CAPS 422 **Mammalian Respiratory Physiology**

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Textbook: Pulmonary Physiology by Michael G. Levitzky. Multiple copies are placed on the course reserve list at Woodward Library and e-book version is accessible using UBC library online—sign in with your CWL.

COURSE OBJECTIVES

1. Mechanics of Breathing (Statics) [Levitzky, Ch. 1 & 2]

1.1 Define and be able to identify the following lung volumes and capacities on a spirogram: tidal volume (V_T), residual volume (RV), inspiratory reserve volume (IRV), expiratory reserve volume (ERV), vital capacity (VC), total lung capacity (TLC) and functional residual capacity (FRC).

1.2 Describe the two-compartment model of the lungs and define FRC in relation to the elastic recoil of the lungs and the chest wall and in relation to the transmural pressure across these two compartments. Specify the alveolar, intrapleural and atmospheric pressures at FRC under static conditions when there is no airflow in or out of the lungs.

1.3 Describe the changes in alveolar pressure (P_A), intrapleural pressure (P_{pl}), atmospheric pressure (P_{atm}) and transpulmonary pressure (P_L) during a single respiratory cycle during normal quiet breathing (eupnea) and relate swings in intrapleural pressure to the two forces that the inspiratory muscles must overcome to inflate the lungs.

1.4 Describe the generation of a pressure gradient between the atmosphere and alveoli. In your description state the relevance of Boyle's Law and include the function of the main respiratory muscles involved both during a normal quiet tidal breath and during forced expiration.

1.5 Describe how static lung compliance is measured with reference to the pressure-volume curve of the lung obtained during deflation of the lungs from TLC to FRC. Contrast this relationship to the pressure-volume curve of a stiff lung (low compliance) and the pressure-volume curve of a highly distensible lung (high compliance) encountered in disease states. Describe the effect of changes in lung compliance in disease states on FRC.

1.6 Discuss the factors that influence the static compliance of the lungs.

1.7 Distinguish between static and specific compliance and describe what information can be derived knowing both values in an individual.

1.8 Discuss the key findings that have led to our understanding of the role of surface tension and pulmonary surfactant in the mechanics of breathing.

1.9 Specify the components of pulmonary surfactant and our understanding of their function.

1.10 Identify conditions where chest wall compliance is altered.

1.11 Draw the static PV curves of the lungs, chest wall and respiratory system from RV to TLC and how interactions between the chest wall and the lungs determine lung volume.

1.12 Explain why FRC is reduced when moving from the sitting to supine position; in pregnancy; in obesity and in bilateral paralysis of the diaphragm.

2. Mechanics of Breathing (Dynamics) [Levitzky, Ch. 2]

2.1 Identify the key resistive force opposing movement of air in and out of the lungs and describe its overall value as well the contribution of airway generations to total resistance in healthy individuals.

2.2 Describe the three patterns of airflow typically found in the airways and their characteristics.

2.3 Compare the relationship between driving pressure, flow and airway resistance in laminar and turbulent flow conditions and specify the physiologic significance of the different relationships.

2.4 Define the Reynolds number and specify its significance to pattern of airflow.

2.5 Describe both active and passive control of the airway caliber. In your description, include the key neural pathways controlling airway function.

2.6 Describe how resistance to airflow is indexed clinically by measuring maximal airflow during a forced vital capacity.

2.7 Define the variables obtained from the expiratory flow volume curve and their significance in determining airway function.

2.8 Using the equal pressure point hypothesis, apply the concept of dynamic compression of airways during forced expiration to explain the concept of “flow limitation” and “effort independence” of expiratory flow.

2.9 Specify the determinants of maximal expiratory flow and describe how each of these factors can be affected by a disease state.

2.10 Describe the “normal” flow volume loop profile and the profiles found in fixed and variable intra and extra-thoracic airway obstructions. Provide the physiologic basis for the abnormal profiles.

3. Distribution of Alveolar Ventilation [Levitzky, Ch. 3]

3.1 Describe the relationship between minute ventilation, alveolar ventilation, anatomic dead space and physiologic dead space.

3.2 Describe two methods used to measure dead space and explain why a discrepancy in the value of dead space obtained between the two methods is significant.

3.3 Distinguish between physiologic and alveolar dead space.

3.4 Define the respiratory quotient [RQ] and the respiratory exchange ratio [RER] . Describe the basis for difference found in R in healthy subjects at rest, during exercise and in patients on intravenous glucose.

3.5 List the partial pressure of oxygen and carbon dioxide in the alveoli and specify their significance in gas exchange. Predict the change in these partial pressures under the following conditions 1) no perfusion to the alveolar unit. 2) no ventilation to the alveolar unit.

3.6 Derive the alveolar ventilation equation and discuss the factors determining alveolar PCO_2.

3.7 Distinguish between hypoventilation, hyperventilation, hypopnea and hyperpnea.

3.8 Use correct terminology in reference to terms used to describe ventilation and breathing patterns.

3.9 State the alveolar-air equation and discuss the factors determining alveolar PO_2.

3.10 Use the alveolar- air equation to predict the alveolar partial pressure of oxygen at about 8,000 feet.

3.11 Describe the regional distribution of ventilation and provide a brief explanation of how it is measured.

3.12 Relate the intrapleural pressure gradient in the upright lung to the static pressure volume curve of the lungs to describe regional alveolar size and alveolar compliance at FRC and explain the greater alveolar ventilation to the base of the upright lungs. How would your description differ if the lungs are inflated from RV? How would your description differ if a person breathes from FRC lying on their side.

4. Distribution of Pulmonary Blood Flow- Ventilation Perfusion Mismatch [Levitzky, Ch. 4 & 5]

4.1 Specify the two sources of blood flow to the lungs.

4.2 Compare and contrast the vascular pressures in the pulmonary and systemic circulations. Provide an anatomic explanation for the lower pressures found in the pulmonary circulation.

4.3 Explain how pulmonary vascular resistance (PVR) is measured and calculated.

4.4 Describe the effect of increasing lung volume on the alveolar and extra alveolar vessel contribution to PVR.

4.5 Describe the role of distention and recruitment in determining PVR.

4.6 Summarize the role of passive factors (lung inflation, pulmonary vessel distention and recruitment) in determining PVR.

4.7 Compare the effect of low alveolar oxygen on pulmonary vessels versus low blood oxygen on systemic vessels and the physiologic significance of this difference.

4.8 Define hydrostatic pressure and the relative arterial, alveolar and venous pressures in the three zones of the upright lung.

4.9 Specify the driving pressure for blood flow in each of the three zones of the lungs and describe the regional distribution of this blood flow at rest, during exercise and in conditions where mean arterial pressure is low [acute hemorrhage or during PEEP].

4.10 Describe graphically the relationship between lung height and 1) ventilation 2) perfusion and 3) the V/Q ratio in the up right lungs.

4.11 Compare the partial pressure of respiratory gases in an "ideal alveolar unit" to 1) a shunt unit (V/Q=0) and 2) dead space unit (V/Q= ∞) and predict the consequences of the regional differences in the ventilation and perfusion ratio on PA_{CO2} and PA_{O2} in the normal upright lung.

4.12 Distinguish between regional variations in partial pressure of respiratory gases in the alveoli in the upright lung and regional variations in the quantity of blood and air flow.

5. GAS EXCHANGE, DIFFUSING CAPACITY & CAUSES OF HYPOXEMIA [Levitzky, Ch.6, Ch. 8]

5.1 Using Fick's law of diffusion, describe the factors influencing the diffusion of gases in the lung. Provide an example for each factor.

5.2 Define solubility and explain the key difference in solubility of physiologically inert gases and gases that do combine chemically with blood and the functional significance of this difference.

5.3 Explain why the respiratory gases, oxygen and carbon dioxide are normally perfusion limited at rest and during exercise in average healthy individuals. Why does oxygen become "diffusion limited" in some elite athletes?

5.4 Using Fick's Law of diffusion, derive the diffusing capacity of the lungs for carbon monoxide.

5.5 Discuss the significance of a reduction in DLCO and the factors that can affect this measure.

5.6 Distinguish between hypoxia, hypoxemia, anoxia and asphyxia.

5.7 Specify the normal range for $P(A\text{-}a)O_2$ [a.k.a. alveolar-arterial oxygen difference, $A\text{-}aDO_2$, and the alveolar-arterial oxygen gradient], determine how it is calculated and what it quantifies.

5.8 Discuss the five major causes of hypoxemia: hypoventilation, low inspired PO_2, right to left shunt, diffusion impairment and ventilation-perfusion mismatch and explain how they may be distinguished from one another.

6. CONTROL OF BREATHING [Ch.9]

6.1 Describe the chemoreceptors involved in the control of breathing, including the site of the receptors, their adequate stimulus and the effect of their stimulation.

6.2 Describe how the cerebrospinal fluid (CSF) is formed and secreted, its buffering properties, and its role in control of ventilation.

6.3 Describe and illustrate graphically the effects of hypercapnia and hypoxia on minute ventilation and discuss the factors that modify these relationships.

6.4 In historic context, discuss the development of hypotheses regarding signal transmission by the glomus cell.

6.5 List the major mechanoreceptors in the lungs; identify their location, major properties and reflex effects.

6.6 List the major sensory receptors in the upper airways; identify their location, afferent pathway, and reflex effects.

6.7 Identify the muscles of respiration, their innervation, and when these muscles are typically activated.

6.8 Describe the central organization of the respiratory control system referring to the locations of the respiratory-related (RRN) neurons and their potential axonal projections.

6.9 A dual control system one voluntary and the other automatic regulates breathing. Provide three examples that reveal the role of a voluntary system.

7. BREATHING DURING SLEEP

7.1 Describe the pattern of breathing during NREM and REM sleep in healthy adults.

7.2 Describe the change in the ventilatory response to CO_2 and in the reflex response to airway irritants that takes place during sleep.

7.3 Identify the arousal mechanisms that protect the sleeper.

7.4 Explain why the upper airway patency may become compromised during sleep.

7.5 Define sleep apnea and describe the three types of sleep apnea characterized in clinical settings.

7.6 Explain how in a laboratory setting the difference between central, obstructive and mixed sleep apneas is distinguished.

8. BREATHING DURING ASCENT TO HIGH ALTITUDE [Ch.11]

8.1 Explain why inspired levels of oxygen decrease with increased elevation.

8.1 Describe the effects of decreased inspired levels of oxygen on the sensory and mental function of individuals with gradual ascent.

8.2 Describe the symptoms of Acute Mountain Sickness (AMS), Chronic Mountain Sickness and High Altitude Pulmonary Edema (HAPE).

8.3 Describe the physiologic changes that take place during acclimatization to high altitude.

9. DIVING AND THE RESPIRATORY SYSTEM [Ch.11] Not examinable (see student presentations)

9.1 Describe the major physiological stresses associated with diving.

9.2 State the key physical principle affecting gas pressures during diving.

9.3 Describe the cause and provide examples of baro-trauma during diving.

9.4 Explain why divers can suffer decompression sickness and discuss its prevention and treatment.

9.5 Describe the symptoms of nitrogen narcosis.

Common symbols used in respiratory physiology

Primary Symbols denoting physical quantities

- P pressure, tension or partial pressure of a gas
- V volume of a gas
- F fractional concentration of a gas
- Q volume of blood
- C content

Secondary Symbols denoting the location of the gas

I inspired gas	a arterial blood
E expired gas	v venous blood
A alveolar gas	c capillary blood

Tertiary Symbols indicating particular gases

O_2=oxygen
CO_2 =carbon dioxide
N_2=nitrogen

In addition

. denotes time derivative of a physical quantity (the given quantity per unit time)

‾ denotes average (mean)

′ denotes end capillary

Examples of Respiratory Symbols

$\dot{V}_E$ minute ventilation

$\dot{V}_{O2}$ oxygen consumption

$\dot{V}_{CO2}$ carbon dioxide production

FE_{N2} fraction of expired nitrogen

$\bar{v}$ mixed venous

B_f breathing frequency

V_T tidal volume

V_D volume of dead space

PA_{O2} partial pressure of oxygen in the alveoli

Pa_{CO2} partial pressure of carbon dioxide in arterial blood

CvO_2 Oxygen content of venous blood

The Laws Governing Behaviour of Gases

Avogadro's Hypothesis Equal volume of different gases at equal temperature contain the same number of molecules. Similarly, equal numbers of molecules in identical volumes and at the same temperature will exert the same pressure. One mole of any gas will contain $6.02X\ 10^{23}$ molecules and will occupy a volume of 22.4 liters at a temperature of O °C and a pressure of 760 mmHg.

Ideal Gas Law **PV =n*R*T** where
R = universal gas constant =62.3656 L.mmHg/mole degree
n= number of moles of gas present
T is temperature in degrees Kelvin
The ideal gas law is the based on the following other laws that specify the relationship between the 3 factors affect the volume of a gas: pressure, temperature and amount.

- At a constant temperature the same amount of gas will decrease in volume with an increase in pressure **(Boyle's Law)**
- At constant pressure, the same amount of gas will increase in volume with an increase in temperature **(Charles' Law** or Gay Lussac's Law). Hence at a constant temperature and pressure, the same amount of gas will remain at constant volume; the only factor that would change the volume would be an increase in the number of moles of gas present.

Dalton's Law of Partial Pressures In a gas mixture the pressure exerted by each individual gas in a space is independent of the pressure of other gases in the same mixture.
e.g. Total pressure of dry air = $P_{O2} + P_{CO2} + P_{N2}$
e.g. Alveolar gas mixture): $P_A = PA_{H2O} + PA_{O2} + PA_{CO2} + PA_{N2}$

Partial Pressure of a Gas in a Liquid Gases such as CO_2, O_2 and N_2 that are in physical solution in a liquid such as plasma, continually escape from the liquid into the gas phase and may also return to the liquid. When the rate of a gas coming out of solution is equal to the rate at which it enters the solution, the system is in equilibrium for that gas and liquid. At equilibrium, the partial pressure of a gas in gas phase is equal to the partial pressure (or tension) of the gas in liquid.

Water Vapor When a gas is in contact with a liquid, and is in equilibrium (saturated) with the liquid, the partial pressure of the gas is a function of temperature. The one gas to which this applies in a normal respiration is water. The lungs and airways are always moist, and inspired gas is rapidly saturated with water vapor in the upper segments of the respiratory system. The temperature in the airways and lungs is almost identical with deep body temperature (approximately 37°C); at this temperature water vapor has a partial pressure of 47 mmHg. We can calculate partial pressure of oxygen and nitrogen in inspired air, after the gas mixture becomes saturated with water vapor in the upper airway (so-called tracheal air): P_{total} = 760 mmHg- P_{H20} = 47 mmHg=713 mmHg for remaining inspired gases (21% O_2 and 79% N_2)
$P_{O2} = 0.21 \cdot 713 = 150$ mmHg
$P_{N2} = 0.79 \cdot 713 = 563$ mmHg

That is, since water vapor partial pressure must be 47 mmHg in a saturated gas mixture at 37°C, the total pressure remaining for the inspired gases is only 760-47 or 713 mmHg. The composition of this remaining gas is 21% O_2 and 79% N_2, giving the partial pressures indicated above.

Henry's Law: The amount of a gas that dissolves in a specific volume of liquid with which it does not combine chemically is almost directly proportional to the partial pressure of that gas in gas phase and its solubility (Bunsen) coefficient. Note that solubility coefficients differ for different gases and are temperature dependant.