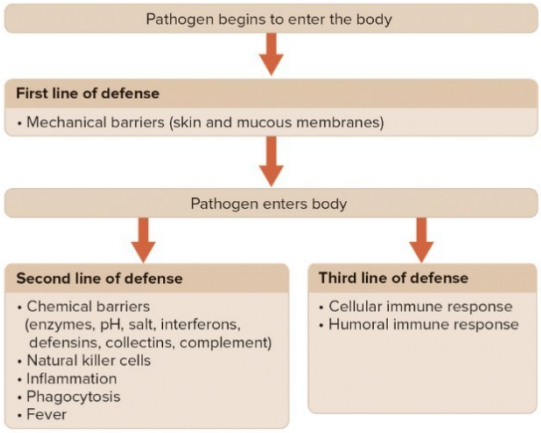
BIOS255 Exam 3 Review

Introduction to immune system

- Functions of the immune system
  - Protect the body from and fight off pathogens
- Two major forms of immunity with three lines of defense
  - Non-specific Resistance (Innate Immunity) – Immune defense mechanisms you are born with
    - Physical and Chemical barriers – first line of defense
      - Skin
      - Mucous membranes
      - Sebum
      - Perspiration
    - Internal defenses - Second line of defense
      - Inflammation
      - Interferon
      - Compliment
      - Fever
      - NK cells (Immunological surveillance)
      - Phagocytosis
  - Specific Resistance (Adaptive Immunity; Third line of defense)
    - Cell mediated immunity
    - Antibody mediated

immunity Overview of Innate (non-specific) defenses



- Non-phagocyte killing
  - Granulocytes release chemical granzymes to attack local pathogens
    - Neutrophils – bacteria
    - Eosinophils – parasitic worms, allergies, and inflammation
  - NK cells
    - Recognition and attachment
    - Secretion of perforins and granzymes
    - Lysis and detachment
- Phagocytosis

- Chemotaxis
- Adhesion
- Engulfment
- Formation of a phagosome
- Add digestive enzymes to vesicle with the pathogen killing the pathogen
- Endocytosis of residual body

- Antimicrobial proteins
  - Interferons – interfere with viral replication
  - Complement – cascade of proteins join to form a membrane attach complex that lyses the membrane of the pathogen
  - Pyrogens – cause a fever
    - Exogenous – from outside the cell
    - Endogenous – released from body cells like neutrophils and macrophages (Ex: Interleukin I)
  - Inflammation is triggered by inflammatory chemicals; the four cardinal signs of inflammation are:
    - Redness (Rubor)
    - Swelling (Tumor)
    - Heat (Calor)
    - Pain (Dolor)

<u>Overview of Adaptive (specific) immunity, antigens, and antigen processing</u>

- Specific defenses
  - Specificity: Highly specific to the antigen against which the third line of defense is directed. Immunity against one disease does not provide immunity for any other disease.
  - Inducibility: Lymphocytes are activated only in response to specific antigens.
  - Clonality: Proliferation of a particular lymphocyte occurs once induced.
  - Unresponsiveness to self: Lymphocytes that attack self-antigens (your own body's cells) are destroyed by a process called clonal deletion. This is also called self-tolerance.
  - Memory: After an initial exposure (sensitization) to an antigen, lymphocytes produce an enhanced response upon subsequent exposures. The rate of production and persistence of antibodies is greatly increased compared to the first exposure. This is also called the secondary or anamnestic response.
- Cell mediated immunity
  - Carried out by T-cell lymphocytes
  - Triggered by endogenous antigens
  - MCH II antigen presenting triggers the activation of Helper T-cells
  - MCH I antigen presenting triggers the activation of Cytotoxic T-cells
  - Required interaction with infected human cells
- Antibody mediated immunity
  - Carried out by B-cell lymphocytes
  - Triggered by exogenous antigens

- MHC II antigen presenting triggers the activation of B cells
  - Memory B-cells
  - Plasma cells that create antibodies
  - Requires antigen and antibody interaction

- Antigens – molecules that the body reacts with to elicit a response from the immune system
  - Proteins in a cell membrane
  - Entire pathogens
    - Epitopes – Usually there is a specific part of the membrane or outer surface of an antigen that our immune system is able to recognize, known as an epitope. If an antigen were a person, the epitope would be that person's nametag, the part that we read to know their name.
  - Chemicals produced by pathogen
  - Found on some food
  - Dust

<u>The role of Lymphocytes in Adaptive (specific, acquired) Immunity</u>

Some comparisons between cellular and humoral immunity

Characteristics	Cellular Immunity	Humoral Immunity
Disease agents	Intracellular viruses, bacteria, yeasts, and protozoans; parasitic worms; cancer cells; transplanted tissues and organs	Extracellular viruses, bacteria, yeasts, and protozoans; toxins, venoms, and allergens; mismatched RBCs
Effector cells	Cytotoxic T cells	Plasma cells (develop from B cells)
Other cells involved in attack	Helper T cells	Helper T cells
Antigen-presenting cells	B cells, macrophages, dendritic cells, nearly all cells	B cells
MHC proteins	MHC-I and MHC-II	MHC-II only
Chemical agents of attack	Perforins, granzymes, interferons, tumor necrosis factor	Antibodies, complement
Mechanisms of counteracting or destroying pathogens	Cytolysis, phagocytosis, apoptosis	Cytolysis, phagocytosis, immune clearance, inflammation, neutralization, agglutination, precipitation
Memory	T cell recall response	Secondary (anamnestic) resposne

- Cell mediated immunity
  - Helper T cells (CD4 cells): recruit other WBCs (B cells; Cytotoxic T Cells; Macrophages) to the area of infection; Activated by MHC II
  - Cytotoxic T cells (CD8 cells): secrete perforin and granzymes to destroy cells infected with a pathogen; Activated by MHC I
  - Memory T cells: live for years to create future immunity
- Antibody mediate immunity (Humoral)
  - Activated B cells: differentiate into plasma cells
  - Plasma cells: create antibodies; Activated by MHC I
  - Memory B cells: live for years to create future immunity

<u>The role of Antibodies in Adaptive (Specific, acquired) immunity and applied immunology</u>

- Antibodies: Y shaped proteins with light and dark chains. Named for how many Y shaped structures there are (monomer is 1; dimer is 2; pentamer is 5)

- 5 classes of antibodies (Immunoglobulins)
    - IgA: Most associated with exocrine secretions; found as a monomer and dimer
    - IgD: Transmembrane protein involved in B cell activation
    - IgE: Involved in response to parasitic infections and allergies, transmembrane protein on mast cells and basophils; important role in allergic reactions
    - IgG: Most common (80%) and longest-lasting antibody in plasma; can cross placenta; is most responsible for secondary immune response
    - IgM: First antibody produced during infection; pentamer
- Primary and Secondary immune response
    - Primary response – slow rise slow decline; IgM first to respond then IgG
    - Secondary response – fast rise, slow decline; IgG first to respond then IgM
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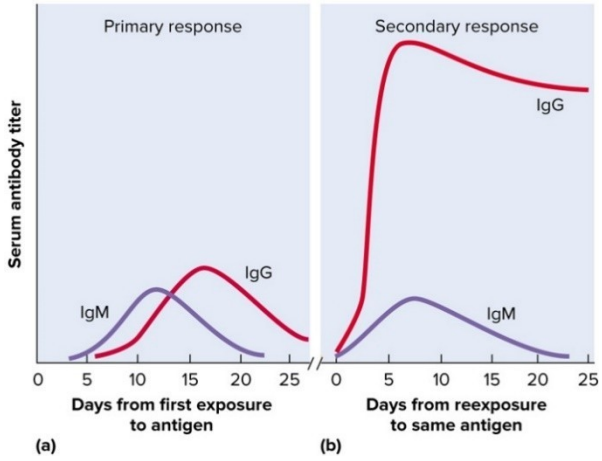


- Types of adaptive immunity
    - Naturally acquired **passive** immunity – example is **passing** of IgA antibodies from placenta and breast milk from mother to infant
    - Naturally acquired **active** immunity – example is exposure to the chickenpox and **creating** antibodies due to the exposure
    - Artificially acquired **passive** immunity – example is **giving** intravenous antibodies to someone exposed to rabies
    - Artificially acquired **active** immunity – example is being given a vaccination of an attenuated virus that your body must fight off and **create** antibodies to

<u>Application of Homeostatic mechanisms and predictions related to disruption of homeostasis</u>

- Elephantiasis
- HIV/AIDS
- Autoimmune disorders
- Allergies/Hypersensitivity
    - Type1: IgE-mediated, topical (atopy), and systemic (anaphylaxis) reactions. Includes food allergies, asthma, and hay fever.
    - Type 2: Antibody-mediated reaction. For example, an incompatible blood transfusion.

- Type 3: Immune complex-mediated, antigen antibody complexes that include autoimmune disorders like rheumatoid arthritis, Grave's disease, Myasthenia gravis, and systemic lupus.
- Type 4: Delayed or T cell-mediated hypersensitivity which is seen with poison ivy, tuberculin test, graft rejections, Type I diabetes, multiple sclerosis, and contact dermatitis.

General functions of Respiratory System

- Ventilation vs Respiration
  - Ventilation – movement of gases into and out of the lungs; between the lungs and external environment
    - Inhalation: air moving from external environment into the lungs
    - Exhalation: air moving from the lungs to the external environment
  - Respiration – exchange of gasses across a membrane into and out of a blood vessel
    - External (Pulmonary) Respiration: Oxygen moves from the alveoli across the alveolar membrane into the pulmonary capillary bed; carbon dioxide moves from the pulmonary capillary bed across the alveolar membrane into the alveoli
    - Internal (Tissue) Respiration: carbon dioxide moves from the interstitial fluid across the systemic capillary membrane into the systemic capillary bed; oxygen moves from the systemic capillary bed across the systemic capillary membrane into the interstitial fluid where it is used by the cell for cellular respiration to create ATP
- Functions of the Respiratory System
  - Communication: Involved in speech, vocalization, crying and laughing.
  - Olfaction: Site for smelling
  - pH balance: This is achieved through the control of the levels of CO_2. When CO_2 dissolves in water it will react to create Carbonic Acid, which will in turn affect the blood pH. Recall from previous topics that the blood pH must remain in a range of 7.35-7.45.
  - Blood Pressure regulation: Lungs are responsible for producing ACE which is involved in the production of Angiotensin II, a strong hormone which assists in blood pressure regulation and promotes the release of Aldosterone.
  - Removal of abdominal contents: Breathing and muscle contractions assists in the removal of abdominal contents as well as other processes such as childbirth, defecation, and micturition.
  - Filtration of Blood: The lungs are capable of filtering small blood clots in the blood.
  - Production of Platelets: Over 50% of the body's platelets are generated from the megakaryocytes in the lungs and not the bone marrow.
  - Promoting blood and lymph flow: Breathing and muscle contractions helps to promote the movement of blood and lymph in the body.

Principle components of the Respiratory System

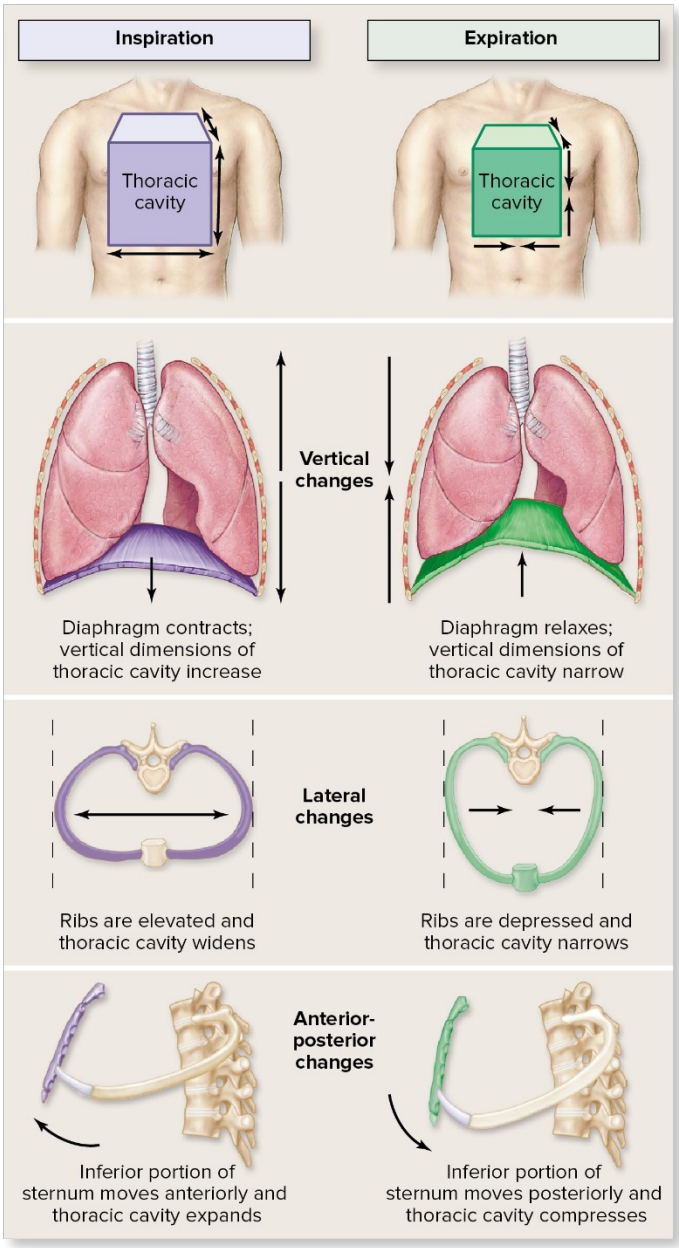
- Principle components of the respiratory system
  - Nose
  - Pharynx
  - Larynx
  - Trachea
  - Lungs
    - Bronchi
    - Bronchioles
    - Alveoli
- Structural Divisions of the Respiratory system
  - Upper respiratory system: Nasal passage, pharynx
  - Lower Respiratory system: Larynx, Trachea, Main bronchus, Bronchioles, and Alveoli
- Functional Divisions of the Respiratory system
  - Conducting zone structures: Everything else
  - Respiratory zone structures: Terminal bronchioles, Respiratory bronchioles, Alveolar ducts, and Alveoli
- Nose/Nasal Cavity
  - External nares
  - Nasal septum
  - Nasal conchae
  - Respiratory membrane
  - Paranasal sinuses: function to filter, humidify, and warm up the air before the lungs as well as to resonate sound and lighten the skull
    - Frontal sinus
    - Maxillary sinus
    - Ethmoid sinus
    - Sphenoid sinus
- Pharynx
  - Nasopharynx: from the sphenoid bone to the soft palate
  - Oropharynx: soft palate to the bottom of the tongue
  - Laryngopharynx: tongue to epiglottis
- Larynx
  - Vocal folds
  - Vestibular folds
  - Cartilages of the larynx
    - Epiglottis
    - Thyroid cartilage
    - Cricoid cartilage
    - Arytenoid cartilage
    - Corniculate cartilage
    - Tracheal cartilage
- Trachea
  - Incomplete c-shaped trachea cartilage

- Carina – coughing reflex
  - Division of the trachea into the two main bronchi
- Right and Left Lungs: Apex, Base, and Hilum
  - Right lungs
    - 3 lobes: Superior, Middle, and Inferior lobes
    - Horizontal and Oblique Fissures
  - Left lungs
    - 2 lobes: Superior and Inferior
    - Cardiac notch
    - Oblique fissure
- Bronchi
  - Have cartilage and smooth muscle in walls
  - Creates a tree of distribution into the lungs
  - Bronchoconstriction and Bronchodilation to help control air flow to the lungs
- Bronchioles
  - Smooth muscle, but no cartilage in walls
  - Dilate and constrict with bronchi to control air flow in lungs
  - Last part of conducting zone
  - Respiratory bronchioles
  - Similar to bronchioles but with occasional alveoli
  - First part of respiratory zone
- Alveoli
  - Site of gas exchange
  - Type I alveolar cells – create respiratory membrane
  - Type II alveolar cells – create surfactant (reduces surface tension in the lungs)
  - Phagocytic dust cells – clears debris in the alveoli
- Pleura: protective tissue surrounding the lungs
  - Parietal pleura – attached to the thoracic wall
  - Interpleural space – filled with serous fluid to reduce friction
  - Visceral pleura – attached to outside of the

lungs <u>Mechanisms of Pulmonary ventilation</u>

- Respiratory cycle: one inhalation followed by one exhalation
- Eupnea: Normal quiet breathing
  - Controlled mostly by contraction of the diaphragm and external intercostal muscles (inhalation), relaxing of the diaphragm and elastic recoil of the lungs (exhalation)
- Forceful breathing: the amount of air that can be forced into and out of the lungs beyond normal breathing
  - Muscles used for forceful inhalation
    - Diaphragm (normal breathing too)
    - External intercostals (normal breathing too)
    - Scalene muscles
    - Sternocleidomastoid

        - Pectoralis minor
    - Muscles used for forceful exhalation
        - Internal intercostals
        - Abdominal muscles (rectus abdominis, transversus abdominis, internal/external obliques)
- Nerves responsible for ventilation
    - Phrenic nerve (C3, C4, and C5) controls the diaphragm
    - Vagus nerve
    - Posterior thoracic nerve controls intercostal muscles
- Airflow and Pressure
    - Air will move from high pressure areas to low pressure areas
    - Volume and pressure are inversely related
        - When volume goes down, pressure goes up
            - To exhale, we need to create less volume in the thoracic cavity thus driving pressure up
        - When volume goes up, pressure goes down
            - To inhale, we need to create more volume in the thoracic cavity thus driving pressure down
- Boyle's Law
    - Pressure and volume are inversely related
    - Volume changes can be used to create pressure changes for ventilation



- Resistance of airflow
  - Airway diameter: bronchoconstriction and bronchodilation
  - Alveolar surface tension: Surfactant produced by Type II Alveolar cells
  - Compliance: ability of the lungs and thoracic cage to expand
    - High compliance = easier to expand thorax
    - Low compliance = more difficult to expand thorax (can occur with emphysema)

Pulmonary air volumes and capacities

- Pulmonary volumes
  - Tidal volume (TV) – amount of air in and out during normal quiet breathing (500 mL)

- Inspiratory reserve volume (IRV) – amount of air that can be forced in after normal breath (3000 mL)
- Expiratory reserve volume (ERV) – amount of air that can be forced out after a normal breath (1200 mL)
- Residual volume (RV) – amount of air that remains in the lungs after maximum amount of air breathed out (1300 mL)
- Anatomical dead space – amount of air that remains in the conducting zone structures (150 mL)

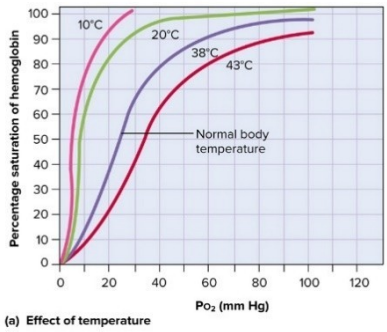
- Composition of Alveolar and Inspired Air
  - Air is a mixture of gasses of which Oxygen is only about 21%
- Minute Ventilation (MV)
  - MV = TV (tidal volume) x RR (respiratory rate)

<u>Mechanisms of Gas exchange in the lungs and tissues</u>

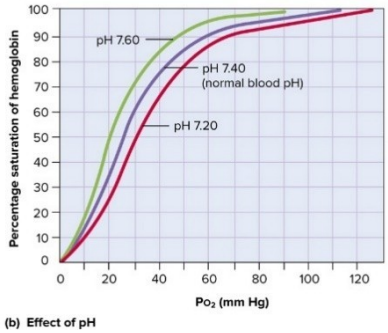
- Dalton's Law – In a mixture of gases each gas exerts a partial pressure as if no other gas is present ($P_{Total} = P_{Gas1} + P_{Gas2} + P_{Gas3}...$)
- Henry's Law – Gases move across a membrane is directly proportional to both the partial pressure of the gas as well as the solubility coefficient (carbon dioxide is 20x more soluble in water than oxygen)
- Ventilation-perfusion coupling: blood will be diverted by precapillary sphincters in the pulmonary capillary beds to areas that have high oxygen concentrations. In other words, blood flow follows oxygen in the lungs
  - This is opposite from the systemic circulation, where blood flows to areas of low oxygen (because they must need more oxygen)

<u>Mechanisms of Gas transport in the blood</u>

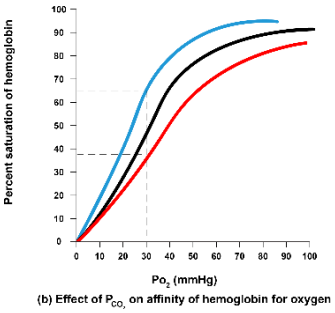
- Transport of oxygen
  - 1.5% of oxygen is transported dissolved in plasma
  - 98.5% of oxygen is transported on the hemoglobin
    - One Hb can bind up to 4 oxygen molecules
- Hemoglobin affinity and oxygen saturation
  - When more oxygen is present, a higher saturation of Hb can occur. There are several factors that can affect Hb saturation with oxygen
    - Partial pressure of carbon dioxide
    - Temperature
    - pH
    - 2,3-BPG (a by-product of glycolysis)
    - The makeup of Hb itself (fetal vs adult hemoglobin)
  - Hb is said to have been LEFT-shifted if it has a greater affinity than normal (stronger attraction to oxygen – so it is more likely to pick-up oxygen)
  - Hb is said to have been RIGHT-shifted if it has a lesser affinity than normal (weaker attraction to oxygen – so it is more likely to release oxygen)



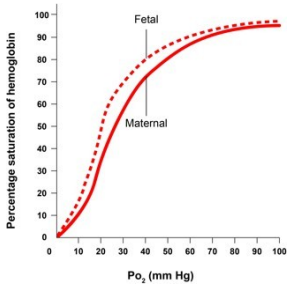
(a) Effect of temperature



(b) Effect of pH



(b) Effect of P_{CO_2} on affinity of hemoglobin for oxygen



- Carbon dioxide transport
  - 7% dissolved in plasma
  - 23% carried by Hb
  - 70% converted in bicarbonate (HCO_3^-): $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$

<u>Control of pulmonary ventilation</u>

- Dorsal respiratory group
  - Sets rate and controls inspiratory muscles (diaphragm and external intercostals) during normal, quiet breathing
- Modifies VRG based on input from chemoreceptors or the cortex (emotions) Ventral respiratory group
  - Controls muscles of inspiration and expiration during forceful breathing under the guidance of the DRG.
- Pontine respiratory group
  - Changes breathing patterns based on sleep, speech, exercise, and emotions
- Breathing patterns

Breathing Pattern	Manifestation
Eupnea	Normal quiet breathing
Hyperventilation	Increased pulmonary ventilation as a compensatory mechanism of metabolic acidosis in order to expel carbon dioxide faster; sometimes associated with anxiety and stress
Hypoventilation	Decreased pulmonary ventilation as a compensatory mechanisms of metabolic alkalosis in order to retain carbon dioxide
Dyspnea	Labored breathing with gasps and shortness of breath
Tachypnea	Accelerated respiration
Bradypnea	Slower than normal respirations
Orthopnea	Dyspnea that occurs when a person is sitting or lying down; typically seen in asthma, emphysema, and heart failure
Apnea	Temporary cessation of breathing; typically during sleep
Kussmaul	Deep, rapid breathing as a result of acidosis; typically seen in cases of diabetes mellitus and ketoacidosis
Biot's	A series of quick shallow breaths followed by periods of apnea; typically caused by stroke within in the medulla oblongata or prolonged opioid use
Cheyenne-Stokes	Progressively deeper inhalations, followed by a decrease in respirations until apnea, repeating every 30 second to 2 minutes; seen in patients with brain tumors, encephalitis, and commonly experienced during dying

Breathing Pattern	Manifestations
Coughing	A long-drawn and deep inhalation with a closure of the vocal cords, leading to a stronger inhalation that will allow air to blast through the upper respiratory tract to dislodge foreign objects.
Crying	Inhalations followed by convulsive exhalations, causing the vocal cords to vibrate, and is typically associated with facial expression changes and tears.
Hiccupping	Spasms of the diaphragm and vocal cords leading to a sharp sound during inhalations. Typically stimulated by nerve irritation in the gastrointestinal tract.
Laughing	Similar breathing pattern to crying but with a slightly different rhythm and facial expressions.
Sighing	A long, deep inhalation followed by a short, forceful exhalation.
Sneezing	Spasms within the muscle of exhalation that will forcefully expel air through the nasal and oral passages. Typically stimulated by irritation within the nasal mucosa.
Sobbing	Convulsive inhalations followed by a single long exhalation. The vocal cords close early after each inhalation, leading to less airflow into the lungs.
Valsalva Maneuver	Forceful exhalations that occur while the rima glottis is closed. Typically associated with straining during defecation.
Yawning	A single deep inhalation with the mouth exaggeratedly depressed. Typically associated with drowsiness.

<u>Application of homeostatic mechanisms</u>

- Effects on cardiovascular function
    - Changing breathing pattern changes oxygen rates and oxygen delivery. A change in oxygen delivery causes chemoreceptors to alter heart rate
        - Hyperventilation – more oxygen saturation, lowers heart rate
        - Hypoventilation – lower oxygen saturation, elevates heart rate
    - Exercise
        - Elevates oxygen demand, elevates respiratory rate, elevates heart rate
- COPD
    - Chronic bronchitis
        - Difficulty exhaling
        - Pink puffer
    - Emphysema
        - Difficulty inhaling: barrel chested
        - Blue bloater
- Lung cancer
    - Squamous cell carcinoma – most common
    - Flat cell carcinoma – uncommon but most dangerous
- SARS
    - Viral infection
    - Flu-like symptoms

- COVID-19