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Chapter 17: Blood Gases, pH, and Buffer Systems

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Definitions: Acid, Base, Buffer

- **Acid:** a substance that can yield a hydrogen ion (H) or hydronium ion when dissolved in water
- **Base:** a substance that can yield hydroxyl ions (OH^-)
- **Dissociation constant** (ionization constant K value): describes relative strengths of acids & bases
- **pK:** negative log of ionization constant & pH in which protonated & unprotonated forms are present in equal concentrations
- **Buffer:** combination of weak acid or weak base & its salt; a system that resists changes in pH
- Carbonic acid-bicarbonate with a pK of 6.1 is the principle buffering system in the blood

Acid–Base Balance

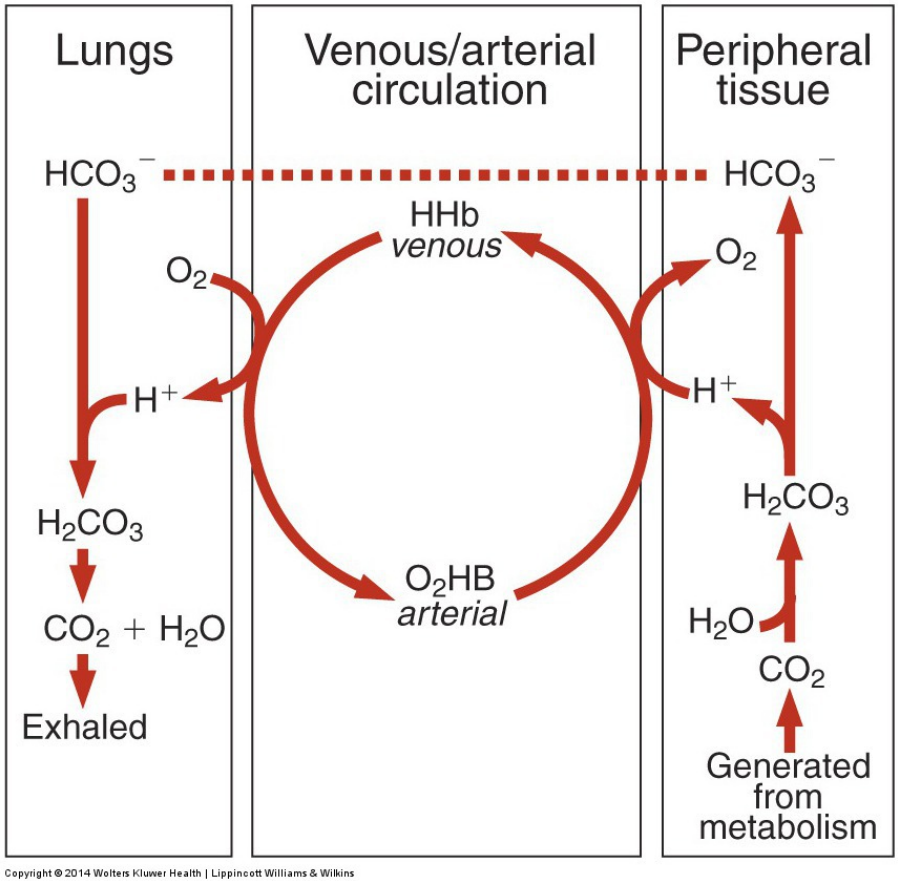
- Maintenance of H^+
  - Normal concentration of H in extracellular body fluid ranges from 36 to 44 nmol/L, but body produces much greater quantities of H.
  - Via lungs & kidneys, body controls & excretes H to maintain pH homeostasis.
  - **Acidosis:** a pH level below reference range (<7.34)
  - **Alkalosis:** a pH level above reference range (>7.44)

Acid–Base Balance (cont'd)

- Buffer Systems: Regulation of H^+
  - Buffer systems are body's first line of defense against extreme changes in H concentration.
  - All buffers consist of a weak acid & its salt or conjugate base.
  - Bicarbonate-carbonic acid system has low buffering capacity, but is still important buffer for 3 reasons:
    - 1. H_2CO_3 dissociates into CO_2 and H_2O, allowing CO_2 to be eliminated by lungs and H as water.
    - 2. Changes in CO_2 modify ventilation (respiration) rate.
    - 3. HCO_3^- concentration can be altered by kidneys.
  - Other buffers: phosphate system & plasma protein (imidazole side chain of His residues)

Regulation of Acid-Base Balance

- Interrelationship of bicarbonate & hemoglobin buffering systems



Regulation of Acid-Base Balance

- Decreased ventilation – lungs do not remove CO_2 as much as it is produced (acidosis)
- Hyperventilation – lungs remove CO_2 faster than it is produce causing alkalosis
- *The lungs and the buffering systems work within seconds to maintain acid-base homeostasis*
- The kidneys can excrete acids and bases ➔ important for acid-base regulation
- Main role is to reabsorb HCO_3^- in the proximal tubules

Acid–Base Balance (cont'd)

- Regulation of Acid–Base Balance: Lungs and Kidneys
  - **Lungs:** Ventilation affects pH of blood.
    - O_2 is inspired & diffuses from alveoli into blood.
    - CO_2 diffuses into alveoli from blood & is eliminated via ventilation.
    - Result is minimal change in H concentration between venous & arterial circulations.
  - **Kidneys:** regulate acid–base balance by excreting acids or bases
    - HCO_3^- is reclaimed from glomerular filtrate to prevent excessive acid gain in blood from loss of HCO_3^- in urine.

TABLE 17-1	ARTERIAL BLOOD GAS REFERENCE RANGE AT 37°C
pH	7.35–7.45
pCO_2 (mm Hg)	35–45
HCO_3^- (mmol/L)	22–26
Total CO_2 content (mmol/L)	23–27
pO_2 (mmol/L)	80–110
SO_2 (%)	>95
O_2Hb (%)	>95

Assessment of Acid–Base Homeostasis

- Bicarbonate Buffering System and the Henderson-Hasselbalch Equation
  - Measurement of components of bicarbonate buffering system provides information on other buffers & systems that regulate production, retention, & excretion of acids & bases.
  - Henderson-Hasselbalch equation expresses acid–base relationships:
  - pH = p*K'* + log cA^-/cHA

$$pH = pK_a' + \log \frac{cHCO_3^-}{0.0307 \times pCO_2}$$

Assessment of Acid–Base Homeostasis (cont'd)

- Acid–Base Disorders: Acidosis and Alkalosis
  - **Acidemia:** excess acid or H concentration (pH < reference range)
  - **Alkalemia:** excess base (pH > reference range)
  - **Nonrespiratory acidosis:** decrease in bicarbonate resulting in decreased pH
  - **Respiratory acidosis:** decrease in alveolar ventilation, causing decreased elimination of CO_2 by lungs
  - **Nonrespiratory alkalosis:** gain in HCO_3^-, causing increase in pH
  - **Respiratory alkalosis:** increase in alveolar ventilation, causing excessive elimination of CO_2 by lungs

Assessment of Acid–Base Homeostasis (cont'd)

- Acid–Base Disorders: Acidosis and Alkalosis
  - **Compensation** – the body responds to pathological conditions by altering the factor not primarily affected by the pathologic process
  - Lungs compensate for nonrespiratory problems rapidly, but the response is short term and often incomplete
  - Kidneys respond to respiratory acidosis or alkalosis slowly (2-4 days), but the response is long term and potentially complete
  - *Fully compensated* – pH returned to normal (20:1 ratio)
  - *Partially compensated* – pH is approaching normal
  - *While compensation may successfully return the ratio to the normal 20:1, the primary abnormality is not corrected.*

CASE STUDY 17-1

A 50-year-old man came to the emergency department after returning from foreign travel. His symptoms included persistent diarrhea (over the past 3 days) and rapid respiration (tachypnea). Blood gases were drawn with the following results:

pH	7.21
pCO_2	19 mm Hg
pO_2	96 mm Hg
HCO_3^-	7 mmol/L
SO_2	96% (calculated) (reference range, >95%)

Question

1. What is the patient's acid–base status?
2. Why is the HCO_3^- level so low?
3. Why does the patient have rapid respiration?

1. Nonrespiratory acidosis

2. Persistent diarrhea causes significant loss of HCO_3^-

3. The patient's rapid respirations reflect a compensatory mechanism to decrease the PCO_2 level and restore the 20:1 ratio (HCO_3^-/PCO_2) and the pH to 7.4.

Assessment of Acid–Base Homeostasis (cont'd)

- **Primary Nonrespiratory Acidosis**
  - Decrease in bicarbonate (<24 mmol/L), resulting in a decreased pH
  - May be caused by:
    - direct administration of an acid-producing substance ($CaCl_2$, NH_4Cl)
    - excessive formation of organic acids as seen with diabetic ketoacidosis and starvation
    - reduced excretion of acids
    - excessive loss of bicarbonate from diarrhea or vomiting

$$\text{pH} \propto \frac{\downarrow c\text{HCO}_3^-}{N(0.0307 \times p\text{CO}_2)} < \frac{20}{1}$$

  - Hyperventilation *compensates* this problem by "blowing off" CO_2
  - The base-to-acid ratio will return toward normal.
  - Secondary compensation occurs when the "original" organ (the kidneys) begins to correct the ratio by retaining bicarbonate.

Assessment of Acid–Base Homeostasis (cont'd)

- **Primary Respiratory Acidosis**
  - A decrease in alveolar ventilation (hypoventilation), causing a decreased elimination of CO_2 by the lungs:

$$\text{pH} \propto \frac{\downarrow cHCO_3^-}{N(0.0307 \times pCO_2)} < \frac{20}{1}$$

  - Many lung diseases may cause defective CO_2 removal from the blood
  - **Chronic obstructive pulmonary disease (COPD):** destructive changes in the airways and alveolar walls increase the size of the alveolar air spaces, with the resultant reduction of the lung surface area available for gas exchange ➔ CO_2 is retained in the blood, causing chronic hypercarbia
  - **Bronchopneumonia:** gas exchange is impeded because of the secretions, white blood cells, bacteria, and fibrin in the alveoli.
  - **Barbiturates and morphine:** drugs that cause hypoventilation will increase blood pCO_2
  - **Mechanical obstruction or asphyxiation** and **decreased cardiac output**

Assessment of Acid–Base Homeostasis (cont'd)

- **Primary Respiratory Acidosis**
  - Compensation:
    - Nonrespiratory processes:
      - The kidneys increase the excretion of H^+ and increase the reclamation of HCO^{3-}.
      - Although the renal compensation begins immediately, it takes days to weeks for maximal compensation to occur.

Assessment of Acid–Base Homeostasis (cont'd)

- **Alkalosis**
  - Result from nonrespiratory and respiratory causes.
  - *Primary nonrespiratory alkalosis* results from a gain in HCO_3^-.
    - May result from:
      - Excess administration of sodium bicarbonate or bicarbonate-producing salts
      - Excessive loss of acid through vomiting, nasogastric suctioning, or prolonged use of diuretics that increase renal excretion of H^+
    - *Response: depressing the respiratory center (hypoventilation)*

Assessment of Acid–Base Homeostasis (cont'd)

- **Alkalosis**
  - *Primary respiratory alkalosis* results from an increased rate of alveolar ventilation ➔ excessive elimination of CO_2.
  - Causes:
    - Hypoxemia
    - Chemical stimulation of the respiratory center by drugs (salicylates)
    - Hysteria (hyperventilation)
  - *Compensation:* The kidneys compensate by excreting HCO_3^- in the urine and reclaiming H^+ to the blood
    - Treatment for hysterical hyperventilation, breathing into a paper bag

CASE STUDY 17-2

An 80-year-old woman fell on the ice and fractured her femur. After several hours, when she arrived at the emergency department, she was anxious, panting, and complaining of severe chest pain and not being able to breathe. Her pulse was rapid (tachycardia) as was her respiration rate (tachypnea). Blood gases were drawn and yielded the following results:

pH	7.31
pCO_2	27 mm Hg
pO_2	62 mm Hg
HCO_3^-	12 mmol/L
SO_2	78% (calculated) (reference range, >95%)

Question

1. What is the patient's acid–base status?
2. Why is the HCO_3^- level so low?
3. What caused the acid–base imbalance?

1. Partially compensated nonrespiratory acidosis

2. The HCO_3^- level is the primary contributor to nonrespiratory acidosis. The PCO_2 level is low as a result of the patient hyperventilating and blowing O_2 in an attempt to restore the 20:1 ratio and return the pH to 7.4.

3. Pulmonary fat emboli are a major, serious complication of long-bone fractures in the elderly. Tachycardia, tachypnea, and low PO_2 values, together with chest pain, are the classic signs. Globules of fatty marrow from the fracture enter small veins in the area of the fracture and travel to the lung, obstructing pulmonary circulation.

CASE STUDY 17-3

A 24-year-old graduate student was brought to the emergency department in a comatose state after being found unconscious in his room. A bottle of secobarbital was there on his bed stand. He did not respond to painful stimuli, his respiration was barely perceptible, and his pulse was weak. Blood gases were drawn and yielded the following results:

pH	7.10
pCO_2	70 mm Hg
pO_2	58 mm Hg
HCO_3^-	20 mmol/L
O_2Hb	80% (reference range, >95%)

Question

1. What is the patient's acid–base status?
2. What caused the profound hypoventilation?
3. Once the respiratory component returns to normal, what will be the patient's expected acid–base status?

1. Respiratory and nonrespiratory acidosis. Respiratory acidosis is indicated by elevated pCO_2; nonrespiratory acidosis is indicated by decreased HCO_3^-.

2. Secobarbital depresses the breathing center; consequently, CO_2 is not eliminated effectively and sufficient O_2 is not taken into the lungs.

3. Nonrespiratory acidosis. Appropriate ventilation will correct the respiratory component, returning pCO_2 and pO_2 to normal. The decreased HCO_3^- level will take longer to return to normal.

Oxygen and Gas Exchange

- Oxygen and Carbon Dioxide
  - 7 conditions necessary for adequate tissue oxygenation:
    1. Available atmospheric oxygen
       - Partial pressure of oxygen = (760 mm Hg – 47 mm Hg) × 20.93% = 149 mm Hg (at 37°C)
    2. Gas exchange between lungs & arterial blood
    3. Loading of O_2 onto hemoglobin
    4. Adequate hemoglobin
    5. Adequate transport (cardiac output)
    6. Release of O_2 to tissue

Oxygen and Gas Exchange

- Gas exchange between lungs & arterial blood
  - Thoracic cavity expands ➔ negative pressure ➔ air is moved into the lungs (many tracheal branches and alveoli)
  - At the beginning of inspiration, these airways are still filled with gas from the previously expired breath (dead space air) which dilutes the air being inspired.
  - Saturation with water vapor and warmed to 37°C ➔ pO_2 ~ 110 mm Hg
  - The fraction of inspired O_2 (FiO_2) can be increased by breathing gas mixtures up to 100% O_2 *(breathing more than 60% O_2 can be toxic to the lungs!)*

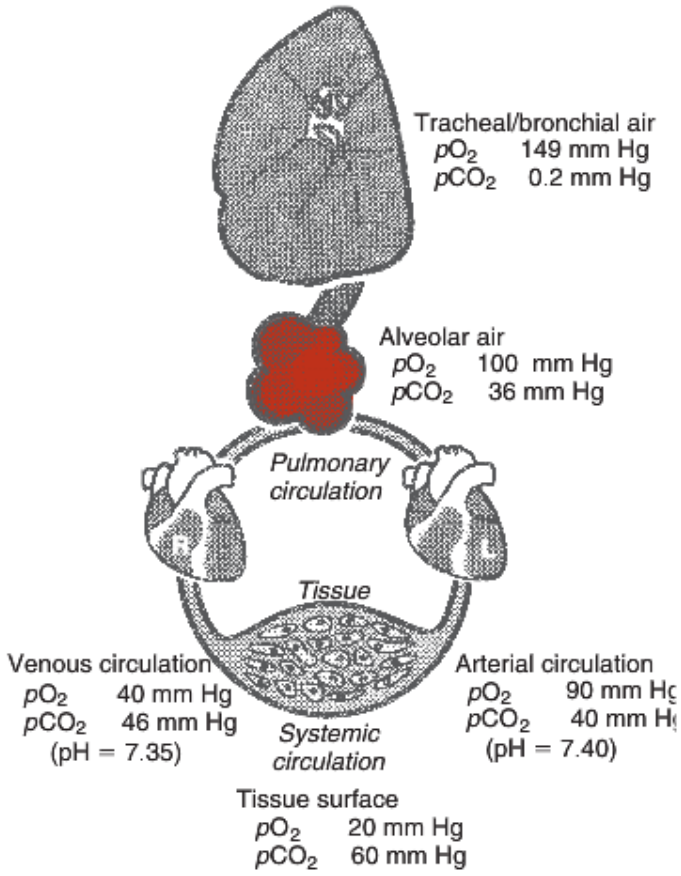


FIGURE 17-3 Gas content in lungs and pulmonary and systemic circulation.

Oxygen and Gas Exchange

- Factors affecting pO_2 in alveoli
  1. pO_2 in air
  2. pCO_2 in expired air (dead space air) which dilutes inspired O_2
  3. Ratio of inspired air volume to dead space air volume

- Clinical conditions can influence pCO_2 in the expired air
  - A patient with increased metabolism (e.g. hyperthermia) produces more CO_2 ➔ pCO_2 (in blood & expired gas) ⇧ ➔ inspired air will be diluted more
  - People with shallow breaths have less "fresh" air entering the lungs than those breathing deeply.

Oxygen and Gas Exchange (cont'd)

- Oxygen and Carbon Dioxide
  - Common factors influencing amount of O_2 that moves through alveoli into blood & then to tissue:
    1. Destruction of alveoli (e.g. emphysema)
    2. Pulmonary edema (fluid in the alveolar space increases distance between the alveoli and capillary walls and causing a barrier to diffusion)
    3. Airway blockage (e.g. Asthma and bronchitis)
    4. Inadequate blood supply (blockage in a pulmonary blood vessel (pulmonary embolism), pulmonary hypertension, or a failing heart)
    5. Diffusion of CO_2 and O_2 (O_2 diffuses 20 times slower than CO_2 ➔ hypoxemia can occur without problems to CO_2 excretion)

Oxygen and Gas Exchange (cont'd)

- Oxygen Transport
  - Most O_2 in arterial blood is transported to tissue by hemoglobin.
  - Blood hemoglobin exists in one of four conditions:
    1. **Oxyhemoglobin (O_2Hb):** O_2 reversibly bound to hemoglobin
    2. **Deoxyhemoglobin (HHb):** hemoglobin not bound to O_2 but capable of forming a bond when O_2 is available
    3. **Carboxyhemoglobin (COHb):** hemoglobin bound to CO
    4. **Methemoglobin (MetHb):** hemoglobin unable to bind O_2 because Fe is in an oxidized rather than reduced state. Fe^{3+} can be reduced by the RBC enzyme *methemoglobin reductase*

Dyshemoglobins

Oxygen and Gas Exchange (cont'd)

- Quantities Associated With Assessing a Patient's Oxygen Status
  - **Oxygen saturation (SO_2):** ratio of O_2 bound to hemoglobin, compared with total amount of hemoglobin capable of binding O_2 *(calculated, not accurate, ignores COHb and MetHb)*

$$SO_2 = \frac{cO_2Hb}{(cO_2Hb + cHHb)} \times 100$$

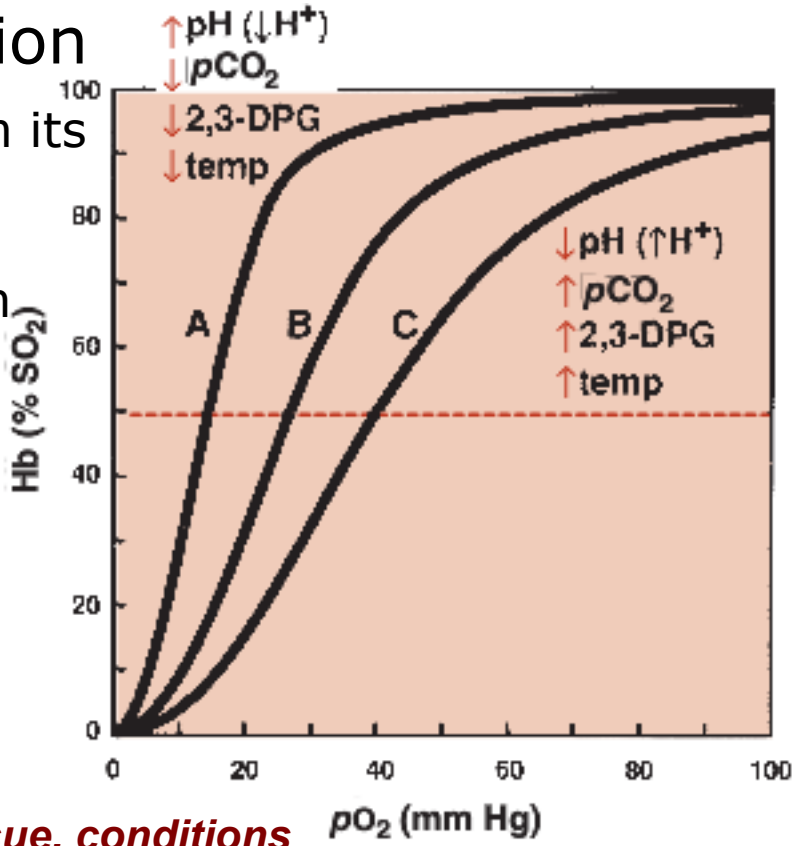
  - **Fractional oxyhemoglobin (FO_2Hb):** ratio of concentration of O_2Hb to concentration of total hemoglobin (*c*tHb)

$$FO_2Hb = \frac{cO_2Hb}{ctHb} = \frac{cO_2Hb}{cO_2Hb + cHHb + cdysHb}$$

  - **Trends in oxygen saturation:** assessed by transcutaneous, pulse oximetry (SpO_2). Pass light of two or more wavelengths through the tissue in the capillary bed of the toe, finger, or ear.
  - **Oxygen content:** total O_2 in blood; sum of O_2 bound to hemoglobin (O_2Hb) & amount dissolved in plasma (pO_2)

Oxygen and Gas Exchange (cont'd)

- Hemoglobin–Oxygen Dissociation
  - O_2 must be released at tissues from its carrier, hemoglobin.
  - Oxygen dissociates from adult (A_1) hemoglobin in characteristic fashion (S-shaped curve).
  - Shape of oxygen-dissociation curve & affinity of hemoglobin for O_2 are affected by:
    - Hydrogen ion concentration
    - pCO_2 & CO levels
    - Body temperature
    - 2,3-DPG



In actively metabolizing tissue, conditions promote release of O_2:

Oxidative metabolism increases the temperature, H^+, CO_2, and 2,3-DPG concentrations, resulting in a right shift of the dissociation curve.

CASE STUDY 17-8

A 23-year-old woman with a history of asthma was brought to the emergency department by ambulance. She was extremely short of breath. Her level of consciousness was diminished greatly, and she was only able to respond to questions with nods or one-word responses. She had a weak cough, with nearly inaudible breath sounds. After drawing blood gases, she was placed on supplemental oxygen. Vital signs: heart rate, 160 bpm; blood pressure, 120/84 mm Hg; temperature, 37°C; and respiratory rate, 36/min. Her initial blood gas and total hemoglobin results were as follows:

pH	7.330
pCO_2	25 mm Hg
pO_2	58 mm Hg
HCO_3^-	13 mmol/L
Hb	12.4 g/L

Questions

1. What is the patient's acid–base and oxygenation status?
2. What is the cause of the acid–base disturbance?
3. Would the pH be normal if the patient's pCO_2 increased to 40 mm Hg?
4. Does asthma typically present in this manner?
5. What clinical findings are most indicative of this patient's impending failure?

1. The acid–base status reflects partially compensated nonrespiratory acidosis. Because the patient was on room air when the blood gases were drawn, a pO2 of 58 mm Hg represents hypoxemia.

2. The acid–base disturbance was a result of lactic acidosis, secondary to severe hypoxemia, that developed when the patient was at home without supplemental oxygen.

3. If the patient's pCO_2 was increased to 40 mm Hg, the pH would fall to approximately 7.20 (11:1 ratio HCO_3^- to H_2CO_3) because the body would not have time to alter the HCO_3^- level to compensate.

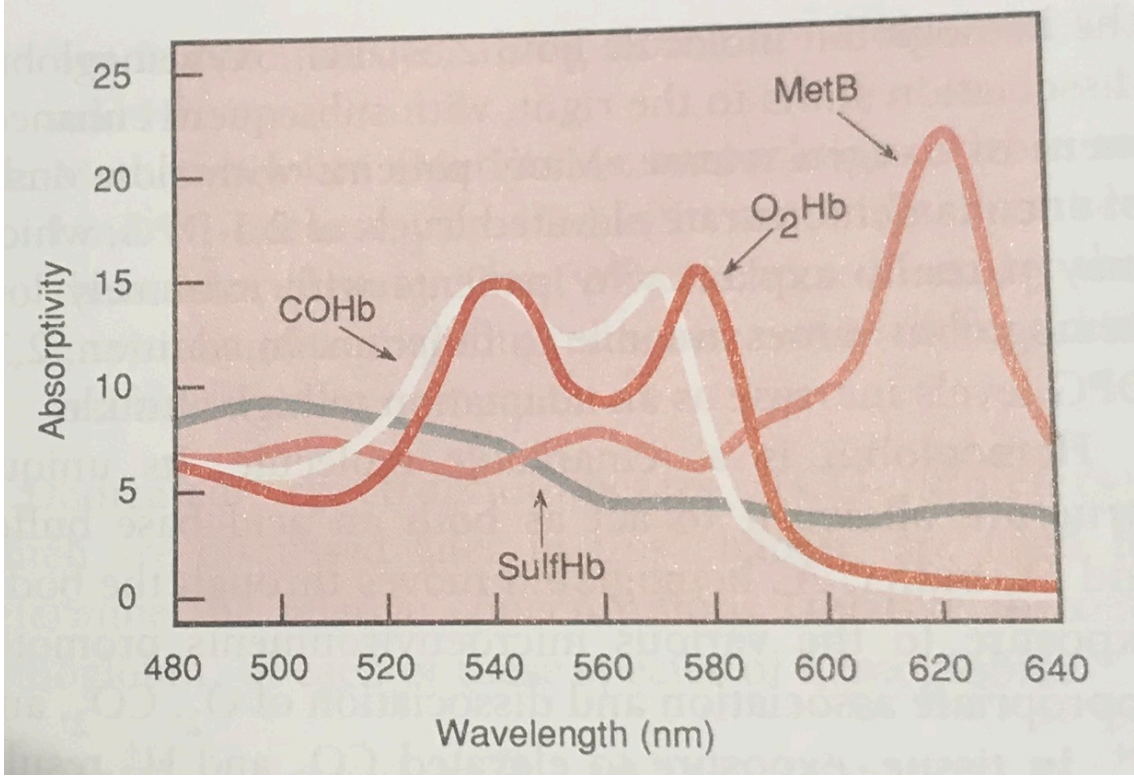
4. No. Initially, patients with asthma tend to hyperventilate and present with acute respiratory alkalemia and hypoxemia. If hypoxemia is not treated, lactic acidosis can develop. As the patient tires, the ability to compensate (via hyperventilation) diminishes. If asthma is not reversed, the most severe acid–base disturbance, mixed acidemia, will develop.

5. The ability to respond to questions with nods and single words only, together with a decreased level of consciousness

Measurement

- Spectrophotometric Determination of Oxygen Saturation
  - Actual percent oxyhemoglobin (O_2Hb) can be determined using CO-oximeter designed to measure various hemoglobin species.
  - Each species has a characteristic absorbance curve.
  - Number of wavelengths incorporated into instrument determines number of species that can be measured, from 4 to hundreds.
  - 4 most common hemoglobin species: HHb, O_2Hb, COHb, MetHb
  - Potential sources of error: faulty instrument calibration & spectral-interfering substances (dyes, pigments)
  - *All blood samples should be collected under anaerobic conditions and mixed immediately with anticoagulant. All samples should be analyzed promptly to avoid changes in saturation resulting from the consumption of oxygen by metabolizing cells.*

Absorbance curves of different Hb species



Measurement (cont'd)

- Blood Gas Analyzers: pH, pCO_2, and pO_2
  - Blood gas analyzers measure pH, pCO_2, & pO_2 with electrodes.
  - **Amperometric:** Amount of current flow indicates oxygen present (pO_2).
  - **Potentiometric:** Change in voltage indicates analyte activity (pCO_2, pH).
  - **Cathode:** 1) negative electrode; 2) site to which cations tend to travel; 3) site at which reduction occurs
  - **Anode:** 1) positive electrode; 2) site to which anions tend to travel; 3) site at which oxidation occurs
  - **Electrochemical cell:** formed when two opposite electrodes are immersed in a liquid that will conduct current.

Measurement (cont'd)

- Measurement of pO_2
  - pO_2 (Clarke) electrodes measure amount of current flow in circuit related to amount of O_2 being reduced at cathode.
  - Sources of error: buildup of protein material on surface of membrane, bacterial contamination within measuring chamber, exposure of sample to room air
  - Continuous measurements for pO_2 are possible using transcutaneous electrodes placed directly on skin.
- Measurement of pH and pCO_2
  - Ion force measurement requires 2 electrodes & a voltmeter.
  - Potential difference is related to concentration of ion of interest by Nernst equation.

$$\Delta E = \Delta E^\circ + \frac{0.05916}{n} \log a_1 \text{ at } 25^\circ C$$

Measurement (cont'd)

- Types of Electrochemical Sensors
  - **Macroelectrode sensors:** used in blood gas instruments since beginning of clinical measurement of blood gases
  - **Microelectrodes:** miniaturized macroelectrodes
  - **Thick and thin film technology:** Sensors are tiny wires embedded in printed circuit card that are disposable.
- Optical Sensors
  - Use fluorescent dyes, into which sample diffuses
  - Have been applied to indwelling blood gas systems

Measurement (cont'd)

- Calibration
  - pH & blood gas measurements are extremely sensitive to temperature.
  - Electrode sample chamber must be maintained at constant temperature.
  - pH electrode is calibrated with 2 buffer solutions, traceable to standards prepared by NIST.
  - Two gas mixtures are used to calibrate for pCO_2 & pO_2.
  - Most instruments are self-calibrating & are programmed to indicate a calibration error if electronic signal from electrode is inconsistent with programmed expected value.

Measurement (cont'd)

- Calculated Parameters
  - **HCO_3^-:** based on Henderson-Hasselbalch equation; can be calculated when pH & pCO_2 are known
  - **Carbonic acid concentration:** can be calculated using solubility coefficient of CO_2 in plasma at 37°C
  - **Total carbon dioxide content:** bicarbonate plus dissolved CO_2 plus associated CO_2 with proteins (carbamates)
- Correction for Temperature
  - By convention, pH, pCO_2, & pO_2 are all measured at 37°C.
  - If patient's body temperature differs from 37°C, blood gas instrument can "correct" values; results at 37°C should be reported, too, however, for reference.

Quality Assurance

- Preanalytic Considerations
  - Proper patient identification
  - Correct labeling of specimen & accurate info provided
  - Experienced, knowledgeable personnel
  - Proper collection & handling of blood gas specimens
  - Transport time
- Analytic Assessments: QC & Proficiency Testing
  - Surrogate liquid control materials, duplicate assays, non-surrogate QC
- Interpretation of Results

Quality Assurance (cont'd)

- Blood gas analysis quality assurance cycle