An Approach to Dyspnea: from atmosphere to hemoglobin

Authors:
Jeff Redinger
Tyler Albert

Definition: a subjective sensation of abnormal or uncomfortable breathing

Pathophysiologic Mechanisms of Dyspnea:
- Decreased arterial O_2 levels
- Increased CO_2 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 O_2 as we breathe

1) <u>Drive to breathe</u>
- 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, O_2 and CO_2 are the major contributors to the complex feedback control system of basic breathing
    - O_2 is sensed by peripheral chemoreceptors in the carotid and aortic bodies
    - CO_2 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) <u>Generating negative pressure</u>
- 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 CO_2 retention
- Abnormal neuromuscular function:
    - Diaphragmatic paralysis
    - Myasthenia gravis
    - Guillain-Barré
- Poor respiratory system compliance
    - Pulmonary fibrosis
    - Pleural effusions
    - Obesity
    - Ascites
    - Pregnancy

3) <u>Airways</u>
- 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) O_2 transport in the blood
- The majority of O_2 is bound to hemoglobin, with some dissolved in blood as well
- Low O_2 content can result from decreased total hemoglobin or functional alterations of hemoglobin leading to impaired O_2 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:

- Banzett RB, Schwartzstein RM. Dyspnea: Don't Just Look, Ask! Am J Respir Crit Care Med 2015; 192:1404.

- Manning HL, Schwartzstein RM. Pathophysiology of dyspnea. N Engl J Med 1995; 333:1547.
- Parshall MB, et al. An Official American Thoracic Society Statement: Update on the Mechanisms, Assessment, and Management of Dyspnea. *Am J Respir Crit Care Med.* Vol 185, 4, 435-452. Feb 2012.
- Schwartzstein RM and Adams L. Dyspnea. In Broaddus VC, Murray JF, Nadel JA, eds. Murray and Nadel's Textbook of Respiratory Medicine. Philadelphia, Elsevier Saunders, 6th edition, 2016: 485-496.
- Mookherjee S, Beste L, Klein J, Wright J, eds. Teaching Scripts in Internal Medicine. New York, Springer, 1st edition, *in press*