An Approach to Dyspnea: from atmosphere to hemoglobin

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Definition: a subjective sensation of abnormal or uncomfortable breathing

Pathophysiologic Mechanisms of Dyspnea:

- Decreased arterial O₂ levels
- Increased CO₂ levels
- Low blood pH
- Neuromechanical dissociation
  - a mismatch between respiratory effort and ventilation
    - elicits dyspnea in cases of abnormal chest wall compliance or airway resistance

Etiologies: follow O₂ as we breathe

1) Drive to breathe
- The impulse to breathe is generated in the brainstem (medulla and pons) via mechanical and chemical stimuli
- Together with pulmonary and skeletal muscle stretch receptors, O₂ and CO₂ are the major contributors to the complex feedback control system of basic breathing
  - O₂ is sensed by peripheral chemoreceptors in the carotid and aortic bodies
  - CO₂ and pH are sensed primarily in the brain by medullary chemoreceptors
- Muted or absent responses can lead to a decreased “drive” to breathe, as in obesity hypoventilation

2) Generating negative pressure
- We generate negative pressure to move oxygen from the atmosphere into the lungs
- Abnormal neuromuscular function and/or poor respiratory system compliance can lead to neuromechanical dissociation and cause CO₂ retention
- Abnormal neuromuscular function:
  - Diaphragmatic paralysis
  - Myasthenia gravis
  - Guillain-Barré
- Poor respiratory system compliance
  - Pulmonary fibrosis
  - Pleural effusions
  - Obesity
  - Ascites
  - Pregnancy

3) Airways
- Large airway disorders:
  - COPD
  - Asthma
  - Bronchospasm
  - Obstructing tumor
  - Foreign body
- Small airway diseases (i.e. bronchiolitis, appearing as “tree-in-bud” opacities on CT imaging):
  - Infectious: viral, bacterial, mycobacterial
- Inflammatory: RA, SLE, vasculitis
- Fibro-proliferative: post lung transplantation
- Inhalational: exposure to tobacco, toxic fumes, mineral dusts

4) Alveolar filling processes
   - Cause dyspnea by impairing gas exchange due to shunt
   - Common etiologies:
     - Blood (alveolar hemorrhage)
     - Pus (pneumonia)
     - Water (pulmonary edema)
     - Atelectasis can cause shunt due to complete collapse of alveoli

5) Alveolar-capillary membrane
   - Gas exchange depends on a thin alveolar-capillary membrane and a large surface area
   - Diseases that destroy (emphysema) or thicken (pulmonary fibrosis) the alveolar-capillary membrane decrease the total membrane surface area and slow the rate of diffusion
   - Membrane abnormalities are rarely a cause of dyspnea. Rather, these disorders have other features as a source of dyspnea, as in COPD (hyperinflation, air trapping) or fibrosis (decreased compliance, increased work of breathing)
   - One exception: alveolar-capillary membrane diseases can result in dyspnea during exercise due to shortened capillary transit time

6) O₂ transport in the blood
   - The majority of O₂ is bound to hemoglobin, with some dissolved in blood as well
   - Low O₂ content can result from decreased total hemoglobin or functional alterations of hemoglobin leading to impaired O₂ binding
   - Two main etiologies:
     - Anemia
     - Dyshemoglobinemias (CO poisoning or methemoglobinemia)

7) Inefficient blood flow
   - Cardiac disorders: systolic or diastolic heart failure, MI, arrhythmia, tamponade
   - Pulmonary vascular diseases: pulmonary hypertension, PE

Pearls:
1. Dyspnea is not always from a pulmonary disorder
2. An easy way to build a differential diagnosis is to follow the oxygen molecule from atmosphere to hemoglobin
3. Blood, pus, or water are the main causes of alveolar shunt

References: