Respiratory Rhythm: Control of Breathing
Linda Costanzo, Ph.D.

OBJECTIVES:

After studying this lecture, the student should understand:

1. The organization of medullary and pontine centers that control breathing.
2. Effects of lung stretch receptors and peripheral and central chemoreceptors on the dorsal respiratory group of neurons.
3. The function of the central chemoreceptors and their effect on ventilation.
4. The function of the peripheral chemoreceptors and their effect on ventilation.

To maintain constant arterial P$_{O_2}$ and P$_{CO_2}$, the frequency and depth (volume) of breathing is tightly controlled. Breathing is normally an involuntary process controlled by the brain stem (we don’t have to think about it.....how nice!) It can be overridden by intentional hyperventilation or hypoventilation (breath-holding).

1. BRAIN STEM CENTERS

Centers that control breathing are located in the medulla and pons of the brain stem. Information from chemoreceptors and lung receptors in the periphery feed afferent information to these brain stem centers. Efferent information from the brain stem controls the function of muscles for breathing (e.g., diaphragm).

Figure 1.
A. **Dorsal respiratory group (inspiratory center)–medulla**

The dorsal respiratory group of neurons, in the reticular formation of the medulla, is the inspiratory center. It controls the frequency of breaths and the **basic rhythm of breathing**. These dorsal neurons cause repetitive **bursts of action potentials** in the **phrenic nerve** that innervates the **diaphragm** (causing the diaphragm to contract). The breathing cycle begins with quiescence, followed by action potentials that ramp up in frequency, followed by quiescence. Contraction of the diaphragm (for inspiration) follows the same pattern: quiescence, contraction, quiescence.

The dorsal group is inhibited by the pontine pneumotaxic center and lung stretch (via the vagus). It is also regulated by peripheral chemoreceptors (via the vagus and glossopharyngeal nerves) and by central chemoreceptors.

B. **Pneumotaxic center–upper pons**

The pneumotaxic center is located in the upper pons. It inhibits the dorsal respiratory group and **turns off inspiration**. In effect, the pneumotaxic center **determines tidal volume** because it ends the period of inspiration. Loss of this center prolongs inspiration.

The **vagus**, like the pneumotaxic center, inhibits the dorsal respiratory group. Specifically, vagal afferents from **lung stretch receptors** are stimulated during inspiration. Firing of the vagus then inhibits, or limits, inspiration. (Information from **peripheral chemoreceptors** is also transmitted to the dorsal respiratory group, both via the vagus and glossopharyngeal nerves.)

C. **Apneustic center–lower pons**

The apneustic center in the lower pons activates the dorsal respiratory group and prolongs the ramped period of action potentials. When stimulated, there are **prolonged inspiratory gasps**, called **apneusis**.

D. **Ventral respiratory group (expiratory center)–medulla**

The ventral respiratory group is the expiratory center of the medulla. In normal quiet breathing, expiration is passive (due to the elastic recoil of the lung) and no ‘center’ is involved. During exercise, the ventral group is activated and drives activity in the abdominal and internal intercostal muscles.
II. RECEPTORS THAT REGULATE BREATHING

A. **Lung stretch receptors** are located in the smooth muscle of the airways and are activated in response to distension (inspiration). The information is carried via the vagus to the dorsal respiratory group, where it inhibits activity and ends inspiration (in collaboration with the pontine pneumotaxic center).

B. **Central chemoreceptors** are located on the ventral surface of the medulla, near the dorsal respiratory group (inspiratory center). They are sensitive to changes in arterial $P_{CO_2}$ and are the most important factor in the minute-to-minute control of breathing.
The central chemoreceptors detect changes in arterial $P_{CO_2}$ and alter the breathing rate as follows. Increases in $P_{CO_2}$ are detected by the central chemoreceptors, which direct an increase in breathing rate; excess CO$_2$ is expired and $P_{CO_2}$ is restored to normal. Decreases in $P_{CO_2}$ direct a decrease in breathing rate; CO$_2$ is retained and $P_{CO_2}$ is restored to normal. The steps in detecting an increase in $P_{CO_2}$ are as follows. Note that the sensor on the central chemoreceptors is for H$^+$, not for CO$_2$.

1. CO$_2$ in blood crosses the blood-brain barrier and enters the CSF, where it combines with H$_2$O to form H$_2$CO$_3$, which dissociates into H$^+$ and HCO$_3^-$.

2. There is an increase in H$^+$ concentration and decrease in pH of CSF.

3. The central chemoreceptors, located in the ventral medulla, detect increased H$^+$ in the CSF and direct the dorsal respiratory group to increase the breathing rate (hyperventilation) to expire extra CO$_2$.

C. Peripheral chemoreceptors for O$_2$, CO$_2$, and H$^+$ are located in the carotid bodies near the bifurcation of the common carotid arteries and in the aortic arch. Information from the peripheral chemoreceptors is carried via the vagus and glossopharyngeal nerves to the dorsal respiratory group (inspiratory center), which directs the appropriate change in breathing rate.

1. The most important role of the peripheral chemoreceptors is to detect decreases in arterial $P_{O_2}$. However, peripheral chemoreceptors are relatively insensitive to $P_{O_2}$ and are activated when $P_{O_2}$ is less than 60 mm Hg. When activated, they increase the breathing rate and attempt to restore $P_{O_2}$ to normal.
2. Peripheral chemoreceptors also detect increases in arterial $P_{CO2}$ and direct an increase in breathing rate. This response is less important than their response to a decrease in $P_{O2}$ and less important than the response of central chemoreceptors to changes in $P_{CO2}$. The effects of increased $P_{CO2}$ and decreased $P_{O2}$ are additive in peripheral chemoreceptors.

3. Peripheral chemoreceptors also detect decreases in arterial $pH$, independent of changes in $P_{CO2}$, and direct an increase in breathing rate. The effect of decreased pH is additive with the effect of decreased $P_{O2}$.

D. Other receptors

1. **Mechanoreceptors** are located in the muscles and joints that detect movement of the limbs. For example, there is an anticipatory response to exercise that involves an early increase in breathing rate.

2. **Irritant receptors** to noxious chemicals and particles, located in the linings of airways, cause constriction of bronchial smooth muscle and an increase in breathing rate.

3. **J receptors**, or juxtacapillary receptors, are located in alveolar walls. Engorgement of pulmonary capillaries with blood, such as in left heart failure (blood backs up into pulmonary circulation) causes rapid shallow breathing.