Lecture Outline for Integrated Basic Health Sciences for Pharmacy

Physiology Component of Module : Respiratory

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Respiration

- *Involves both the respiratory and the circulatory systems*
- *Four processes that supply the body with O_2 and dispose of CO_2*
- *Pulmonary ventilation (breathing):movement of air into and out of the lungs*
- *External respiration: O_2 and CO_2exchange between the lungs and the blood*
- *Transport: O_2 and CO_2in the blood*
- *Internal respiration: O_2 and CO_2exchange between systemic blood vessels and tissues*

Respiratory System: Functional Anatomy

- *Major organs*
  - Nose, nasal cavity, and paranasal sinuses
  - Pharynx
  - Larynx
  - Trachea
  - Bronchi and their branches
  - Lungs and alveoli

Functional Anatomy

- *Respiratory zone: site of gas exchange*
  - Microscopic structures: respiratory bronchioles, alveolar ducts, and alveoli
- *Conducting zone: conduits to gas exchange sites*
  - Includes all other respiratory structures
- *Respiratory muscles: diaphragm and other muscles that promote ventilation*

The Nose

- *Functions*
  - Provides an airway for respiration
  - Moistens and warms the entering air
  - Filters and cleans inspired air
  - Serves as a resonating chamber for speech
  - Houses olfactory receptors

Nasal Cavity and Respiratory Defences

- *Respiratory mucosa*
  - Pseudostratified ciliated columnar epithelium

- Mucous and serous secretions contain lysozyme and defensins
- Cilia move contaminated mucus posteriorly to throat
- Inspired air is warmed by plexuses of capillaries and veins
- Sensory nerve endings triggers sneezing

Nasal Cavity

- *Superior, middle, and inferior nasal conchae*
  - Protrude from the lateral walls
  - Increase mucosal area
  - Enhance air turbulence

Functions of the Nasal Mucosa and Conchae

- *During inhalation, the conchae and nasal mucosa*
  - Filter, heat, and moisten air
- *During exhalation these structures*
  - Reclaim heat and moisture

Paranasal Sinuses

- *In frontal, sphenoid, ethmoid, and maxillary bones*
- *Lighten the skull and help to warm and moisten the air*

Respiratory Zone

- *Respiratory bronchioles, alveolar ducts, alveolar sacs (clusters of alveoli)*
- *~300 million alveoli account for most of the lungs' volume and are the main site for gas exchange*

Respiratory Membrane

- *~0.5-μm-thick air-blood barrier*
- *Alveolar and capillary walls and their fused basement membranes*
- *Alveolar walls*
  - Single layer of squamous epithelium (type I cells)
- *Scattered type II cuboidal cells secrete surfactant and antimicrobial proteins*

Alveoli

- *Surrounded by fine elastic fibers*
- *Contain open pores that*
  - Connect adjacent alveoli
  - Allow air pressure throughout the lung to be equalized
- *House alveolar macrophages that keep alveolar surfaces sterile*

Mechanics of Breathing

- *Pulmonary ventilation consists of two phases*
  1. Inspiration: gases flow into the lungs
  2. Expiration: gases exit the lungs

Pressure Relationships in the Thoracic Cavity

- *Atmospheric pressure (P_{atm})*
  - Pressure exerted by the air surrounding the body

- 760 mm Hg at sea level
- *Respiratory pressures are described relative to P_{atm}*
  - Negative respiratory pressure is less than P_{atm}
  - Positive respiratory pressure is greater than P_{atm}
  - Zero respiratory pressure = P_{atm}

Intrapulmonary Pressure

- *Intrapulmonary (intra-alveolar) pressure (P_{pul})*
  - Pressure in the alveoli
  - Fluctuates with breathing
  - Always eventually equalizes with P_{atm}

Intrapleural Pressure

- *Intrapleural pressure (P_{ip}):*
  - Pressure in the pleural cavity
  - Fluctuates with breathing
  - Always a negative pressure ($<P_{atm}$ and $<P_{pul}$)

Intrapleural Pressure

- *Negative P_{ip} is caused by opposing forces*
  - Two inward forces promote lung collapse
    - Elastic recoil of lungs decreases lung size
    - Surface tension of alveolar fluid reduces alveolar size
  - One outward force tends to enlarge the lungs
    - Elasticity of the chest wall pulls the thorax outward

Pressure Relationships

- *If $P_{ip} = P_{pul}$ the lungs collapse*
- *($P_{pul} – P_{ip}$) = transpulmonary pressure*
  - Keeps the airways open
  - The greater the transpulmonary pressure, the larger the lungs

Homeostatic Imbalance

- *Atelectasis (lung collapse) is due to*
  - Plugged bronchioles → collapse of alveoli
  - Wound that admits air into pleural cavity (pneumothorax)

Pulmonary Ventilation

- *Inspiration and expiration*
- *Mechanical processes that depend on volume changes in the thoracic cavity*
  - Volume changes → pressure changes
  - Pressure changes → gases flow to equalize pressure

Boyle’s Law

- *The relationship between the pressure and volume of a gas*
- *Pressure (P) varies inversely with volume (V): $P_1V_1 = P_2V_2$*

Inspiration

- *An active process*

- Inspiratory muscles contract
- Thoracic volume increases
- Lungs are stretched and intrapulmonary volume increases
- Intrapulmonary pressure drops (to –1 mm Hg)
- Air flows into the lungs, down its pressure gradient, until $P_{pul} = P_{atm}$

Expiration

- *Quiet expiration is normally a passive process*
  - Inspiratory muscles relax
  - Thoracic cavity volume decreases
  - Elastic lungs recoil and intrapulmonary volume decreases
  - P_{pul} rises (to +1 mm Hg)
  - Air flows out of the lungs down its pressure gradient until Ppul = 0
- *Note: forced expiration is an active process: it uses abdominal and internal intercostal muscles*

Physical Factors Influencing Pulmonary Ventilation

- *Inspiratory muscles consume energy to overcome three factors that hinder air passage and pulmonary ventilation*
  1. Airway resistance
  2. Alveolar surface tension
  3. Lung compliance

Airway Resistance

- *Friction is the major nonelastic source of resistance to gas flow*
- *The relationship between flow (F), pressure (P), and resistance (R) is:*

$$F = \Delta P/R$$

  - ΔP is the pressure gradient between the atmosphere and the alveoli (2 mm Hg or less during normal quiet breathing)
  - Gas flow changes inversely with resistance

Airway Resistance

- *Resistance is usually insignificant because of*
  - Large airway diameters in the first part of the conducting zone
  - Progressive branching of airways as they get smaller, increasing the total cross-sectional area
- *Resistance disappears at the terminal bronchioles where diffusion drives gas movement*

Airway Resistance

- *As airway resistance rises, breathing movements become more strenuous*
- *Severely constricting or obstruction of bronchioles*
  - Can prevent life-sustaining ventilation
  - Can occur during acute asthma attacks and stop ventilation
- *Epinephrine dilates bronchioles and reduces air resistance*

Alveolar Surface Tension

- *Surface tension*

  - Attracts liquid molecules to one another at a gas-liquid interface
  - Resists any force that tends to increase the surface area of the liquid

Alveolar Surface Tension

- *Surfactant*
  - Detergent-like lipid and protein complex produced by type II alveolar cells
  - Reduces surface tension of alveolar fluid and discourages alveolar collapse
  - Insufficient quantity in premature infants causes infant respiratory distress syndrome

Lung Compliance

- *A measure of the change in lung volume that occurs with a given change in transpulmonary pressure*
- *Normally high due to*
  - Distensibility of the lung tissue
  - Alveolar surface tension

Lung Compliance

- *Diminished by*
  - Nonelastic scar tissue (fibrosis)
  - Reduced production of surfactant
  - Decreased flexibility of the thoracic cage

Lung Compliance

- *Homeostatic imbalances that reduce compliance*
  - Deformities of thorax
  - Ossification of the costal cartilage
  - Paralysis of intercostal muscles

Respiratory Volumes

- *Used to assess a person’s respiratory status*
  - Tidal volume (TV)
  - Inspiratory reserve volume (IRV)
  - Expiratory reserve volume (ERV)
  - Residual volume (RV)

Respiratory Capacities

- *Inspiratory capacity (IC)*
- *Functional residual capacity (FRC)*
- *Vital capacity (VC)*
- *Total lung capacity (TLC)*

Dead Space

- *Some inspired air never contributes to gas exchange*
- *Anatomical dead space: volume of the conducting zone conduits (~150 ml)*
- *Alveolar dead space: alveoli that cease to act in gas exchange due to collapse or obstruction*
- *Total dead space: sum of above nonuseful volumes*

Pulmonary Function Tests

- *Spirometer: instrument used to measure respiratory volumes and capacities*
- *Spirometry can distinguish between*
  - Obstructive pulmonary disease—increased airway resistance (e.g., bronchitis)
  - Restrictive disorders—reduction in total lung capacity due to structural or functional lung changes (e.g., fibrosis or TB)

Pulmonary Function Tests

- *Minute ventilation: total amount of gas flow into or out of the respiratory tract in one minute*
- *Forced vital capacity (FVC): gas forcibly expelled after taking a deep breath*
- *Forced expiratory volume (FEV): the amount of gas expelled during specific time intervals of the FVC*

Pulmonary Function Tests

- *Increases in TLC, FRC, and RV may occur as a result of obstructive disease*
- *Reduction in VC, TLC, FRC, and RV result from restrictive disease*

Alveolar Ventilation

- *Alveolar ventilation rate (AVR): flow of gases into and out of the alveoli during a particular time*
- *Dead space is normally constant*
- *Rapid, shallow breathing decreases AVR*

Control of Respiration

- Involves neurons in the reticular formation of the medulla and pons

Medullary Respiratory Centers

1. Dorsal respiratory group (DRG)
   - Near the root of cranial nerve IX
   - Integrates input from peripheral stretch and chemoreceptors

Medullary Respiratory Centers

2. Ventral respiratory group (VRG)
   - Rhythm-generating and integrative center
   - Sets eupnea (12–15 breaths/minute)
   - Inspiratory neurons excite the inspiratory muscles via the phrenic and intercostal nerves
   - Expiratory neurons inhibit the inspiratory neurons

Pontine Respiratory Centers

- Influence and modify activity of the VRG
- Smooth out transition between inspiration and expiration and vice versa

Genesis of the Respiratory Rhythm

- Not well understood
- Most widely accepted hypothesis
  - Reciprocal inhibition of two sets of interconnected neuronal networks in the

medulla sets the rhythm

Depth and Rate of Breathing

- Depth is determined by how actively the respiratory center stimulates the respiratory muscles
- Rate is determined by how long the inspiratory center is active
- Both are modified in response to changing body demands

Chemical Factors

- Influence of Pco_2:
  - If Pco_2 levels rise (hypercapnia), CO_2 accumulates in the brain
  - CO_2 is hydrated; resulting carbonic acid dissociates, releasing H^+
  - H^+ stimulates the central chemoreceptors of the brain stem
  - Chemoreceptors synapse with the respiratory regulatory centers, increasing the depth and rate of breathing

Depth and Rate of Breathing

- Hyperventilation: increased depth and rate of breathing that exceeds the body's need to remove CO_2
  - Causes CO_2 levels to decline (hypocapnia)
    - May cause cerebral vasoconstriction and cerebral ischemia
- Apnea: period of breathing cessation that occurs when Pco_2 is abnormally low

Chemical Factors

- Influence of Po_2
  - Peripheral chemoreceptors in the aortic and carotid bodies are O_2 sensors
    - When excited, they cause the respiratory centers to increase ventilation
- Substantial drops in arterial Po_2 (to 60 mm Hg) must occur in order to stimulate increased ventilation

Chemical Factors

- Influence of arterial pH
  - Can modify respiratory rate and rhythm even if CO_2 and O_2 levels are normal
  - Decreased pH may reflect
    - CO_2 retention
    - Accumulation of lactic acid
    - Excess ketone bodies in patients with diabetes mellitus
  - Respiratory system controls will attempt to raise the pH by increasing respiratory rate and depth

Summary of Chemical Factors

- Rising CO_2 levels are the most powerful respiratory stimulant
- Normally blood Po_2 affects breathing only indirectly by influencing peripheral chemoreceptor sensitivity to changes in Pco_2

Summary of Chemical Factors

- When arterial Po_2 falls below 60 mm Hg, it becomes the major stimulus for respiration (via the peripheral chemoreceptors)
- Changes in arterial pH resulting from CO_2 retention or metabolic factors act indirectly through the peripheral chemoreceptors

Influence of Higher Brain Centers

- Hypothalamic controls act through the limbic system to modify rate and depth of respiration
  - Example: breath holding that occurs in anger or gasping with pain
- A rise in body temperature acts to increase respiratory rate
- Cortical controls are direct signals from the cerebral motor cortex that bypass medullary controls
  - Example: voluntary breath holding

Pulmonary Irritant Reflexes

- Receptors in the bronchioles respond to irritants
- Promote reflexive constriction of air passages
- Receptors in the larger airways mediate the cough and sneeze reflexes

Inflation Reflex

- Hering-Breuer Reflex
  - Stretch receptors in the pleurae and airways are stimulated by lung inflation
    - Inhibitory signals to the medullary respiratory centers end inhalation and allow expiration to occur
    - Acts more as a protective response than a normal regulatory mechanism

END OF OUTLINE

References

Marieb, E. N. & Hoehn K (2010). Human Anatomy and Physiology. 8th Edition, Pearson, Benjamin Cummings.