Respiratory System

- **Major function:**
  - To supply the body with oxygen and dispose of carbon dioxide

- **Four processes that define respiration:**
  - Pulmonary ventilation (breathing)
  - External respiration (oxygen loading; CO2 unloading)
  - Transport (via blood circulation)
  - Internal respiration (oxygen unloading; CO2 loading)
Respiratory System:

Functional Anatomy

- Major organs:
  - Nose, nasal cavity & paranasal sinuses
  - Pharynx
  - Larynx
  - Trachea
  - Bronchi and their branches
  - Lungs and alveoli
Respiratory System

- Nasal cavity
- Nostril
- Oral cavity
- Pharynx
- Trachea
- Larynx
- Carina of trachea
- Right main (primary) bronchus
- Right lung
- Left main (primary) bronchus
- Left lung
- Diaphragm
The Nose

Functions:
- Provides an airway for respiration
- Moistens & warms the entering air
- Filters and cleans inspired air
- Houses olfactory receptors
- Aids in speech resonation
Structure of the Nose

Root: between the eyebrows, frontal bone

Bridge: shallow indentation between the eyes

Dorsum nasi: anterior margin - cartilage

Apex: tip

Philtrum: vertical groove below apex

External nares: nostrils - openings

Ala: flare on lateral portion of the nostrils
Nasal Cavity

- Air enters > External nares (nostrils) > internal nares > Conchae
- Bottom of nasal cavity – palate – separates from oral
  - Hard Palate: bone – maxilla & palatine bones
  - Soft palate: muscle
- Nasal vestibule (above nostrils) lined with *vibrissae*
  - Hairs that filter coarse debris
- Rest of cavity lined with mucous membranes
  - Olfactory mucosa: superior; smell receptors
  - Respiratory mucosa: Pseudostratified ciliated columnar epithelium with goblet cells (mucus)
Nasal Cavity

- Superior, medial, and inferior conchae (chambers)
  - Increase mucosal area
  - Enhance air turbulence and help filter air
- Respiratory mucosa
  - Lines the nasal cavity is continuous with rest of respiratory tract
  - Pseudostratified columnar epithelial and goblet cells
  - Moisturizes the air & warm the air
  - Triggers sneezing when stimulated by irritating particles
  - Mucous contains lysozyme & defensins
Nasal Cavity:

**Paranasal Sinuses**

- Open areas in bones that surround the nasal cavity
- Lighten the skull
- Help to warm and moisten the air
- *Sinusitis*- inflamed sinuses
  - can lead to blocked passageways that lead from the sinus to nasal cavity > headache
Nasal Cavity

- Sphenoidal sinus
- Nasal meatuses (superior, middle, and inferior)
- Pharyngeal tonsil
- Opening of pharyngotympanic (auditory) tube
- Nasopharynx
- Posterior nasal aperture
- Uvula
- Palatine tonsil
- Isthmus of the fauces
- Oropharynx
- Laryngopharynx
- Vestibular fold
- Vocal fold
- Esophagus

- Frontal sinus
- Cribriform plate of ethmoid bone
- Nasal conchae (superior, middle and inferior)
- Nasal vestibule
- Nostril
- Hard palate
- Soft palate
- Tongue
- Lingual tonsil
- Epiglottis
- Hyoid bone
- Thyroid cartilage
- Cricoid cartilage
- Laryngeal cartilages
- Thyroid gland
- Trachea
Pharynx

- a.k.a. *throat*; Common food and air passageway
- Connects nasal and oral airways to the larynx
- It is divided into three regions
  - Nasopharynx (superior) – air only
    - protected by uvula when eating; eustachian tube entrance; location of pharyngeal tonsils (adenoids)
  - Oropharynx (middle) – food & air
    - Lined with stratified squamous epithelium; location of palatine & lingual tonsils
  - Laryngopharynx (inferior) – food & air
    - Lined with stratified squamous epithelium;
Pharynx

Nasopharynx

Oropharynx

Laryngopharynx
Larynx (Voice Box)

- Superiorly attaches to hyoid bone; opens to laryngopharynx; attaches to trachea

- Three functions:
  - To provide a patent (open) airway
    - Glottis open
  - To act as a switching mechanism to route air and food into the proper channels
    - Epiglottis closes glottis – swallowing
  - Houses vocal chords – voice production
Framework of the Larynx

- Arrangement of 9 Cartilages of the larynx
  - Mostly hyaline cartilage (except epiglottis)
  - Major ones:
    - Thyroid cartilage
      - with a midline laryngeal prominence (Adam’s apple)
      - Thicker in males due to testosterone
    - Cricoid cartilage: ring anchoring larynx to trachea
    - Arytenoid cartilage: anchors vocal cords within walls of larynx
    - Epiglottis: elastic cartilage that covers the laryngeal inlet during swallowing
Framework of the Larynx

- Epiglottis
- Thyrohyoid membrane
- Cuneiform cartilage
- Corncilulate cartilage
- Arytenoid cartilage
- Arytenoid muscles
- Cricoid cartilage
- Cricothyroid ligament
- Cricotracheal ligament
- Tracheal cartilages
Larynx: Vocal Cords

- Vocal ligaments attach to arytenoid cartilage
- Made of elastic fibers which vibrate as air comes from lungs
- Opening between vocal ligaments is the glottis

- Speech: intermittent release of expired air while open/closing glottis
- Pitch: determined by length & tension of vocal cords (tighter=higher pitch)
- Loudness: depends on force at which air rushes across the vocal cords
Trachea “windpipe”

- from larynx into mediastinum; ends by dividing into two main (primary) bronchi

- Tracheal wall has three layers (deep to superficial)
  - Mucosa (deepest; lines airway)
    - Made of pseudostratified ciliated columnar epithelial cells
      - With goblet cells (mucus secreting)
      - smoking damages cilia > smoker’s cough > clear respiratory mucus
  - Submucosa (middle)
    - Made of connective tissue which contains seromucosa glands - creates sheets of mucus within trachea
  - Adventitia (superficial)
    - made of connective tissue surrounding C-shaped rings of hyaline cartilage
    - trachealis muscle- between trachea & esophagus
Trachea

(a) Cross section of the trachea and esophagus
Respiratory Tree

Trachea branches into L and R primary bronchi at Carina (last tracheal cartilage)

↓

secondary bronchi (supply to lobes of lung)

↓

tertiary bronchi

↓

bronchioles

↓

terminal bronchioles

↓

Alveoli (create sacs – site for gas exchange)
Bronchi & Bronchioles

- Bronchi tissues are like that of the trachea

- Bronchioles have these changes:
  - No cartilage support
  - Epithelium types change
    - Cubodial (not columnar), cilia & goblet cells are sparse (so little mucus)
  - Amount of smooth muscle increases
Bronchi & Bronchioles

- Superior lobe of right lung
- Middle lobe of right lung
- Inferior lobe of right lung
- Superior lobe of left lung
- Left main (primary) bronchus
- Lobar (secondary) bronchus
- Segmental (tertiary) bronchus
- Inferior lobe of left lung
Bronchioles → Alveoli

- Respiratory bronchioles branch into clusters of alveolar sacs composed of alveoli

- Alveoli:
  - Account for most of the lungs’ volume
  - Begin “respiratory zone”
  - Provide tremendous surface area for gas exchange
    - Gas exchange (CO₂ and O₂) via diffusion
Respiratory Zone

(a) Diagram showing the respiratory zone with labels for Alveolar duct, Alveoli, Respiratory bronchioles, Terminal bronchiole, and Alveolar sac.

(b) Microscopic image of the respiratory zone with labels for Respiratory bronchiole, Alveolar duct, Alveoli, and Alveolar sac.
Alveoli: Composition

- Alveolar walls are composed of a single layer of simple squamous epithelial cells (Type I Cells)
  - Basal lamina of the alveoli and capillaries form a respiratory membrane
    - Gases diffuse across; much thinner than tissue paper

- Scattered amongst Type I Cell layer are Type II cells
  - Cubodial cells which secrete surfactant & antimicrobial proteins
    - Surfactant: coats alveoli surfaces, preventing collapse
      - Premature infants do not produce enough surfactant > infant respiratory distress syndrome > lung collapse

- Alveolar macrophages present to keep surfaces sterile
Alveoli Composition

Type I form part of respiratory membrane—gases diffuse across
Type II cells secrete surfactant
Lung Gross Anatomy

- Occupy most of thoracic cavity
  - Each lung within its own pleural cavity flanking the mediastinum
- Costal surface (interfaces with rib cage)
  - Anterior, lateral and posterior surfaces
- Apex: deep to clavicle; most superior tip of lung
- Base: inferior surface that rests on diaphragm
- Hilum: indentations on mediastinal surface
  - Site for attachment of blood vessels, bronchi, lymphatic vessels, nerves
- Cardiac notch: on L lung; accommodates heart
Lungs

(a) Anterior view. The lungs flank mediastinal structures laterally.
Lung Gross Anatomy

- **Left lung**
  - smaller than the right
  - Has cardiac notch: cavity that accommodates the heart
  - Separated into upper and lower lobes by the oblique fissure

- **Right lung**
  - separated into three lobes by the oblique and horizontal fissures
Serous membranes of lungs: Pleurae

- Parietal pleura
  - On thoracic wall and superior surface of diaphragm
  - Continues around heart and between lungs

- Visceral, or pulmonary, pleura
  - Covers the external lung surface

- Pleural cavity with fluid between
  - Filled with fluid to provide lubrication & decrease surface tension

- Pleurisy: inflammation of pleura > pleura becomes rough > increased friction
  - Pleural effusion: fluid accumulation in pleural cavity
Transverse Thoracic Section

- Esophagus (in posterior mediastinum)
- Right lung
- Parietal pleura
- Visceral pleura
- Pleural cavity
- Right main bronchus
- Right pulmonary artery
- Right pulmonary vein
- Pericardial membranes
- Vertebral
- Root of lung at hilum
- Left lung
- Thoracic wall
- Pulmonary trunk
- Heart (in mediastinum)
- Anterior mediastinum
- Sternum

Figure 22.10c
Breathing, or pulmonary ventilation, consists of two phases

**Inspiration**
- Contraction of inspiratory muscles (diaphragm & external intercostal muscles) > dec air pressure in lungs
- Now air flows into lungs (high > low pressure)

**Expiration**
- Inspiratory muscles relax & recoil
- Thoracic volume decreases
- Compresses alveoli > gases flow out of lungs
Mechanism of Breathing: Pressure Relationships in the Thoracic Cavity

- Respiratory pressure is always described relative to atmospheric pressure.

- Atmospheric pressure
  - Pressure exerted by the air surrounding the body
  - 760 mmHg (at sea level)
Mechanisms of Breathing: Pressure Relationships in the Thoracic Cavity

- **Intrapulmonary pressure** $(P_{pul})$
  - Pressure in the alveoli
  - Rises and falls with the phases of breathing
  - Always eventually equalizes with atmospheric pressure

- **Intrpleural pressure** $(P_{ip})$
  - Pressure in pleural cavity
  - Also fluctuates with breathing phases
  - Always less than intrapulmonary pressure

- **Transpulmonary pressure** $(P_{pul} - P_{ip})$
  - Difference in pressures that keeps air spaces in lungs (alveoli) open
  - keeps them from collapsing
  - The greater the transpulmonary $> \text{larger the lungs}$
  - If $P_{pul} = P_{ip}$ the lungs collapse
Pressure Relationships

![Diagram of lung with pressure relationships]

- Atmospheric pressure
- Parietal pleura
- Visceral pleura
- Pleural cavity
- Transpulmonary pressure: 760 mm Hg
- Intrapleural pressure: 756 mm Hg (−4 mm Hg)
- Intrapulmonary pressure: 760 mm Hg (0 mm Hg)

http://www.youtube.com/watch?v=gYSIWCeGMxY&feature=related
http://www.youtube.com/watch?v=HiT621Prro0&feature=related
Atelectasis (lung collapse)

- Caused by equalization of the intrapleural pressure with the intrapulmonary pressure
- Can be caused by:
  - Plugged bronchioles > collapse of alveoli
  - Wound that lets air into pleural cavity (pneumothorax)
Inspiration

- Active process (requires energy)
- Inspiratory muscles contract (diaphragm and external intercostals muscles)
  - causes an increase in the volume and size of the thoracic cavity
    - Diaphragm contracts and moves down (descends)
    - External intercostals contract and move up and out
  - Intrapulmonary pressure drops below atmospheric pressure > vacuum to draw in air > air flows into lungs until intrapulmonary pressure = atmospheric pressure
- Forced inspiration (deep breathing) requires additional muscles
Inspiration

<table>
<thead>
<tr>
<th>Sequence of events</th>
<th>Changes in anterior-posterior and superior-inferior dimensions</th>
<th>Changes in lateral dimensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>① Inspiratory muscles contract (diaphragm descends; rib cage rises)</td>
<td>Ribs elevated and sternum flares as external intercostals contract</td>
<td>External intercostals contract</td>
</tr>
<tr>
<td>② Thoracic cavity volume increases</td>
<td>Diaphragm moves inferiorly during contraction</td>
<td></td>
</tr>
<tr>
<td>③ Lungs stretched; intrapulmonary volume increases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>④ Intrapulmonary pressure drops (to $-1$ mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>⑤ Air (gases) flows into lungs down its pressure gradient until intrapulmonary pressure is 0 (equal to atmospheric pressure)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Inspiration:
Role of Pleural Membranes

- Adhesion of the visceral pleura to the parietal pleura provided by the pleural fluid
  - increase in the volume of the thoracic cavity > parietal pleura “pulls” the visceral pleura > increase in volume of alveoli

- increased volume creates a vacuum that pulls air into the lungs/alveoli
Boyle’s Law

- Boyle’s law: the relationship between the pressure and volume of gases
  - States that when temperature is constant, pressure is inversely related to volume
    - as volume of lungs goes up, the pressure of gases goes down
  - Increasing the volume of an area (lungs) creates a vacuum that draws air (gases) in
Expiration

- Normally a passive process
  - alternate – forced expiration requires muscles (active)
- Relaxation of inspiratory muscles
- Depends a lot on elasticity of lungs (recoil)
- Alveoli size decreases to smallest diameter (but not sticking or collapsing because of surfactant)
  - without surfactant to decrease surface tension the alveoli would close completely = collapse
Expiration

<table>
<thead>
<tr>
<th>Sequence of events</th>
<th>Changes in anterior-posterior and superior-inferior dimensions</th>
<th>Changes in lateral dimensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>① Inspiratory muscles relax (diaphragm rises; rib cage descends due to recoil of costal cartilages)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>② Thoracic cavity volume decreases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>③ Elastic lungs recoil passively; intrapulmonary volume decreases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>④ Intrapulmonary pressure rises (to +1 mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>⑤ Air (gases) flows out of lungs down its pressure gradient until intrapulmonary pressure is 0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Ribs and sternum depressed as external intercostals relax
- Diaphragm moves superiorly as it relaxes
- External intercostals relax
Active Expiration

- used when extra CO2 must be removed or voluntarily for actives like blowing up a balloon

- contraction of internal intercostals (mostly) the abdominal muscles also helps

- These actions force air out
Physical Factors Influencing Pulmonary Ventilation

- **Airway resistance**
  - Gas flow friction; considers pressure & resistance in airway; highly dependant on airway diameter, air viscosity
    - Greatly affected in acute asthma attack (histamines!!)

- **Alveolar surface tension**
  - Surfactant creates detergent-like film > dec surface tension > allowing easy passage of air
    - Like how laundry detergent increases the ability of water to permeate fabric
    - Deeper breaths stimulate Type II cells to make more surfactant

- **Lung compliance**
  - Distensibility of lungs; how lung volume responds to pressure
    - Decreased in people with TB > scar tissue in lungs
Respiratory Volumes

Used to assess a person’s respiratory status

- **Tidal volume (TV)**
  - Amount of air that moves into and out of the lungs with each breath--resting conditions (~500 ml)

- **Inspiratory reserve volume (IRV)**
  - air that can be forcefully inhaled beyond the tidal volume (3100 ml)

- **Expiratory reserve volume (ERV)**
  - air that can be forcefully exhaled from the lungs after a tidal expiration (1200 ml)

- **Residual volume (RV)**
  - air left in the lungs after forced exhale (1200 ml)

**averages are for 20 yr old 155 lb male**
Respiratory Capacities

- Calculated values based on respiratory volumes

- **Inspiratory capacity (IC)** \((IRV + TV)= 3600 \text{ ml}\)
  - total amount of air that can be inspired after a normal expiration

- **Functional residual capacity (FRC)** \((RV + ERV)= 2400 \text{ ml}\)
  - amount of air remaining in the lungs after a tidal expiration

- **Vital capacity (VC)** \((TV + IRV + ERV)= 4800 \text{ ml}\)
  - the total amount of exchangeable air

- **Total lung capacity (TLC)** \((\text{approximately } 6000 \text{ ml in males})\)
  - sum of all respiratory volumes
Respiratory Volumes and Capacities

(a) Spirographic record for a male
<table>
<thead>
<tr>
<th>Measurement</th>
<th>Adult male average value</th>
<th>Adult female average value</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tidal volume (TV)</td>
<td>500 ml</td>
<td>500 ml</td>
<td>Amount of air inhaled or exhaled with each breath under resting conditions</td>
</tr>
<tr>
<td>Inspiratory reserve volume (IRV)</td>
<td>3100 ml</td>
<td>1900 ml</td>
<td>Amount of air that can be forcefully inhaled after a normal tidal volume inhalation</td>
</tr>
<tr>
<td>Expiratory reserve volume (ERV)</td>
<td>1200 ml</td>
<td>700 ml</td>
<td>Amount of air that can be forcefully exhaled after a normal tidal volume exhalation</td>
</tr>
<tr>
<td>Residual volume (RV)</td>
<td>1200 ml</td>
<td>1100 ml</td>
<td>Amount of air remaining in the lungs after a forced exhalation</td>
</tr>
<tr>
<td>Total lung capacity (TLC)</td>
<td>6000 ml</td>
<td>4200 ml</td>
<td>Maximum amount of air contained in lungs after a maximum inspiratory effort: TLC = TV + IRV + ERV + RV</td>
</tr>
<tr>
<td>Vital capacity (VC)</td>
<td>4800 ml</td>
<td>3100 ml</td>
<td>Maximum amount of air that can be expired after a maximum inspiratory effort: VC = TV + IRV + ERV</td>
</tr>
<tr>
<td>Inspiratory capacity (IC)</td>
<td>3600 ml</td>
<td>2400 ml</td>
<td>Maximum amount of air that can be inspired after a normal expiration: IC = TV + IRV</td>
</tr>
<tr>
<td>Functional residual capacity (FRC)</td>
<td>2400 ml</td>
<td>1800 ml</td>
<td>Volume of air remaining in the lungs after a normal tidal volume expiration: FRC = ERV + RV</td>
</tr>
</tbody>
</table>

(b) Summary of respiratory volumes and capacities for males and females
Pulmonary Function Tests

- Spirometer: instrument used to measure respiratory volumes & capacities

- Spirometry can distinguish between
  - Increased airway resistance
    - As with CODP or other obstructive disease
  - Or reduction in lung capacity
    - due to structural or functional lung changes
Gas Exchange Between the Blood, Lungs, & Tissues:

Characteristics of Blood Gases

- Basic Properties of Gases
  - Dalton’s Law of Partial Pressures
  - Henry’s Law
- Oxygen transport
  - Hemoglobin (Hb) saturation/oxygenation
  - Bohr effect
- CO2 transport
  - Haldane effect
Basic Properties of Gases:

Dalton’s Law of Partial Pressures

- The total pressure exerted by a mixture of gases is the sum of the pressures exerted independently by each gas in the mixture.

  - Additionally, the pressure exerted by each gas – its partial pressure – is directly proportional to the percentage of that gas in the mixture.

  - Ex: at sea level atmospheric pressure is 760mmHg
    - Nitrogen makes up 79% of air or 597mmHg (760x79%)
    - Oxygen makes up 21% of air or 159mmHg (760x21%)
    - 1% carbon and water vapor
Basic Properties of Gases: Henry’s Law

- When a mixture of gases is in contact with a liquid, each gas will dissolve in the liquid in proportion to its partial pressure.
  - Gases diffuse down their partial pressure gradients - even across liquid/gas interface.
  - Greater gas concentration = more & faster it will go into a liquid.
    - Also depends on solubility of a gas in a liquid (or plasma).

- Hyperbaric chambers apply this law clinically.
  - Chambers contain higher than normal pressures of oxygen > more oxygen forced into body.
Molecular oxygen is carried in the blood

- majority (98.5%) is loosely bound to hemoglobin (Hb) in RBCs
  - termed oxyhemoglobin (Hb-O2 combo)
  - Oxygen binds to Iron (Fe) in heme
  - 4 oxygen molecules can bind each Hg in RBCs
- Dissolved in plasma (1.5%)
O2 and Hemoglobin

- Oxygenation: Hb affinity for O2
  - is described as Hb saturation (influenced by pH, CO2, O2, temp, etc)
    - Binding of one oxygen will increase binding of others
  - Conditions with High CO2, high H+ (Low pH) acidosis = ↓ oxygenation (↓ Hb affinity for O2)
  - Conditions with low CO2, low H+ (high pH) alkalosis = ↑ oxygenation (↑ Hb affinity for O2)

- Bohr effect: declining blood pH and increasing CO2 weaken the Hb-O2 bond
Gas exchange at the tissues

(a) Oxygen release and carbon dioxide pickup at the tissues
Gas exchange in the lungs

(b) Oxygen pickup and carbon dioxide release in the lungs
Hyperbaric oxygen chambers

- Can be used to increase partial pressure of O2 and increase O2 dissolved in the blood
- Prolonged exposure to higher O2 pressures can be toxic
  - Produces free radicals in the body > damage CNS > coma and possibly death
- Helpful for treating carbon monoxide poisoning, tissue damage, gas gangrene, scuba diving (bends)
The “bends”

- Decompression sickness or air embolism
- Occurs when divers descend to great depths under water
  - Every 10m descent = 1 atm increase in pressure
    - Forces larger than normal amounts of nitrogen into the blood
      - Surfacing slowly allows nitrogen to be removed from blood
      - Surfacing too fast > nitrogen “bubbling” to get out of blood > gas bubbles create emboli
  - Compressed air and pressurized suits help
Transport of Respiratory Gases by Blood: Carbon dioxide transport

- Most (70%) transported as HCO3 (bicarbonate) in plasma
- Small amount (20%) bound to globin of Hb (carbaminohemoglobin)
- Smaller (10%) dissolved in blood

\[
\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3
\]

Carbon dioxide diffuses into RBCs and combines with water to form **carbonic acid** (\(\text{H}_2\text{CO}_3\)), which quickly dissociates into hydrogen ions and bicarbonate ions.
CO2 transport

- At the tissues:
  - Bicarbonate quickly diffuses from RBCs into the plasma
  - Chloride shift occurs
    - Outrush of negative bicarbonate ions from the RBCs is balanced as chloride ions (Cl–) move in from the plasma
Gas exchange at the tissues

(a) Oxygen release and carbon dioxide pickup at the tissues

Figure 22.22a
At the lungs, the process is reversed and the HCO$_3$ moves into RBC and is converted back into CO$_2$ and H$_2$O

- With help from carbonic anhydrase enzyme

- CO$_2$ diffuses out of the plasma into the alveloi and is exhaled
Gas exchange in the lungs

(b) Oxygen pickup and carbon dioxide release in the lungs
Carbon dioxide transport in blood: Haldane Effect

- The lower the oxygen partial pressure > the lower Hb saturation with oxygen = more CO2 can be carried

- Reduced Hb (oxygen has been unloaded) has a greater ability to form carbaminohemoglobin
Respiration is under the neural control of the medulla and pons (neurons in the reticular formation)

- **Medulla**
  - Dorsal and ventral respiratory groups

- **Pons**
  - Pneumotatxic (pontine) center

Other factors can influence rate
Pontine respiratory centers interact with the medullary respiratory centers to smooth the respiratory pattern.

Ventral respiratory group (VRG) contains rhythm generators whose output drives respiration.

Dorsal respiratory group (DRG) integrates peripheral sensory input and modifies the rhythms generated by the VRG.

To inspiratory muscles

External intercostal muscles
Neural Control of Respiration: Medullary Respiratory Centers

- dorsal respiratory group (DRG)
  - Integrates input from peripheral stretch & chemoreceptors

- ventral respiratory group (VRG)
  - Rhythm-generating & integrative center
  - Sets eupnea (normal breathing rate) 12-15 breaths/min
    - Inspiration
      - Inspiratory neurons excite the inspiratory muscles to tell them to contract
    - Exhalation
      - Exhalation neurons inhibit the inspiratory neurons
  - Can be suppressed by drugs/ alcohol
Neural Control of Respiration: Pons Respiratory Centers

- **Pneumotaxic (pontine) center**
  - Influence and modify activity of the VRG during
    - Talking
    - Sleep
    - Exercise

- Smooths out inspiration and expiration transitions as needed
Several factors influence:

- Stretch receptors (Hering-Breuer reflex)
- Chemical factors
- Hypothalamic controls
- Cortical controls (voluntary)
Neural & Chemical Influences on Brain Stem Respiratory Centers

Higher brain centers (cerebral cortex—voluntary control over breathing)

Other receptors (e.g., pain) and emotional stimuli acting through the hypothalamus

Peripheral chemoreceptors
- \(O_2\downarrow, CO_2\uparrow, H^+\uparrow\)

Central chemoreceptors
- \(CO_2\uparrow, H^+\uparrow\)

Receptors in muscles and joints

Respiratory centers (medulla and pons)

Stretch receptors in lungs

Irritant receptors
Reflexes

- Inflation reflex (Hering-Breuer)
  - Stretch receptors in the lungs are stimulated by lung inflation
  - At inflation, inhibitory signals are sent to the medullary inspiration center to end inhalation and allow expiration
    - Prevents excessive stretching of the lungs (protective)

- Pulmonary irritant reflexes
  - Irritants promote reflexive constriction of air passages and coughing
Chemical factors are the most important regulators of respiratory rate from greatest stimuli to lesser are CO2, pH, O2.

Chemoreceptors in the medulla (central) and the carotid and aortic bodies (peripheral) detect levels of the above chemicals and mediate a response.
Peripheral Chemoreceptors

- Brain
- Sensory nerve fiber in cranial nerve IX (pharyngeal branch of glossopharyngeal)
- External carotid artery
- Internal carotid artery
- Carotid body
- Common carotid artery
- Cranial nerve X (vagus nerve)
- Sensory nerve fiber in cranial nerve X
- Aortic bodies in aortic arch
- Aorta
- Heart
Blood CO2 is the MOST powerful respiratory stimulus

- CO2 levels rise (hypercapnia), CO2 accumulates in brain > diffuses into CSF > CO2 gets hydrated > forms carbonic acid > acid dissociates > raises H+ > lowers pH > prompts hyperventilation > flush CO2 from the blood

- Too much hyperventilation can lead to low levels of CO2 in blood (hypocapnia) > dizziness and fainting
  - Low CO2 > constriction of cerebral vessels > reduces cerebral perfusion > ischemia of cerebral tissue
  - Apnea (cessation of breathing) can occur until CO2 levels rise
Depth and Rate of Breathing: low blood pH

- Changes in arterial pH can modify respiratory rate even if carbon dioxide and oxygen levels are normal.

- Increased ventilation in response to falling pH is mediated by peripheral chemoreceptors.
Rate of Breathing: low blood pH

- Acidosis may reflect:
  - Carbon dioxide retention - COPD (emphysema, chronic bronchitis)
  - Accumulation of lactic acid
  - Excess fatty acids/ ketone bodies in patients with diabetes mellitus

- Respiratory system controls will attempt to raise the pH by increasing respiratory rate and depth
Rate of Breathing: $P_{O_2}$

- Cells sensitive to O2 are found in the peripheral chemoreceptors
  - Only important in extreme depression of blood oxygen > increased respiratory rate

- In cases of chronic build up of CO2 (e.g. COPD), chemoreceptors become unresponsive to CO2 stimuli
  - In such cases, O2 levels become the principal respiratory stimulus (hypoxic drive)
  - Not a good idea to administer high O2, as this will only decrease breathing rate > inc CO2 levels even further
Rate of Breathing:

**Higher Brain Centers**

- **Hypothalamic controls** act through the limbic system to modify rate and depth of respiration
  - Example: breath holding that occurs in anger
  - Fever > inc respiratory rate

- **Cortical controls** are direct signals from the cerebral motor cortex that bypass medullary controls
  - Examples: voluntary breath holding, taking a deep breath
  - Can hold breath but when pCO2 rises will trigger medullary control - drowning
Respiratory Adjustments: Exercise

- During exercise there are adjustments to breathing rate (increases) that maintain the PCO2 and PO2 levels at normal

- Neural factors:
  - Psychological stimuli
    - Our conscious anticipation of exercise
  - Cortical motor activation of skeletal muscles & respiratory centers
  - Excitatory impulses from proprioceptors
Terminology: related to breathing

- Hyperventilation: increase in rate and depth of breathing
- Hypoventilation: insufficient ventilation
- Dyspnea: difficult or labored breathing
- Apnea: cessation of breathing
  - Sleep apnea: cessation of breathing during sleep
Types of Hypoxia

- Hypoxia: inadequate tissue perfusion of O2
  - Anemic hypoxia: reflects poor O2 delivery resulting from too few RBCs or low Hb
  - Ischemic hypoxia: results when blood circulation is impaired or blocked
  - Histotoxic hypoxia: occurs when body cells are unable to use O2, even when adequate amounts are delivered (i.e. cyanide poisoning)
  - Hypoxemic hypoxia: reduced arterial O2 (i.e. pulmonary diseases, breathing air with low O2 content)
Respiratory diseases & abnormalities

- Asthma
- Chronic obstructive pulmonary disease
  - Emphysema
  - Chronic bronchitis
- Cystic Fibrosis
- TB (Tuberculosis)
- Pneumonia
- Lung cancer
Asthma

- inflammation of trachea and bronchi causing an individual to be hypersensitive to many irritants

- Airway inflammation is an immune response caused by release of factors, which stimulate IgE and recruit inflammatory cells

- Acute attacks of coughing and dyspnea
Why asthma makes it hard to breathe

Air enters the respiratory system from the nose and mouth and travels through the bronchial tubes.

In an asthmatic person, the muscles of the bronchial tubes tighten and thicken, and the air passages become inflamed and mucus-filled, making it difficult for air to move.

In a non-asthmatic person, the muscles around the bronchial tubes are relaxed and the tissue thin, allowing for easy airflow.

Inflamed bronchial tube of an asthmatic

Normal bronchial tube

Source: American Academy of Allergy, Asthma and Immunology
Chronic Obstructive Pulmonary Disease (COPD)

- Exemplified by chronic bronchitis and obstructive emphysema (enlarged alveolar sacs)
- Patients have a history of:
  - Smoking
  - Dyspnea
  - Coughing and frequent pulmonary infections
- COPD victims develop respiratory failure accompanied by hypoxia, carbon dioxide retention, and respiratory acidosis
Pathogenesis of COPD

- Tobacco smoke
  - Air pollution
- α-1 antitrypsin deficiency

Continual bronchial irritation and inflammation

Chronic bronchitis
- Bronchial edema
- Chronic productive cough
- Bronchospasm

Emphysema
- Destruction of alveolar walls
- Loss of lung elasticity
- Air trapping

Breakdown of elastin in connective tissue of lungs

- Airway obstruction or air trapping
- Dyspnea
- Frequent infections

- Abnormal ventilation-perfusion ratio
- Hypoxemia
- Hypoventilation
Chronic Bronchitis and Emphysema

- Chronic bronchitis

Chronic bronchitis is caused most often by exposure to airborne pollutants such as cigarette smoke.

- Emphysema

Enlarged view of air sacs (alveoli)

Emphysema: weakened and collapsed air sacs with excess mucus.

Normal healthy air sacs
Cystic fibrosis

1 out of 2500 Caucasians will have this

- abnormal build up of mucous fluids in respiratory and digestive tract
- genetic basis: transmembrane conductance regulator (CFTR) protein that regulates chlorine movement (and water movement)
**Organs affected by cystic fibrosis**

**Sinuses:** sinusitis (infection)

**Lungs:** thick, sticky mucus buildup, bacterial infection, and widened airways

**Skin:** sweat glands produce salty sweat.

**Liver:** blocked biliary ducts

**Pancreas:** blocked pancreatic ducts

**Intestines:** cannot fully absorb nutrients

**Reproductive organs:** (male and female) complications

**Normal airway**
- Airway wall
- Airway lined with a thin layer of mucus

(Airway in cross-section)

**Airway with cystic fibrosis**
- Thick, sticky mucus blocks airway
- Widened airway
- Blood in mucus
- Bacterial infection
Tuberculosis

- Infectious disease caused by the bacterium *Mycobacterium tuberculosis*

- Tubercles

- Immune response $\rightarrow$ damage

- Antibiotics
Lung Cancer

- #1 cause of all cancer deaths in the U.S.
- 90% of all patients with lung cancer were smokers
Developmental Aspects: Fetus

- During fetal life, the lungs are filled with fluid and blood bypasses the lungs.
  - Gas exchange takes place via the placenta.
- Respiratory system developed at **28 weeks**.
- Respiratory rate is highest in newborns and slows until adulthood.
  - Respiratory efficiency decreased in old age.
**TABLE 22.3 Nonrespiratory Air (Gas) Movements**

<table>
<thead>
<tr>
<th>MOVEMENT</th>
<th>MECHANISM AND RESULT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>Taking a deep breath, closing glottis, and forcing air superiorly from lungs against glottis; glottis opens suddenly and a blast of air rushes upward. Can dislodge foreign particles or mucus from lower respiratory tract and propel such substances superiorly.</td>
</tr>
<tr>
<td>Sneeze</td>
<td>Similar to a cough, except that expelled air is directed through nasal cavities as well as through oral cavity; depressed uvula routes air upward through nasal cavities. Sneezes clear upper respiratory passages.</td>
</tr>
<tr>
<td>Crying</td>
<td>Inspiration followed by release of air in a number of short expirations. Primarily an emotionally induced mechanism.</td>
</tr>
<tr>
<td>Laughing</td>
<td>Essentially same as crying in terms of air movements produced. Also an emotionally induced response.</td>
</tr>
<tr>
<td>Hiccups</td>
<td>Sudden inspirations resulting from spasms of diaphragm; believed to be initiated by irritation of diaphragm or phrenic nerves, which serve diaphragm. Sound occurs when inspired air hits vocal folds of closing glottis.</td>
</tr>
<tr>
<td>Yawn</td>
<td>Very deep inspiration, taken with jaws wide open; not believed to be triggered by levels of oxygen or carbon dioxide in blood. Ventilates all alveoli (not the case in normal quiet breathing).</td>
</tr>
</tbody>
</table>

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