Respiratory Physiology: Control and Regulation of Breathing

Respiration is the process by which our body takes air into the lungs and exchanges oxygen with carbon dioxide in the alveoli. Breathing is the involuntary, rhythmic process of inhalation and exhalation. Respiration includes both breathing and ventilation (gas exchange in the alveoli). Lungs, along with the respiratory tract, are the major organs involved in respiration. The part of the respiratory tract where gas exchange occurs is the alveolar space. The part of the respiratory tract where no gas exchange occurs is called the dead space.

Introduction to Respiratory

A normal adult breathes with a respiratory rate of less than 25 breaths per minute. The rate of respiration varies with the state of the body. It changes with body activity, body temperature, heart status, and during various disease processes. The goal of the mechanism controlling respiration is to maintain arterial partial pressure of oxygen ($pO_2$) and partial pressure of carbon dioxide ($pCO_2$) in the normal range, even in a state of respiratory distress.
What Can Be Controlled?

1. Frequency of breathing
2. Depth of breathing maintaining the tidal volume

Neural Inputs or Sensors

1. **Chemoreceptors**
   a. Central chemoreceptors in the central nervous system (CNS), i.e. the brain and the spinal cord
   b. Peripheral chemoreceptors that are in the carotid artery and the aorta.

2. **Pulmonary receptors (mechanoreceptors) - receptors in the lungs**
   a. Stretch receptors which prevent over-inflation of the lungs.
   b. Juxta-capillary receptors and bronchial C fibers sense chemicals, stretch, and pulmonary edema and respond by producing shallow breathing and mucus secretion.
   c. Joint and muscle receptors responsible for chest wall position and muscle tension.

3. **Irritant receptors**: sense the presence of dust, chemicals, and cold air and respond by producing a cough reflex and/or bronchoconstriction.

Chemoreceptors in the CNS sense changes in H⁺ ion concentration, while the peripheral chemoreceptors sense changes in pO₂ and pCO₂ in the blood, as well as H⁺ ion concentration.

Pulmonary receptors are present in the visceral pleura surrounding the lungs and in the lung parenchyma. These receptors sense the stretch in the lungs when the lungs expand.

Feedback Mechanism

Feedback from the chemoreceptors, pulmonary receptors, and receptors in the joints and muscles around the chest stimulates the respiratory control center, which in return commands the effectors.
Effectors

Effectors are the muscles and related tissues controlled by the CNS to regulate respiratory effort. They maintain respiratory activity as ordered by the brain through the respiratory control center. Effectors include the diaphragm and respiratory muscles (external and internal intercostal muscles, accessory muscles, and abdominal muscles). Inspiration is controlled by the external intercostal muscles and the accessory muscles.Expiration is controlled by the internal intercostal and abdominal muscles.

Respiratory Control Center

The respiratory center in the CNS lies in the brainstem in the pons and medulla. Effectors are signaled by the neurons in the medulla. These centers control the automatic, unconscious breathing activity. Voluntary control is located in the motor cortex of the cerebrum.
The control centers in the brainstem include the following:

1. The apneustic center
2. The pneumotaxic center
3. Medullary respiratory centers (in the reticular formation of the brain)
   a. Ventral respiratory group of nuclei
   b. Dorsal respiratory group of nuclei

Originally, the apneustic center and pneumotaxic center were thought to be essential for normal breathing, but they are now known as accessory centers.

### Input to the Inspiratory Center

Sensory fibers from the peripheral chemoreceptors reach the respiratory control center through the **glossopharyngeal nerve** and the **vagus nerve** and from the mechanoreceptor in the lungs through the vagus nerve. **Stretch receptors** in the lungs send signals through the vagus nerve. pCO₂ receptors in the bone-dura arachnoid mater in the cerebrospinal fluid (CSF) space also send signals through IX and X cranial nerves.

### Output from the Inspiratory Center

Output or efferent fibers signal the diaphragm through the phrenic nerve and through the spinal cord synapse on the lower motor neuron in the cervical and thoracic region, and intercostal nerves signal the intercostal muscles. Contraction of these muscles produces inspiratory activity. Inspiration usually lasts for 2 seconds, followed by expiration, in which the inspiratory muscles relax and the expiratory muscles contract.

### Expiratory Center

The center for expiration lies in the ventral respiratory neurons in the medulla. These neurons are not fully active during quiet breathing. They are activated during exercise or other circumstances when more gas exchange is required.
Apneustic Center

**Location**: reticular formation in the lower pons

**Function**: This center is responsible for the coordination between inhalation and exhalation. It specifically facilitates the process of inspiration. This center sends signals to the dorsal respiratory group of neurons to prevent inspiratory ramp signals from switching off. The apneustic center is responsible for deeper and longer inspiration. When stimulated, the duration of inspiration is increased, resulting in deeper and prolonged inspiratory effort.

Pneumotaxic Center

The **pneumotaxic center** is located in the upper pons. When activated, it sends inhibitory impulses to the inspiratory area and turns off inspiration. It helps limit action in the phrenic nerve to control the function of the diaphragm. The pneumotaxic center therefore limits the size of tidal volume and regulates the respiratory rate. If strong signals are produced, the rate of breathing is increased to 30–40 breaths/min. Weak signals reduce the rate to a few breaths/min.

Chemical Regulation Respiration

The respiratory system functions to maintain proper levels of CO$_2$ and O$_2$ and is very responsive to changes in the levels of these gases in body fluids.

Chemoreceptor

Sensory neurons responsive to chemicals monitor levels of CO$_2$, H$^+$ and O$_2$ and provide input to the respiratory center, which adjusts pulmonary ventilation to keep these variables within the homeostatic limit.

Blood-brain barrier prevents H$^+$ and HCO$_3^-$ from affecting brain ECF or CSF

![Central chemoreceptor](image: Central chemoreceptor. Primary sensor in basal conditions, by Lecturio)
Stimuli for Central Chemoreceptors

H+ ions in CSF are the main stimuli for the central chemoreceptors. CO₂ in blood passes through the brain barrier and forms carbonic acid in CSF, which dissociates into H and HCO₃ ions. The H ion stimulates the respiratory center.

Function of Central Chemoreceptors

The main function is to maintain pCO₂ within limits in the brain and the CSF. The H⁺ generated maintains the pH of the CSF and stimulates the respiratory center, causing an increase in the breathing rate. This rise in the respiratory rate leads to washing out of more CO₂, and the pCO₂ falls to normal.

Peripheral Chemoreceptors

Peripheral chemoreceptors are located at the carotid bifurcation in the carotid body and in the arch of the aorta in the aortic bodies. They may also be present in the thoracic and abdominal regions along major arteries. These receptors detect changes in arterial O₂, along with changes in CO₂ and pH. Signals from these receptors are transmitted to respiratory centers to regulate respiratory activity. Each chemoreceptor receives a special blood supply.

Stimulus for Peripheral Chemoreceptors

1. **Decrease in arterial pO₂**: Any decrease in arterial pO₂ is detected by these receptors. They respond when pO₂ is decreased to less than 60 mm Hg. With a pO₂ of 60–100 mm Hg, the rate remains almost constant, but if arterial pO₂ falls below 60 mm Hg, respiratory rate increases slowly.
2. **Increase in arterial pCO₂**: These receptors also detect increases in pCO₂, but they have less of a response. Changes in pCO₂ are detected and responded to properly by the central chemoreceptors.
3. **Decrease in arterial pH**: A fall in the arterial pH leads to an increase in ventilation, mediated by the peripheral chemoreceptors after sensing an increase in the H⁺ ions in the arterial blood. Only chemoreceptors of the carotid bodies respond to this change, not the aortic bodies.
In conditions like metabolic acidosis, decreased arterial pH stimulates the peripheral chemoreceptors directly and increases the respiratory rate. This is called Kussmaul breathing.

References

Respiration Control via courses.lumenlearning.com

Regulation of Respiration via http://accessmedicine.mhmedical.com

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