

- Describe why administering oxygen to patients with chronic hypercapnia poses a special risk that is not present in healthy individuals.
Objectives (cont.)

- Describe why ascending to a high altitude has different immediate- and long-term effects on ventilation.

- State why mechanically ventilated patients with head injuries may benefit from deliberate hyperventilation.

- Describe the characteristics of abnormal breathing patterns.
Medullary Respiratory Center

- The rhythmic cycle of breathing originates in the medulla.

- Higher brain centers, systemic receptors, and reflexes modify the medulla’s output.

- No truly separate inspiratory and expiratory centers

- The medulla does contain several widely dispersed groups of respiratory-related neurons.
  - These form dorsal and ventral respiratory groups.
Medullary Respiratory Center (cont.)

Dorsal respiratory groups (DRG)
- Composed mainly of inspiratory neurons located bilaterally in the medulla
- These neurons send impulses to the motor nerves of diaphragm and external intercostal muscles.
- DRG nerves extend into the VRG not the reverse.
- Vagus and glossopharyngeal nerves bring sensory impulses to the DRG from the lungs, airways, peripheral chemoreceptors, and joint proprioceptors.
  - Input modifies the breathing pattern.
Medullary Respiratory Center (cont.)

Ventral respiratory groups (VRG)
- Contain both inspiratory and expiratory neurons located bilaterally in the medulla
- VRG sends inspiratory impulses to
  - Laryngeal and pharyngeal muscles
  - Diaphragm and external intercostals
- Other VRG neurons send expiratory signals to abdominal muscles and internal intercostals.

Inspiratory ramp signal
- Signal starts low and gradually increases to produce a smooth inspiratory effort instead of a gasp.
Pontine Respiratory Centers

- The pons modifies the output of medullary centers.
  - Two pontine centers are apneustic and pneumotaxic.

- Apneustic center
  - Its function only identified by cutting connection to medullary centers
  - Apneustic breathing is characterized by long gasping inspirations interrupted by occasional expirations.

- Pneumotaxic center
  - Controls “switch-off,” so controls $I_T$
  - Increased signals increase RR, while weak signals prolong $I_T$ and large $V_T$. 
Reflex Control of Breathing

The Hering-Breuer inflation reflex

- Lung distention causes stretch receptors to send inhibitory signals to DRG, stopping further inspiration.
  - In adults active only on large $V_T (>800 \text{ ml})$
  - Regulates rate and depth of breathing during moderate to strenuous exercise

Deflation reflex

- Sudden lung collapse results in hyperpnea as seen in pneumothoraces.
Reflex Control of Breathing (cont.)

Head’s paradoxic reflex
- May maintain large $V_T$ during exercise and deep sighs
- May be responsible for babies first breaths at birth

Irritant receptors
- Stimulated by inhaled irritants or mechanical factors
- Cause bronchospasm, cough, sneeze, tachypnea, and narrowing of glottis
  - These are vasovagal reflexes.
- In hospital triggered by
  - Suctioning, bronchoscopy, endotracheal intubation
Reflex Control of Breathing (cont.)

- **J-receptors**
  - Located in lung parenchyma juxtacapillary
  - Stimulated by pneumonia, CHF, pulmonary edema
  - Cause rapid, shallow breathing and dyspnea

- **Peripheral proprioceptors**
  - Found in muscles, tendons, joints, and pain receptors
  - Movement stimulates hyperpnea.
  - Moving limbs, pain, cold water all stimulate breathing in patients with respiratory depression
Chemical Control of Breathing

- Body works to maintain proper levels of O₂, CO₂, and pH through mediation of chemoreceptors as it affects $V_E$

Central chemoreceptors
- Located bilaterally in the medulla

- Stimulated directly by H⁺ ions, indirectly by CO₂
  - The BBB is almost impermeable to H⁺ and HCO₃⁻ but CO₂ freely crosses.
  - In CSF, CO₂ is hydrolized, releasing H⁺.
  - An increased CO₂ increases H⁺ in CSF, causing hyperventilation to restore normal levels pH and CO₂.
    - $V_A$ increased 2–3 L/min for 1–mm Hg rise in PaCO₂.
Peripheral chemoreceptors
- Located in the aortic arch and bifurcations of common carotid arteries

Peripheral chemoreceptors’ response to ↓ PaO₂
- Hypoxemia increases receptors sensitivity for H⁺.
  - ↓PaO₂ causes ↑Vₑ for any pH, and vice versa.
  - In severe alkalosis, hypoxemia has little affect on Vₑ.

- Only affected by PaO₂, not CaO₂ (anemia, COHb)
Chemical Control of Breathing (cont.)

Peripheral chemoreceptors’ response to ↓PaO₂ (cont.)

- Not a significant response until PaO₂ falls to ~60 mm Hg
  - A further fall results in sharp increase in Vₑ.
  - This means the under normal circumstances, oxygen plays no role in drive to breathe.

- Hypoxemia the most common cause of hyperventilation
Chemical Control of Breathing (cont.)

Peripheral chemoreceptors’ response to $\uparrow$ PaCO$_2$ and [H$^+$]

- Less responsive than central chemoreceptors (CCRs)
  - One-third of hypercapnic response, but a more rapid response to changes in [H$^+$]

- In hyperoxia, PCRs are almost totally insensitive to changes in PaCO$_2$, so any response is due to CCRs.

- Low PaCO$_2$ renders PCRs almost unresponsive to $\downarrow$ PaO$_2$.
Chemical Control of Breathing (cont.)

- Coexisting acidosis, hypercapnia, and hypoxemia maximally stimulate PCRs

- Hypercapnic COPD patients depressed response to $\uparrow \text{CaO}_2$
Chemical Control of Breathing (cont.)

Control of breathing in chronic hypercapnia

- Sudden rise in PaCO\(_2\) causes immediate rise in \(\dot{V}_E\)

- In slow-rising PaCO\(_2\) (severe COPD), kidneys retain HCO\(_3^-\), which maintains CSF pH, so no hyperventilation response

- Hypoxemia seen with hypercapnia becomes the minute-to-minute breathing stimulus via altered response to \([H^+]\).
  - Hypoxemia is always present in severe COPD due to severe mismatches in V/Q.

- An increased FIO2 raises the PaO2 making the PCR less sensitive to \([H^+]\) resulting in a higher PaCO2
Chemical Control of Breathing (cont.)

Oxygen-induced hypercapnia

- $O_2$ therapy may cause a sudden rise in $PaCO_2$ in severe COPD with chronic hypercapnic.

- Possible explanations include
  - Hypoxic drive is removed (traditional view).
  - $\uparrow FIO_2$ may worsen $\bar{V}/\bar{Q}$ mismatch
    - Hypoxic pulmonary vasoconstriction is reversed to poorly ventilated alveoli
  - $\uparrow FIO_2$ may make patient susceptible to absorption atelectasis.
Chemical Control of Breathing

A

Venous

Hypoxic vasoconstriction:

\[ P_{CO_2} \uparrow \]
\[ P_{O_2} \downarrow \]

\[ Q \downarrow \]

\[ V/Q \] normal

Arterial

\[ FIO_2 = 0.21 \]

\[ P_{CO_2} \] normal
\[ P_{O_2} \] normal

\[ \dot{V} \rightarrow \]

\[ \dot{Q} \rightarrow \]

\[ \dot{V}/Q \]

B

Arterial

\[ FIO_2 = 0.50 \]

\[ \dot{V} \rightarrow \]

\[ \dot{Q} \rightarrow \]

\[ \dot{V}/Q \] normal

Vasoconstriction relieved:

\[ P_{CO_2} \uparrow \]
\[ P_{O_2} \uparrow \]

\[ \dot{V} \rightarrow \]

\[ \dot{Q} \rightarrow \]

\[ \dot{V}/Q \]
Chemical Control of Breathing (cont.)

Oxygen-induced Hypercapnia: KEY POINTS

- “COPD” does NOT signify chronic hypercapnia or that $O_2$ therapy will induce hypoventilation.
  - These characteristics are only in end-stage disease.
  - Present in small percent of COPD patients

- Concern about $O_2$-induced hypercapnia and acidemia is not warranted in most COPD patients.

- $O_2$ should NEVER be withheld in hypoxemic COPD patients as tissue oxygenation is an overriding priority.

- Be prepared to provide MV to the rare COPD patient who does have severe hypoventilation due to oxygen therapy.
Chemical Control of Breathing (cont.)

CCR response to acute CO\(_2\) increase in chronic hypercapnia

- Acute rises in PaCO\(_2\) continues to stimulate the CCRs.
- Resulting ventilatory response is depressed due to chemical and mechanical reasons.
  - Increased HCO\(_3^-\) prevents as large a fall in pH, as would be seen in a healthy patient.
  - Abnormal mechanics impair lung ability to increase \(V_E\).
Ventilatory Response to Exercise

- Strenuous exercise can increase CO$_2$ production and O$_2$ consumption 20-fold.
  - Ventilation normally keeps pace so all ABG values are held constant.
- Mechanism for increased $V_E$ poorly understood: may be
  - CNS sends concurrent signals to skeletal muscles and to medullary respiratory centers.
  - Joint movement stimulates proprioceptors, which send excitatory signals to medullary centers.
  - May also be due to repeated experience causing anticipatory changes in ventilation.
Abnormal Breathing Patterns

- Cheyne-Stokes respirations (CSR)
  - Characterized by cyclic waxing and waning ventilation with apnea gradually giving way to hyperpneic.
  - Seen with low cardiac output states (CHF)
    - Creates lag of CSF CO$_2$ behind arterial PaCO$_2$ and results in characteristic cycle

- Biot’s respiration
  - Similar to CSR but $V_T$ is constant except during apneic periods
  - Seen with patients with elevated ICP
Abnormal Breathing Patterns (cont.)

- Apneustic breathing (previously described)
  - Indicates damage to pons

- Central neurogenic hyperventilation
  - May be caused by head trauma, severe brain hypoxia, or lack of cerebral perfusion

- Central neurogenic hypoventilation
  - Medulla respiratory centers are not responding to appropriate stimuli.
  - Associated with head trauma, cerebral hypoxia, and narcotic suppression
CO₂ and Cerebral Blood Flow (CBF)

- CO₂ plays an important role in autoregulation of CBF mediated through its formation of H⁺.

- Increased CO₂ dilates cerebral vessels and vice versa.

- In traumatic brain injury (TBI), the brain swells acutely, raising ICPs > cerebral arterial pressure (perfusion stops).
  - Cerebral hypoxia/ischemia

- Mechanical hyperventilation lowers PaCO₂ and ICP.
  - Controversial as reduces O₂ and CBF to injured brain

- All agree must avoid hypoventilation in TBI patients