Respiratory System and Disorders

Lesson 3

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Control of Respiration

- In spite of widely differing demands for O_2 uptake and CO_2 output made by the body, the arterial Po_2 and Pco_2 are normally kept within close limits.

- This remarkable regulation of gas exchange is made possible because the level of ventilation is so carefully controlled.

The three basic elements of the respiratory control system are:

1. ***Sensors*** that gather information and feed it to the
2. ***Central controller*** in the brain, which coordinates the information and, in turn, sends impulses to the
3. ***Effectors*** (respiratory muscles), which cause ventilation.

Central Controller

- There are two main anatomical components of the **medullary respiratory center:**
  - The **dorsal respiratory group** (**DRG**)
  - The **ventral respiratory group** (**VRG**)
- The neurons of the **DRG** primarily fire during inspiration.
- The **VRG** contains expiratory neurons. They are quiet during normal breathing, but they become important when large increases in ventilation are required (for example, during strenuous physical activity).

Respiratory Rhythm Generator

- The **respiratory rhythm generator** is located in the **pre-Bötzinger complex** of neurons in the upper part of the VRG.
- During quiet breathing, the respiratory rhythm generator activates inspiratory neurons **(in a ramp-type pattern)** in the DRG that depolarize the inspiratory spinal motor neurons, causing the inspiratory muscles to contract.
- When the inspiratory motor neurons stop firing, the inspiratory muscles relax, allowing passive expiration.

Central Controller

- **Apneustic center** is in the lower pons.
  - The impulses from this center have an excitatory effect on the inspiratory area of the medulla, tending to prolong the ramp action potentials.
- **Pneumotaxic center** is in the upper pons. modulates the activity of the apneustic center.
  - It can turn off the inspiratory ramp. Inspiration is shortened and, as a consequence, the breathing rate increases.
- **Cortex**
  - Breathing is under voluntary control to a considerable extent, and the cortex can override the function of the brainstem within limits.

Effectors

- The muscles of respiration include:
  - The diaphragm
  - Intercostal muscles
    - Internal
    - External
  - Abdominal muscles
  - Accessory muscles *(sternomastoids, scalenes, pectoralis minor etc.)*

(a) normal inspiration **(b)** maximal inspiration

(a) normal expiration; **(b)** maximal expiration;

Sensors

1. **Peripheral Chemoreceptors**
   - Located at the bifurcation of the common carotid arteries and on the arch of the aorta are called the **carotid bodies** and **aortic bodies,** respectively.

2. **Central Chemoreceptors**
   - Located in the medulla and, provide excitatory synaptic input to the medullary inspiratory neurons

Control by Po_2

- Little increase in ventilation is observed until the oxygen concentration of the inspired air is reduced enough to lower arterial Po_2 to 60 mmHg.
- Beyond this point, any further decrease in arterial Po_2 causes a marked reflex increase in ventilation.

Control by Po_2

- This reflex is mediated by the <u>peripheral</u> chemoreceptors.
- Peripheral chemoreceptors are not sensitive to **«oxygen content»** of the blood they are sensitive to Po_2».
- They respond to decreases in arterial Po_2, as occurs in lung disease or exposure to high altitude.
- They don't respond to total oxygen content changes such as anemia or CO poisoning. Because they sense the «dissolved O_2 in plasma not the O_2 binds to Hb»

Control by Po_2

- Remember the oxygen–hemoglobin dissociation curve
- Small reductions in arterial Po_2 is not important for body.
  - Total oxygen transport by the blood is not really decreased very much until the arterial Po_2 decreases below about 60 mmHg.
- Therefore, increased ventilation would not result in much more oxygen being added to the blood until that point is reached.

Control by Pco_2

- Even a very small increase in arterial Pco_2 causes a marked reflex increase in ventilation.
- The arterial Pco_2 is stabilized tightly near the normal value of 40 mmHg.
- The ability of changes in arterial Pco_2 to reflexively control ventilation is largely due to associated changes in H^+ concentration.

Control by Pco_2

- The **peripheral** chemoreceptors are stimulated by the increased arterial H^+ concentration resulting fromthe increased Pco_2.
- At the same time, CO_2 diffuses rapidly across the blood-brain barrier (H^+ ions cannot pass). This increased Pco_2 increases brain extracellular fluid H^+ concentration, which stimulates the **central** chemoreceptors.
- The central chemoreceptors are the more important, accounting for about 70% of the increased ventilation.

Control by Pco_2

- It should also be noted that the effects of increased Pco_2 and decreased Po_2 not only exist as independent inputs to the medulla but potentiate each other's effects.

- The acute ventilatory response to combined low Po_2 and high Pco_2 is considerably greater than the sum of the individual responses.

1

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Arterial H^+ Concentration

- Retention or excessive elimination of carbon dioxide causes **respiratory acidosis** and **respiratory alkalosis**, respectively.
- Arterial H^+ concentration may change due to some cause other than a change in Pco_2.
- This is termed ***metabolic acidosis*** when H^+ concentration is increased and ***metabolic alkalosis*** when it is decreased.

Arterial H^+ Concentration

- In such cases, the **peripheral** chemoreceptors provide the major afferent inputs to the brain in altering ventilation.

- **Central** chemoreceptors are blind to metabolic acidosis/alkolosis because blood-brain barrier are impermeable to H^+ ions.

Arterial H^+ Concentration

- An example to metabolic acidosis is lactic acid accumulation after strenuous exercise.
- Lactic acid in the blood, causes hyperventilation almost entirely by stimulation of the peripheral chemoreceptors.

Arterial H^+ Concentration

- The converse of the previous situation is also true:
  - When arterial H^+ concentration is decreased by any means other than by a reduction in Pco_2 (for example, by the loss of H^+ from the stomach when vomiting), ventilation is reflexively depressed because of decreased peripheral chemoreceptor output.

Control of Respiration in Exercise

- During exercise, the alveolar ventilation may increase as much as 20-fold.
- On the basis of our three variables—Po_2, Pco_2, and H^+ concentration—it may seem easy to explain the mechanism that induces this increased ventilation.

Increased Pco_2 as the Stimulus

- Active muscles produce more CO_2, so the blood Pco_2 would increase in exercise.
- This is true, however, only for systemic venous blood but not for systemic arterial blood.
  - During moderate exercise, the alveolar ventilation increases in exact proportion to the increased carbon dioxide production, so alveolar and therefore arterial Pco_2 do not change.
- In fact, in very strenuous exercise, the alveolar ventilation increases relatively more than carbon dioxide production.

Decreased Po_2 as the Stimulus

- Although systemic *venous* Po_2 decreases during exercise, alveolar Po_2 and, therefore, *arterial* Po_2 usually remain unchanged.
- This is because cellular oxygen consumption and alveolar ventilation increase in exact proportion to each other, at least during moderate exercise.
- In healthy individuals, ventilation is not the limiting factor in strenuous exercise—cardiac output is.

Increased H^+ Concentration

- Because the arterial Pco_2 does not change during moderate exercise and decreases during strenuous exercise, there is no accumulation of excess H^+ resulting from carbon dioxide accumulation.

- However, during strenuous exercise, there *is* an increase in arterial H^+ concentration due to the generation and release of lactic acid into the blood.

Other Factors

- A variety of other factors are involved in stimulating ventilation during exercise. These include:
  1. Reflex input from mechanoreceptors in joints and muscles,
  2. An increase in body temperature,
  3. Inputs to the respiratory neurons via branches from axons descending from the brain to motor neurons supplying the exercising muscles (central command),
  4. An increase in the plasma epinephrine concentration,
  5. An increase in the plasma K^+ concentration due to movement of K^+ out of the exercising muscles
  6. A conditioned (learned) response mediated by neural input to the respiratory centers.

Other Ventilatory Responses

Protective Reflexes

- A group of responses protect the respiratory system from irritant materials
  - Cough reflex
    - Receptors are in the larynx, trachea, and bronchi
    - When the receptors are stimulated, the medullary respiratory neurons reflexively cause a deep inspiration and a violent expiration.
  - Sneeze reflex
    - Receptors are in the nose or pharynx

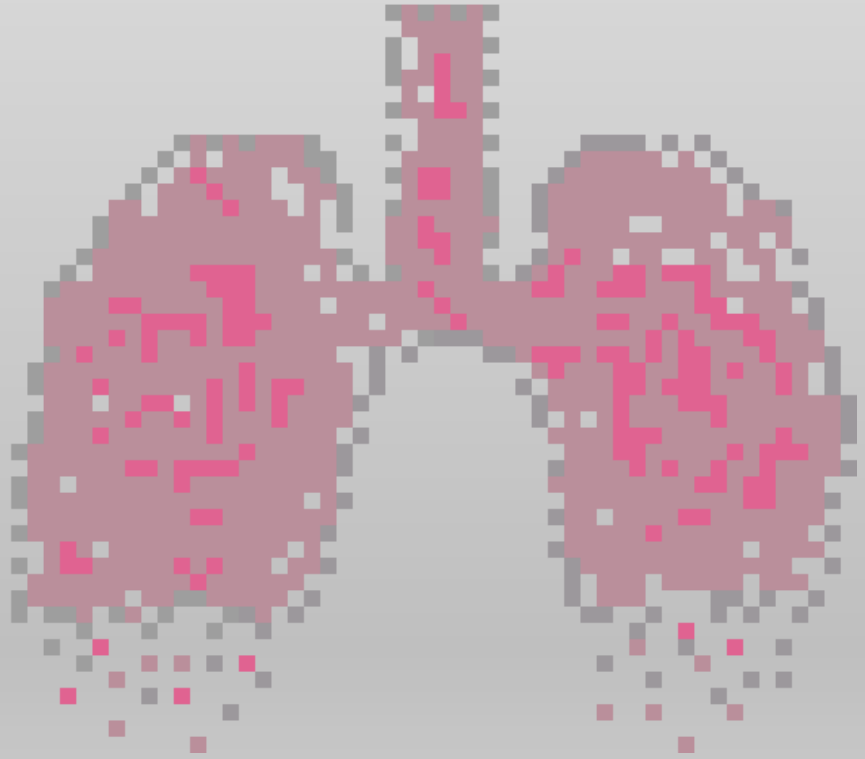
Other Ventilatory Responses

Reflexes from J Receptors

- In the lungs, either in the capillary walls or the interstitium, are a group of sensory receptors called **J receptors.**

- They are normally dormant but are stimulated by an increase in lung interstitial pressure caused by the collection of fluid in the interstitium.

- The main reflex effects are rapid breathing (tachypnea) and a dry cough. In addition, neural input from J receptors gives rise to sensations of pressure in the chest and ***dyspnea***—the feeling that breathing is labored or difficult.



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Thank you for your patience!