AUTONOMIC NERVOUS SYSTEM

The autonomic nervous may be characterized as primarily a motor system.

Types of tissue are innervated by the ANS.
1. Smooth muscle
2. Cardiac muscle
3. Exocrine glands

SENSORY INPUT TO ANS:

Visceral afferents:
- mechanical, thermal, pain
Central influences over the ANS:

Hypothalamus – head ganglion
Brainstem and spinal cord – mediate ANS reflexes

Two (three) divisions of the ANS:
Sympathetic division (SNS)
Parasympathetic division (PNS)
(Enteric division)

Output or efferent pathway of the ANS compared to somatic motor system
Preganglionic neurons are located in the central nervous system.
Postganglionic neurons are located outside of the central nervous system.

**LOCATION OF POSTGANGLIONIC NEURONS:**
- **SYMPATHETIC DIVISION -** PARAVERTEBRAL GANGLION NEAR THE SPINE
- **PARASYMPATHETIC DIVISION -** PREVERTEBRAL GANGLIA NEAR THE EFFECTOR ORGAN

**Neurotransmitters:**
- **Pre to postganglionic synapse:**
  - SNS: Acetylcholine (n)
  - PNS: Acetylcholine (n)
- **Postgang. to effector:**
  - SNS: ACh (m), NE (alpha 1 and 2), NE (beta 1 and 2)
  - PNS: ACh (m)
### ACTIONS ON THE EFFECTOR ORGANS

<table>
<thead>
<tr>
<th>Organ</th>
<th>Function</th>
<th>Sympathetic effect (receptor)</th>
<th>Parasympathetic effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye</td>
<td>Diameter</td>
<td>Increase (alpha 1)</td>
<td>Decrease</td>
</tr>
<tr>
<td></td>
<td>Curvature of lens</td>
<td>Increase</td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>Rate</td>
<td>Increase (beta 1)</td>
<td>Decrease</td>
</tr>
<tr>
<td></td>
<td>Contraction</td>
<td>Increase (beta 1)</td>
<td></td>
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<tr>
<td>Blood Vessels</td>
<td>Vasoconstriction</td>
<td>Increase (alpha 1)</td>
<td></td>
</tr>
<tr>
<td>Lungs</td>
<td>Bronchial Diameter</td>
<td>Increase (beta 2)</td>
<td>Decrease</td>
</tr>
<tr>
<td>Sweat Glands</td>
<td>Production of sweat</td>
<td>Increase (Ach m)</td>
<td></td>
</tr>
<tr>
<td>Salivary Glands</td>
<td>Thick secretion</td>
<td>Increase (Alpha 1)</td>
<td></td>
</tr>
<tr>
<td>Adrenal medulla</td>
<td>Thin, watery secretion</td>
<td>Increase</td>
<td></td>
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<tr>
<td>Gastrointestinal Tract</td>
<td>Peristalsis</td>
<td>Decrease</td>
<td>Increase</td>
</tr>
<tr>
<td></td>
<td>Secretions</td>
<td>Decrease</td>
<td>Increase</td>
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<tr>
<td>Bowel/Bladder</td>
<td>Emptying</td>
<td>Decrease</td>
<td>Increase</td>
</tr>
<tr>
<td>External Genitalia</td>
<td>Erection of penis or clitoris</td>
<td>Increase</td>
<td></td>
</tr>
</tbody>
</table>

### MICTURITION REFLEX

An example of an ANS reflex that involves several different parts of the nervous system

Adequate stimulus for micturition:

Intravesicular pressure

*Lundy Ekman, 2007 Fig 12-16*
PNS controls voiding. PNS output leads to contraction of the detrusor muscle.

SNS prevents voiding:
1. Inhibits PNS pre to post synapse
2. Inhibits detrusor muscle
3. Contracts internal sphincter

Somatic motor system controls the external sphincter, prevents voiding.
Central influences to influence voiding:
e.g. Facilitates emptying
1. Inhibit SNS preganglionic neurons
2. Excite PNS preganglionic neurons
3. Inhibit somatic motor neurons

EFFECT OF LESIONS OF THE SPINAL CORD

1. Lesion of sacral spinal cord:
   - No PNS elicited contraction, flaccid bladder
   - No central control of external sphincter
2. Lesion of above sacral spinal cord
   - No sensation
   - Reflex control of the bladder
   - No central control of external sphincter
   - No central facilitation of emptying

CIRCULATORY SYSTEM
The circulatory system as a hydraulic circuit

The relationship of flow (Q), pressure (P), and resistance (R) as it pertains to blood flow:

\[ Q = \frac{(P_1 - P_2)}{R} \]

or

\[ P_1 - P_2 = QR \]

\[ P_1 = \text{pressure at end 1 of tube} \]

\[ P_2 = \text{pressure at end 2 of tube} \]

Disproportionate role of vessel diameter:

\[ R = \frac{8L}{\pi n^4} \]

\[ L = \text{length of tube} \]

\[ n = \text{viscosity} \]

\[ r = \text{radius of tube} \]
Heart (pump):
- Blood flow through the heart
- Driving force is pulsatile
  - Diastole – during relaxation
  - Systole – during contraction

Arteries (distribution system)
- Wall composition:
  - Elastin
  - Collagen
  - Smooth muscle
- Function:
  - Store pressure

Terminal arteries/arterioles (resistance arteries)
- Wall composition:
  - Smooth muscle
  - Elastin
  - Collagen
- Function:
  - Regulate peripheral resistance
  - \[ R = 8Lr^4 \]
Mechanisms that control arteriolar tone (diameter):

**Neural mechanisms:**
- Vasoconstriction: sympathetic activation
- Vasodilation: mostly passive

**Local factors:**
- Release of vasodilators (adenosine)
- Vasodilation with exercise

**Humoral factors:**
- Vasoconstriction: epinephrine, angiotensin, vasopressin
- Vasodilation: bradykinin, histamine, prostaglandins

---

**Arterioles have a high degree of resistance to flow**

\[ Q = \frac{(P_1 - P_2)}{R} \]

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**Capillaries (exchange system)**

- Large cross-sectional area
- Wall composition:
  - single layer of endothelial cells and basement membrane
- Exchange of substances:
  - Diffusion: lipid soluble (O\(_2\), CO\(_2\))
  - Ultrafiltration: water soluble (ions)
  - Pinocytosis: large substances
Resistance in capillaries is low and flow velocity is low

Microcirculation
- Microcirculation occurs in capillaries
- Balance of filtration and reabsorption
- Driving forces:
  - Hydrostatic pressure
  - Oncotic pressure
- Driving forces are in both capillary and tissue

Filtration
- Capillary hydrostatic pressure
- Tissue oncotic pressure

Schmidt and Thews, 1983  Fig 17-1
Absorption
Capillary oncotic pressure
Tissue hydrostatic pressure
Capillary
Arterial end 25 mm Hg Venous end

Balance of Filtration and Absorption
Filtration Absorption
Capillary
Arterial end 25 mm Hg Venous end

The lymphatic system
Thin walled, closed end vessels that drain into venous system interrupted by lymph nodes
Lymph vessel
Proteins
Capillary
Arterial end Venous end
**Edema: excess interstitial fluid**

Causes of edema: Disruption of driving forces

- Increased oncotic pressure in interstitial fluid due to proteins collected in interstitial space
  - Lymph system blockage
- Decreased oncotic pressure in the blood due to loss of proteins
  - Albumin loss in extensive burns
  - Albumin loss in kidney disease
  - Nutritional cause
- Increased hydrostatic
  - Venous obstruction
  - Arteriolar dilation

---

**Veins (collection system)**

Wall composition:
- thin walled
- elastin
- smooth muscle

Function:
- Store volume
- Distendable, compliant

---

**Veins store volume**

*Schmidt and Thews, 1983* Fig 18-1

*Mohrman & Heller, 2006* Fig 6-5
Factors controlling venous pressure

1. Venous tone:
   - Dilated at rest
   - Venocontriction: Sympathetic NS

2. Arterial resistance:
   - Constriction: reduces volume and pressure
   - Dilation: increases volume and pressure

3. Venous pump:
   - Squeezing action of skeletal muscle
   - Role of venous valves

4. Respiratory pump:
   - Inspiration decreases pressure in large veins in chest
   -Expiration increases pressure in large veins in chest

ELECTRICAL EVENTS OF THE CARDIAC CYCLE

Anatomical components of the heart

Chambers
- Atria, ventricles

Separation of chambers
- Atrioventricular ring

Valves
- Four valves in AV ring

Muscle fibers
- Working, contractile muscle
- Conductive muscle
Electrical characteristics of cardiac muscle fibers.

**Atrial and ventricular (working) muscle**

Resting membrane potential:
- inside negative 85-90 mV and stable due to potassium current

Action potential:
- rapid rise due to sodium current
- plateau due to calcium current increase and potassium decrease
- repolarization due to potassium current

**Conductive muscle**

Resting membrane potential:
- less negative - potassium current dependent, unstable – sodium and calcium leakage

Action potential:
- slow rise, no plateau
- calcium current increase and potassium decrease
- repolarization – potassium current
Pacemaker potential:

Unstable resting membrane potential of conductive muscle leads to spontaneous depolarization and generation of action potential.

Sinoatrial node reaches threshold for action potential first and normally controls the rhythm of contraction of the heart.

Syncitial connection and spread of excitation through the heart:

Propagation of electrical activity through the heart:
SA node - fast
Atria - slow
AV node - slower
Bundle of His – fast
Bundle branches – fast
Purkinje fibers – fast
Ventricles – slow
Repolarization is the reverse
Influence of the autonomic nervous system on cardiac muscle cells

SNS (beta 2) increases HR: increases Na⁺ and Ca²⁺ permeability and increases slope of depolarization.

PNS (Ach) decreases HR: increases K⁺ permeability and increases hyperpolarization.

Electrocardiogram:
Field potential caused by the electrical activity of the heart recorded from the surface of the body

P wave: Atrial depolarization

QRS: ventricular depolarization

T: ventricular repolarization

ST: ventricular excitation
Electrocardiogram and Diagnosis of Electrical Abnormalities and Arrhythmias:

**Supraventricular Abnormalities:**
- Bradycardia: slowed HR, insufficient cardiac output
- Tachycardia: high HR, insufficient filling time
- Conduction blocks: occur at AV node
  - First-degree heart block
  - Second-degree heart block
  - Third degree heart block
- Atrial fibrillation: loss of synchrony

**Ventricular Abnormalities:**
- Ventricular tachycardia: driven by ectopic focus
- Ventricular fibrillation: loss of synchrony

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**MECHANICAL EVENTS OF THE CARDIAC CYCLE**

**Heart valves:**
- AV valves:
  - mitral (left)
  - tricuspid (right)
- Semilunar:
  - aortic (left)
  - pulmonic (right)

**Diastole:**
- Relaxation
- Begins with mitral opening
- Ends with start of ventricular contraction

**Systole:**
- Contraction
- Begins with start of ventricular contraction
- Ends with mitral opening

Mohrman & Heller, 2003 Fig 1-4
**Heart sounds**

Caused by closure and vibration of valves

- **First sound (S1):** closure of AV valves
- **Second sound (S2):** closure of semilunar valves
- **Third sound:** in children, filling of ventricle

---

**Pathological conditions detected by heart sounds**

**Valvular stenosis**
- narrowing of valve opening
- occurs when valve becomes thickened or calcified
- prevents normal blood flow and leads to backup

**Valvular insufficiency**
- incomplete closure of valve
- abnormal valve structure
- leads to regurgitation or backflow

---

**Pathological conditions detected by heart sounds**

- **Systolic murmurs:**
  - Aortic (pulmonic) stenosis
  - calcific degeneration, aging
  - left ventricle hypertrophy
  - Mitral insufficiency
  - regurgitation into left atrium

- **Diastolic murmurs:**
  - Mitral (tricuspid) stenosis
  - common, nearly always rheumatic
  - blood backs up in left atrium
  - Aortic insufficiency
  - regurgitation from aorta to left ventricle
Cardiac output

\[ C.O. = \text{Heart rate} \times \text{Stroke volume} \]

Regulation of heart rate

Heart rate without external influence: 100 beats/min

Parasympathetic influences:
- Decrease HR
- Reduce PNS – increase HR to 100 beats/min

Sympathetic influence:
- Increase HR
- Increases over 100 beats/min
- With increased HR there is less time for filling

Regulation of stroke volume

Cardiac cycle

[Diagram of cardiac cycle]
**Determinants of stroke volume: Preload and Afterload**

*Preload (Frank-Starling Law):*
- degree of filling of ventricles
- increased filling leads to increased contraction

*Afterload (arterial pressure):*
- Resistance the ventricle must overcome
- Ventricle must develop pressure that exceeds arterial pressure

Morhman & Heller, 2003, Fig 3-5b and 3-6b

**Determinants of stroke volume: Force of contraction:**

Sympathetic NS increases Ca++ permeability in sarcoplasmic reticulum and leads to increased contractility

Morhman & Heller, 2003, Fig 3-7b

**Relationship between cardiac output and venous return**

Cardiac output:
- Filling is proportional to central venous pressure (CVP)
- Increase in CVP leads to increased cardiac output

Peripheral venous pool → Central venous pool → Heart

PVP → CVP → Cardiac output
Relationship between cardiac output and venous return

Venous return = Peripheral Venous Pressure (PVP) – CVP

If PVP constant, increased CVP leads to decreased VR
If CVP constant, increased PVP leads to increased VR

Venous return CVP

Venous return

PVP

CVP

Heart

Peripheral venous pool

Central venous pool

Venous volume:
Blood volume
Arterial resistance
Venous pump
Respiratory pump
Venous Tone
Dilated at rest
SNS venoconstriction

INTERACTION OF CARDIAC OUTPUT AND VENOUS RETURN: Equilibrium

FAMILY OF CARDIAC OUTPUT AND VENOUS RETURN CURVES: blood volume, SNS influence
CARDIOVASCULAR CONTROL MECHANISMS

Relationship between blood pressure, cardiac output, and peripheral resistance:

Arterial Blood Pressure (BP)
= cardiac output X peripheral resistance
= heart rate X stroke volume X peripheral resistance

Short term regulation: Baroreceptor reflex

Sensory receptors:
Baroreceptors located in aortic arch and carotid sinus
Adequate stimulus: pressure
Nervous innervation:
Afferent pathway over IX and X cranial nerves (glossopharyngeal and vagus)
Action potentials increase with increased blood pressure
Brain areas involved:
Cardiovascular integrating centers in the medulla
Output to SNS and PNS
For example:
Decrease arterial pressure:
decreased baroreceptor activity
decreased activity in IX and X
increase output to SNS
decrease output to PNS
increase HR
increase ventricular contraction
increase vasoconstriction
increase venoconstriction

Long term regulation of blood pressure
Arterial pressure directly related to blood volume:
Peripheral venous pool proportional to blood volume
Venous return proportional to PVP
Cardiac output proportional to venous return
Arterial pressure proportional to cardiac output
Blood volume is proportional to urine output
Urine output = glomerular filtration – reabsorption

Cardiac Output
Venous Return
Peripheral venous pool
Central venous pool
Heart:
BP = HR x SV x R

Long term regulation
Arterial pressure and glomerular filtration
Filtration directly related to arterial pressure
Filtration is inversely related to renal vasoconstriction
Long term regulation
Arterial pressure and fluid reabsorption

Reabsorption is proportional to sodium retention. Sodium is pumped out of renal tubules back into the capillaries.

Long term regulation
Regulation of sodium retention:
Renin is released from the kidney into the circulation in response to:
- SNS stimulation of kidney
- Low glomerular filtration

Renin is converted to angiotensin in the blood
Angiotensin releases aldosterone from the adrenal gland
Aldosterone regulates sodium retention in the kidney

THE CARDIOVASCULAR SYSTEM
AND HOMEOSTATIC DISTURBANCES
Exercise

Circulatory adjustments

Oxygen utilization: quantification of exercise $\text{VO}_2$

Physiological mechanisms for increasing oxygen utilization:
- Heart rate
- Stroke volume
- Arteriovenous oxygen difference: extraction of $\text{O}_2$
Cardiac output increases proportional to VO\textsubscript{2} and is similar in fit and unfit individuals.

Heart rate increases in both fit and unfit individuals.

Stroke volume does not change appreciably in either fit or unfit individuals but is larger if fit individuals.

O\textsubscript{2} extraction same for fit and unfit individuals.

Acute exercise: HR
Training: stroke volume

Postural hypotension:
Decreased arterial pressure when proceeding from a recumbent to standing or sitting position

What happens to blood when standing?
What mechanism corrects for this?
What mechanisms assist the venous system in returning blood to the heart?
How is the response to postural hypotension altered by spinal cord injury?

If lesion below T6, regulation is normal.
If lesion is above T6, regulation is abnormal.

CIRCULATORY SHOCK

Insufficient cardiac output to maintain adequate tissue nutrition

1. Cardiogenic shock (myocardial failure)
   Cardiac disorder
   Myocardial contraction failure
   Filling or emptying disorder
   Extracardiac disorder
   Chronic high blood pressure
   Chronic increased venous return

2. Hypovolemic shock (fluid loss)
   Hemorrhage (whole blood)
   Plasma loss (intestinal obstruction, burns, dehydration)

3. Low resistance shock (decreased peripheral R)
   Neurogenic (loss of sleep, brain damage, anesthesia)
   Septic (endotoxins from bacteria)
   Anaphylactic (allergic reaction)
Compensatory mechanisms

Short term:
Decreased arterial pressure
initiates baroreceptor reflex

Treatment
- Fluid loss: replacement
- Low R: sympathomimetics
- Recumbent posture to promote
veinous return

RESPIRATORY PHYSIOLOGY AND PATHOPHYSIOLOGY

Respiration During Exercise

- \( O_2 \) consumption increases linearly with work
- Cardiac output is proportional to \( O_2 \) consumption
Respiration During Exercise

- O₂ consumption increases linearly with work
  - 300 to 3500 l/min
- Cardiac output is proportional to O₂ consumption
  - 5 to 25 l/min
- Ventilation increases linearly until blood lactate increases
  - 10 to 150 l/min
- Cardiac output does not increase as much as ventilation

Mechanics of Ventilation

Inspiration:
- Quiet breathing: diaphragm (C3-C5/phrenic n.) - downward
  external intercostals (thoracic) - upward
- Heavy breathing: increase diaphragm, intercostals and scalenes and sternocleidomastoid (Sp Acc N)

Expiration:
- Quiet breathing: diaphragm relaxes, elastic recoil
- Heavy breathing: abdominal muscles (lower thoracic) internal intercostals

Air flow in and out of lungs

- Boyle’s Law: Pressure in inversely related to volume.
- At rest, negative intrapleural pressure holds airways open
- Pneumothorax: Opening of the pleural cavity to atmospheric pressure.
- As thoracic cavity expands, intrapleural pressure decreases, intraalveolar pressure decreases.
- As thoracic cavity recoils, intrapleural pressure lessens and intraalveolar pressure lessens.
- With forced contraction and high intrapleural pressure, airways can collapse.

Role of surfactants and alveoli distension
- Compliance: expression of expandability
Respiratory passageways

Lung volumes
Anatomic dead space
Physiologic dead space

Clinical measures of ventilation

• Volumes
  Tidal (TV) – normal breathing
  Residual (RV) – gas remaining after forced expiration

• Capacities
  Vital (VC) – expired amount after maximum inspiration/expiration
  Total lung (TLC) = VC + RV
  Functional residual (FRC) – gas after normal expiration
Clinical measures of ventilation

- Forced expiration volume
  - Measures rate of flow

Changes in Ventilation in Spinal Cord Injury

- SCI causes restrictive changes in ventilation
- Decreased VC, FRC, TLC, FEV1
- Severity of changes depends on level of injury
  - Cervical 1,2: paralysis of respiratory muscles
    - minimal VC, no cough
  - Cervical 3 to 6: diaphragm intact, no intercostals, no abdominal
    - reduced VC ineffective cough
  - High thoracic: diaphragm and some intercostals intact, no abdominal
    - reduced VC, weak cough
  - Low thoracic: diaphragm, intercostals, some abdominal intact
    - improving function

Respiratory capillaries

- Pulmonary arteries are more compliant than systemic
- Numerous - when distended form a near continuous "sheet" of blood
- Respiratory wall has several layers (epithelium, basement membranes, interstitial space, capillary wall) but is quite thin 2-6 microns
Gas exchange

- Physics of diffusion
  - Pressure is related to the force that molecules exert on the walls of their container
  - Diffusion
    - Random movement of molecules
    - Higher concentration to lower
  - Rate of diffusion depends on
    - Concentration
    - Area of membrane
    - Thickness of membrane
    - Diffusion coefficient – directly related to solubility, inversely related to square root of molecular wt.

Partial pressure

- Mixture of gases – each gas exerts a partial pressure proportional to its fraction
- Total pressure sum of individuals
  - At sea level total pressure of air is 760 mmHg
  - Oxygen is 21% of air and therefore exerts (0.21 x 760 mmHg) 160 mmHg partial pressure
- Vapor pressure - water molecules in a gas exerts pressure – 47 mmHg
  - Partial pressure of oxygen is reduced by vapor pressure

Table of partial pressures

<table>
<thead>
<tr>
<th>Gas</th>
<th>Atmospheric air</th>
<th>Alveolar air</th>
<th>Pulmonary arterial blood</th>
<th>Pulmonary venous blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrogen</td>
<td>597 mmHg</td>
<td>569 mmHg</td>
<td></td>
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<tr>
<td>Oxygen</td>
<td>159 mmHg</td>
<td>104 mmHg</td>
<td>40 mmHg</td>
<td>100 mmHg</td>
</tr>
<tr>
<td>Carbon Dioxide</td>
<td>0.3 mm Hg</td>
<td>40 mmHg</td>
<td>46 mmHg</td>
<td>0 mmHg</td>
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<tr>
<td>Water</td>
<td>Variable</td>
<td>Variable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>760 mm Hg</td>
<td>760 mmHg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Transport of gas in blood - oxygen

- Normally by hemoglobin, slightly dissolved in blood
- Combines with heme portion of hemoglobin
- Factors affecting $O_2$ affinity to hemoglobin
  - pH
  - Temperature
  - $CO_2$
- Decreased affinity in muscle (right shift)
  - low pH, high $CO_2$, high temperature

Transport of gas in blood – $CO_2$

- By combination with proteins (carbaminohemoglobin)
- Slightly dissolved in blood
- Mostly by bicarbonate ion
  \[ CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^- \]
- $CO_2$ combines with water to form carbonic acid which dissociates to hydrogen ion and bicarbonate
- Rapid in red blood cells - enzyme carbonic anhydrase

Normal physiology – high altitude (hypoxia)

- Lower $O_2$ in air
- Lower $O_2$ in alveoli
- Lower $O_2$ in tissue
- Counteract with hyperventilation
Hyperventilation and CO₂

Hyperventilation reduces CO₂ in alveoli
Reducing CO₂ alters acid – base balance
Normal pH is 7.4
Acids formed by metabolism are carbonic, lactic, acetic, phosphoric, uric
Alteration in hydrogen concentration (pH) alters chemical reaction in all cells
1. Acidosis - coma
2. Alkalosis - tetany or convulsions

Regulation of acid – base balance: CO₂ and bicarbonate ion

pH results from solution of CO₂ in blood and dissociation of carbonic acid

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

Henderson- Hasselbalch equation:

\[
pH = pK_a + \frac{[\text{HCO}_3^-]}{0.030 \text{ P CO}_2} \quad \text{Bicarbonate regulated by kidney}
\]

\[
\text{pH} = pK_a + \frac{[\text{HCO}_3^-]}{0.030 \text{ P CO}_2} \quad \text{CO}_2 \text{ regulated by lung}
\]

Respiratory Alkalosis

\[ \uparrow \text{pH} = pK_a + \frac{[\text{HCO}_3^-]}{0.030 \text{ P CO}_2} \downarrow \text{Hyperventilation} \]

Examples:
- high altitude
- anxiety
- over ventilation during anesthesia

Compensation: Kidney eliminates bicarbonate in urine
Respiratory Acidosis

\[ pK_A + \frac{[HCO_3^-]}{0.030 \times P_{CO_2}} \]  

[Increased plasma bicarbonate levels]  

Examples:
- Barbiturate overdose
- Ventilation-perfusion ratio inequality as in COPD

Compensation: Kidney retains bicarbonate

Metabolic Acidosis

\[ pK_A + \frac{[HCO_3^-]}{0.030 \times P_{CO_2}} \]  

[Decreased plasma bicarbonate levels]  

Examples of accumulation of acids in blood:
- Uncontrolled diabetes mellitus
- Tissue hypoxia releases lactic acid

Compensation: Respiratory compensation (hyperventilation)

Metabolic Alkalosis

\[ pK_A + \frac{[HCO_3^-]}{0.030 \times P_{CO_2}} \]  

[Increased plasma bicarbonate levels]  

Examples:
- Ingestion of alkalis
- Loss of acid gastric secretion (e.g. prolonged vomiting)

Compensation: Slight respiratory compensation (hypoventilation)
Control of ventilation

Central nervous system controller

- Brainstem: collection of areas controlling aspects of respiration
  - Dorsal medulla: inspiration
  - Ventral medulla: expiration
  - Upper pons: pneumotaxic area shuts off inspiration
- Cortex: voluntary control of breathing

Sensors

- Central chemoreceptors: near ventral surface of medulla
  - Surrounded by cerebrospinal fluid
    - Blood brain barrier blocks H+ but allows CO2
    - Respond to H+ concentration
      - Hypercapnia: high CO2 (high H+) stimulates breathing
- Peripheral chemoreceptors
  - Located in carotid bodies (also in aortic bodies)
  - Sense low O2: rapid response, responsible for response to arterial hypoxemia
  - Sense CO2 but response is less than CNS response
- Mechano receptors: located in lungs
  - Stretch receptors sense lung expansion – inhibit inspiration
  - Irritant receptors in airways – elicit bronchoconstriction and increased ventilation
Control of ventilation

1. CO₂ – most important factor, normally arterial P CO₂ held to within 3 mm Hg
2. O₂ – relatively minor control under normal circumstances, ventilation doesn’t increase until P O₂ less than 50 mm Hg
3. pH – reduced pH in pathological conditions increases ventilation.

Obstructive Airway Disease

Chronic obstructive pulmonary disease (COPD)
Asthma

COPD
(chronic obstructive pulmonary disease)

Symptoms:
- Shortness of breath
- Poor exercise tolerance
- Persistent cough
- Barrel chested
- Accompanying bronchitis
**COPD**
(chronic obstructive pulmonary disease)

Pathology:
- Emphysema characterized by enlarged air spaces distal to terminal bronchioles with breakdown of alveolar walls.
- Chronic bronchitis characterized by inflammation of bronchial wall and excessive mucous production.

**West, 2007, Fig 3-2**

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**COPD**
(chronic obstructive pulmonary disease)

Lung volumes:
- Vital capacity decreased
- FRC and TLC increased
- Increased compliance
- Reduced elastic recoil

<table>
<thead>
<tr>
<th>Lung Capacity</th>
<th>Observed</th>
<th>Predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC</td>
<td>3.3</td>
<td>4.8</td>
</tr>
<tr>
<td>FRC</td>
<td>6.5</td>
<td>3.7</td>
</tr>
<tr>
<td>TLC</td>
<td>8.1</td>
<td>7.1</td>
</tr>
</tbody>
</table>

**West, 2007, Fig 3-13**

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**COPD**
(chronic obstructive pulmonary disease)

Ventilation-perfusion inequality

**West, 2007, Fig 3-18**
Asthma

Symptoms:
- Shortness of breath
- Wheezing
- Cough
- Poor exercise tolerance

Measures of forced expiration are reduced
- FEV1
- Static lung volumes are increased
  - TLC
  - FRC
  - RV

Treatment:
- Bronchodilators
- Anticholinergics
- Leukotriene blockers

Restrictive lung disease: Pulmonary fibrosis

Symptoms:
- Dypnea
- Reduced exercise tolerance
- Small lungs, reduced compliance
Restrictive lung disease: Pulmonary fibrosis

- Reduced lung volumes
- VC
- FRC
- TLC
- FVC
- FEV 1 – rapid expiration

West, 2007, Fig 3-13

Restrictive lung disease: other examples

- Destruction of lung tissue
  - Pulmonary fibrosis
  - Silicosis
  - Asbestosis
- Reduced expansion of rib cage
  - Kyphosis
  - Scoliosis
  - Fibrotic pleurisy
  - Paralyzed or fibrotic muscles