Acid-base balance

Acid-base balance

- The data are used to assess patients in life-threatening situations
- Blood hydrogen ion concentration [H+] is maintained within tight limits in health. Normal levels lie between 36 and 44 nmol/L (pH 7.35-7.45)
- Any H+ values outside this range will cause alteration in the rates of chemical reactions within the cell and affect many metabolic processes of the body
- Values greater than 120 nmol/L or less than 20 nmol/L are usually incompatible with life

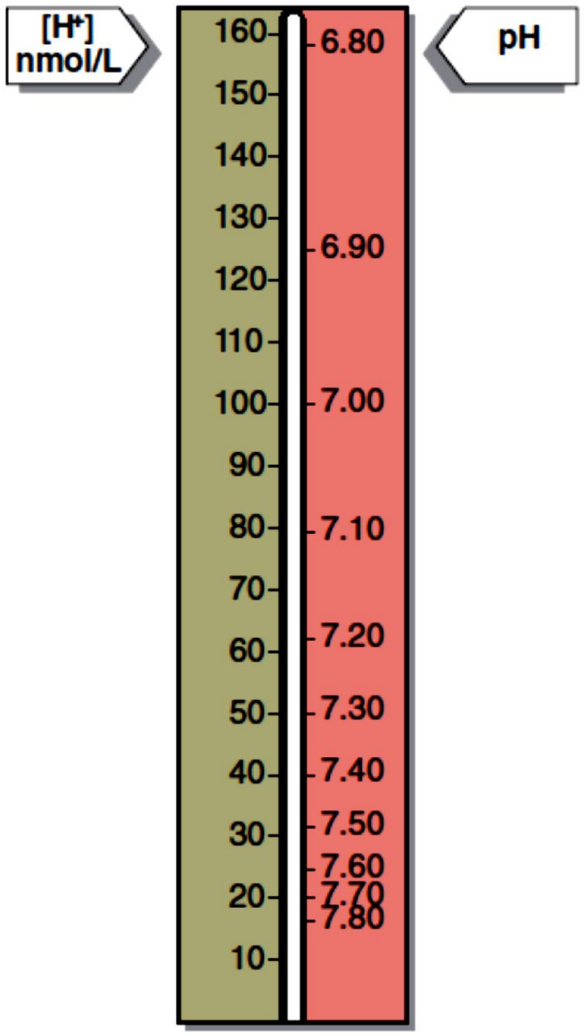


Fig 20.1 **The negative logarithmic relationship between [H+] and pH.**

H+ Production

- Hydrogen ions are produced in the body as a result of **metabolism** (from the oxidation of the sulphur-containing amino acids of protein ingested as food)

- The total amount of H+ produced each day in this way is of the order of 60 mmol but all the H+ produced are efficiently excreted in urine. Everyone who eats a diet rich in animal protein passes an acidic urine

- Large amounts of **CO2** are produced by cellular activity each day with the potential to upset acid-base balance

- Under normal circumstances all of this CO2 is excreted via the **lungs**. Having been transported in the blood, Only when **respiratory function** is impaired do problems occur

Buffering and buffers

- Buffer is a solution of the salt of a weak acid that is able to bind H+. Buffering does not remove H+ from the body but mop up any excess H+ produced (as a sponge)

- **Buffering** is only a short term solution to the problem of excess H. Ultimately, body must get rid of H by renal excretion

- The body contains a number of buffers to correct sudden changes in H production

- **Proteins** can act as buffers and the haemoglobin in the erythrocytes has a high capacity to bind H

Buffers

- In the ECF, **bicarbonate buffer** is the most important. In this buffer system, bicarbonate (HCO_3^-) combines with H^+ to form carbonic acid (H_2CO_3)

- The association of H with bicarbonate occurs rapidly, but the breakdown of carbonic acid to CO_2 and water happens relatively slowly.

- The reaction is accelerated by an enzyme, **carbonic anhydrase**, which is present particularly in the erythrocytes and in the kidneys.

- Only when all the bicarbonate is used up does the system have no further buffering capacity

- The acid base status of patients is assessed by consideration of the bicarbonate system in plasma

Buffers

- The **bicarbonate buffer** system is unique in that:
  - The (H_2CO_3) can dissociate to water and CO_2 allowing CO_2 to be eliminated by lung
  - Changes in CO_2 modify the ventilation rate
  - HCO_3^- concentration can be altered by the kidney

- **Phosphate buffer** system ($HPO_4^{=}$ - $H_2PO_4^-$) plays a role in plasma and RBC‘s and is involved in the exchange of Na/H^+ ion in the urine filtrate

- **Plasma proteins**, especially the imidazole groups of histidine, forms important buffer system in plasma. Most circulating proteins has net negative charge capable of H^+ binding

Regulation of the acid-base balance

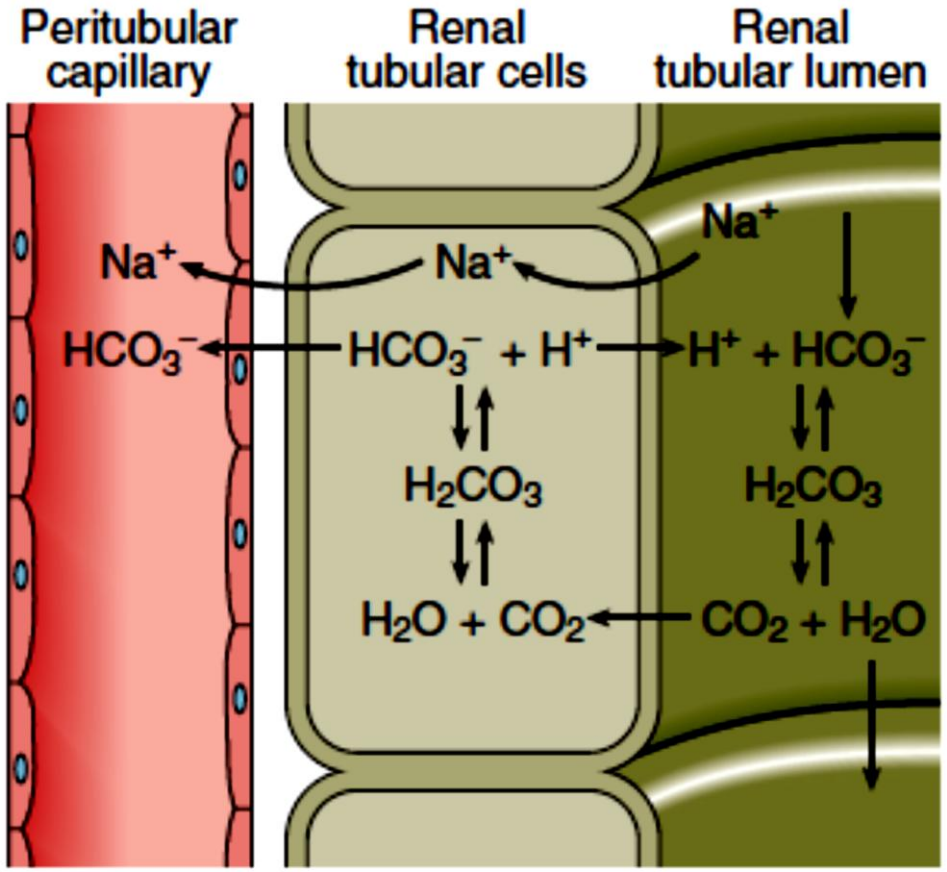
- In plasms at 37oC, the value for the combination of the solubility constant for PCO2 and the factor to convert mm Hg to mmol/L is 0.0307 mmol L-1. mm Hg-1

$$pH = pK' + \log \frac{cHCO_3^-}{0.031 \times PCO_2}$$

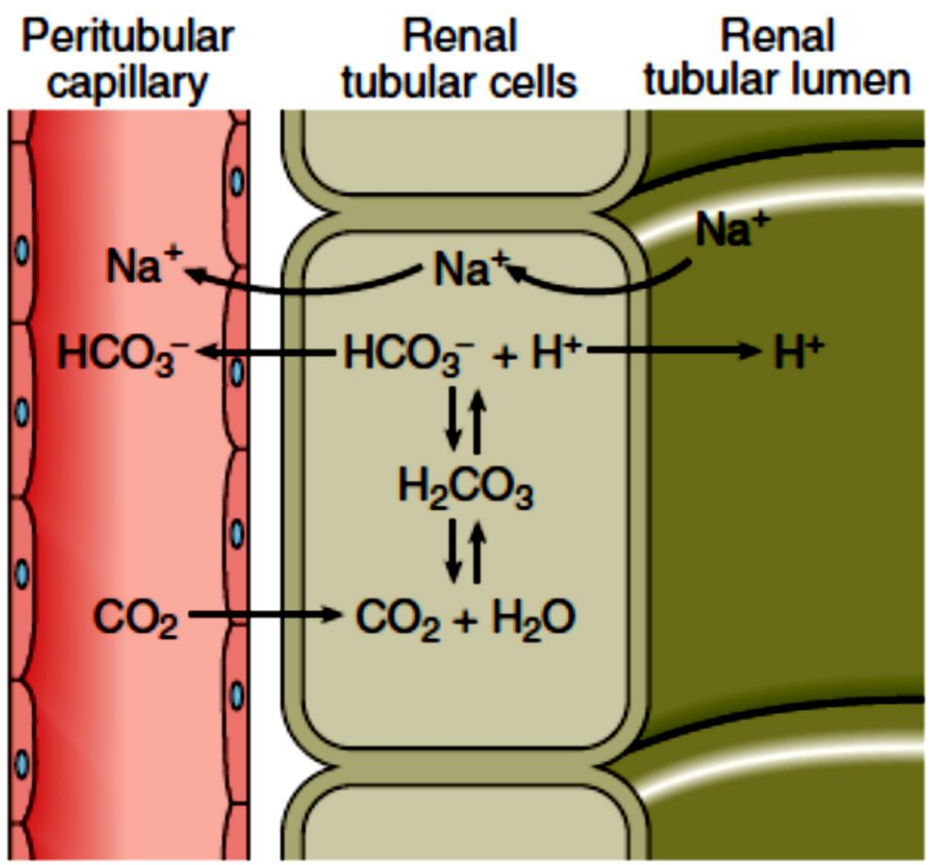
H+ excretion in the kidney

- All the H+ that is buffered must eventually be excreted from the body via the kidneys, regenerating the bicarbonate used up in the buffering process and maintaining the plasma bicarbonate concentration within normal limits.
- Secretion of H+ by the tubular cells serve initially to reclaim bicarbonate from the glomerular filtrate so that it is not lost from the body
- When all bicarbonate has been recovered, any deficit due to the buffering process is regenerated.
- The mechanisms for bicarbonate recovery and for bicarbonate regeneration are very similar and sometimes confused.
- The excreted H+ must be buffered in urine or the [H+] would rise to very high levels, phosphate acts as one such buffer, while ammonia is another

H+ excretion in the kidney

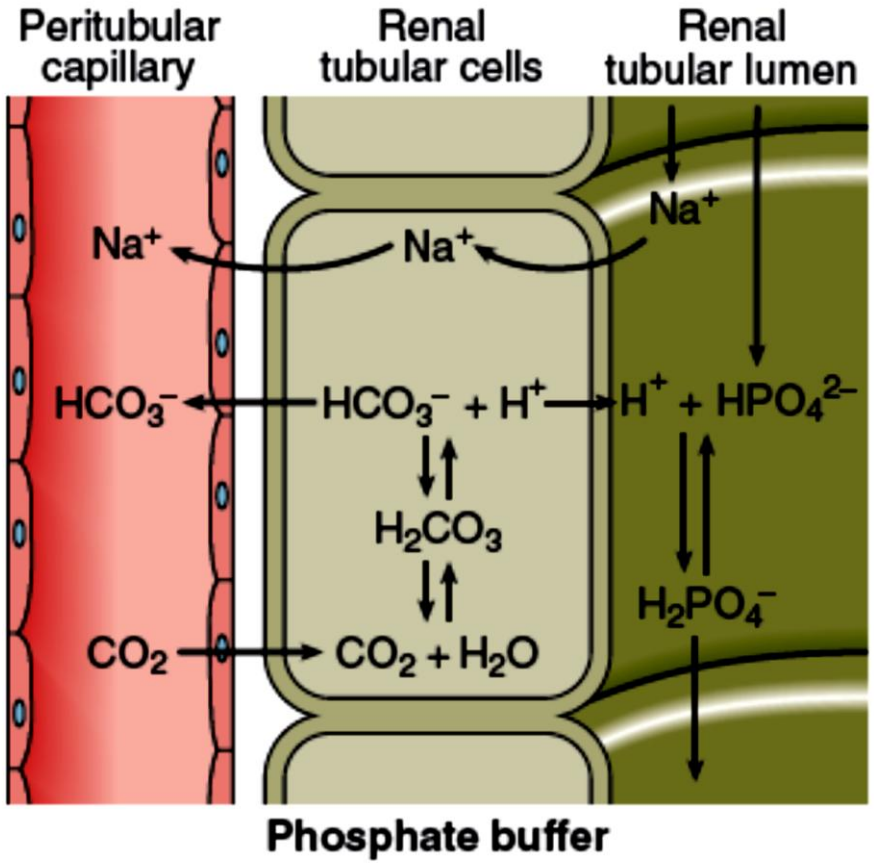


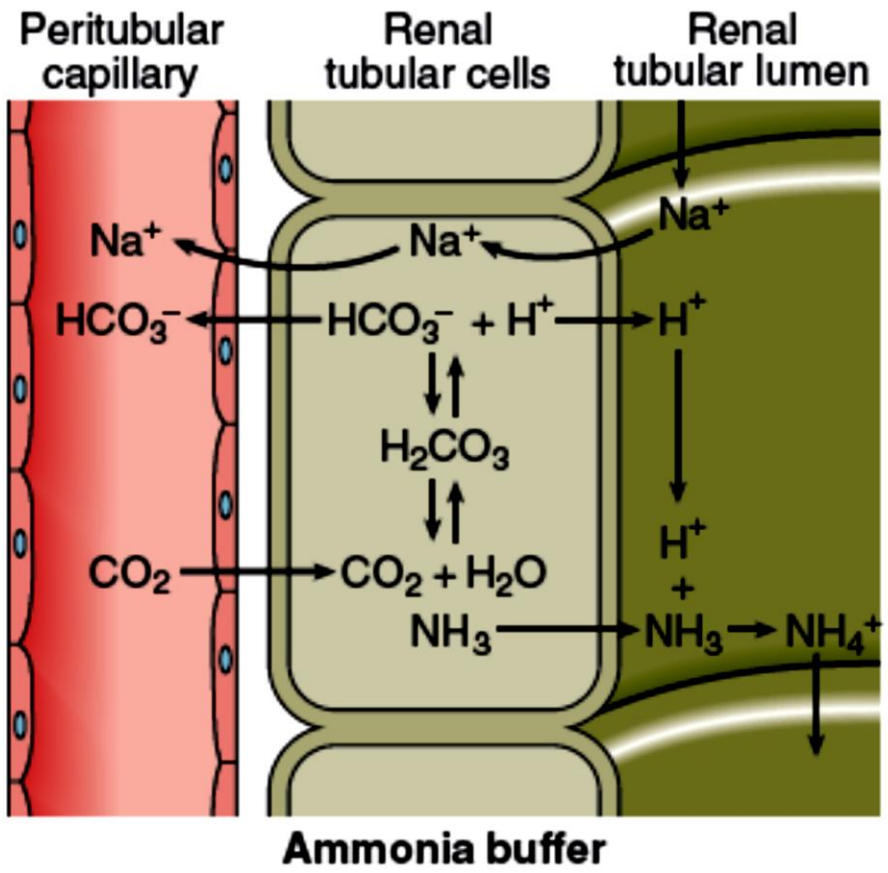
'Recovery' of bicarbonate



'Regeneration' of bicarbonate — excretion of hydrogen ion

H+ excretion in the kidney





Assessing status

- The carbonic acid (H_2CO_3) component is proportional to carbon dioxide, which is in turn proportional to the partial pressure of the CO_2
- Because the body's cellular and metabolic activities are pH dependent, the body tries to restore acid-base homeostasis whenever an imbalance occurs (**Compensation**)
- The body accomplishes this by altering the factor not primarily affected by the pathologic process. For example, if the imbalance is of **non-respiratory** origin, the body compensates by altering **ventilation** (fast response).

- For disturbances of the **respiratory** components. The **kidneys compensate** by selectively excreting or reabsorbing anions and cations. The kidneys are slower to respond (2-4 days)

Assessing status

- The H concentration in blood varies as the bicarbonate concentration and pCO2 change. If everything else remains constant.
- Adding H, removing bicarbonate or increasing the pCO2 will all increase [H+]
- Removing H, adding bicarbonate or lowering pCO2 will all cause the [H+] to fall.
- An indication of the acid base status of the patient can be obtained by measuring the components of the bicarbonate buffer system

Normal ranges

TABLE 16-1 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

Causes of metabolic acidosis

- Metabolic acidosis with an **elevated anion gap** occurs in:

- **Renal disease.** Hydrogen ions are retained along with anions such as sulphate and phosphate.

- **Diabetic ketoacidosis.** Altered metabolism of fatty acids, as a consequence of lack of insulin causes endogenous production of acetoacetic and β–hydroxybutyric acids

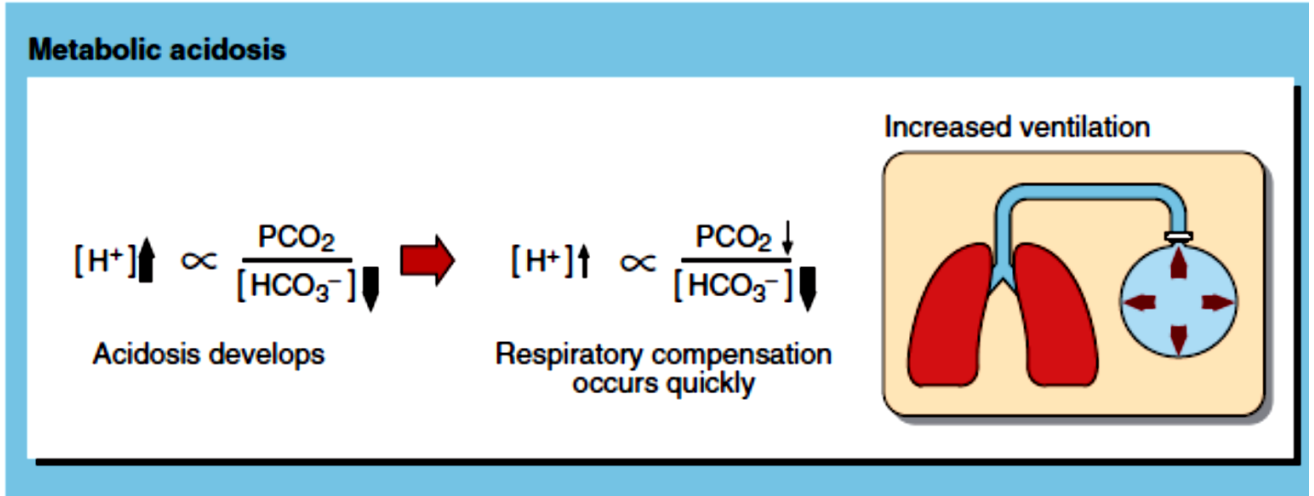
- **Lactic acidosis.** Particularly tissue anoxia. In acute hypoxic states such as respiratory failure or cardiac arrest. It can be caused by liver disease. The presence of lactic acidosis can be confirmed by the measurement of plasma lactate concentration.

- Certain disease of overdosage or **poisoning**. As in **salicylate** overdose where build-up of lactate occurs, or **methanol** poisoning when formate accumulates, or **ethylene glycol** poisoning where oxalate is formed.

Causes of metabolic acidosis

- Metabolic acidosis with a normal anion gap is sometimes referred to as **hyperchloraemic acidosis** because a reduced HCO3 is balanced by increased Cl concentration. It is seen in chronic diarrhea or intestinal fistula. Fluids containing bicarbonate are lost from the body

- **Renal tubular acidosis**: Renal tubular cells are unable to excrete hydrogen ions efficiently and bicarbonate is lost in urine



Clinical effect of acidosis

- The compensatory response to metabolic acidosis is hyperventilation, since the **increased [H+]** acts as a powerful stimulant of the respiratory centre.

- The deep rapid and gasping respiratory pattern is known as Kussmaul breathing. Hyperventilation is the appropriate physiological response to acidosis and it occurs rapidly.

- The raised [H+] leads to increased neuromuscular irritability. There is a hazard of arrhythmia progressing to cardiac arrest and this is more likely by the presence of hyperkalemia, which will accompany the acidosis.

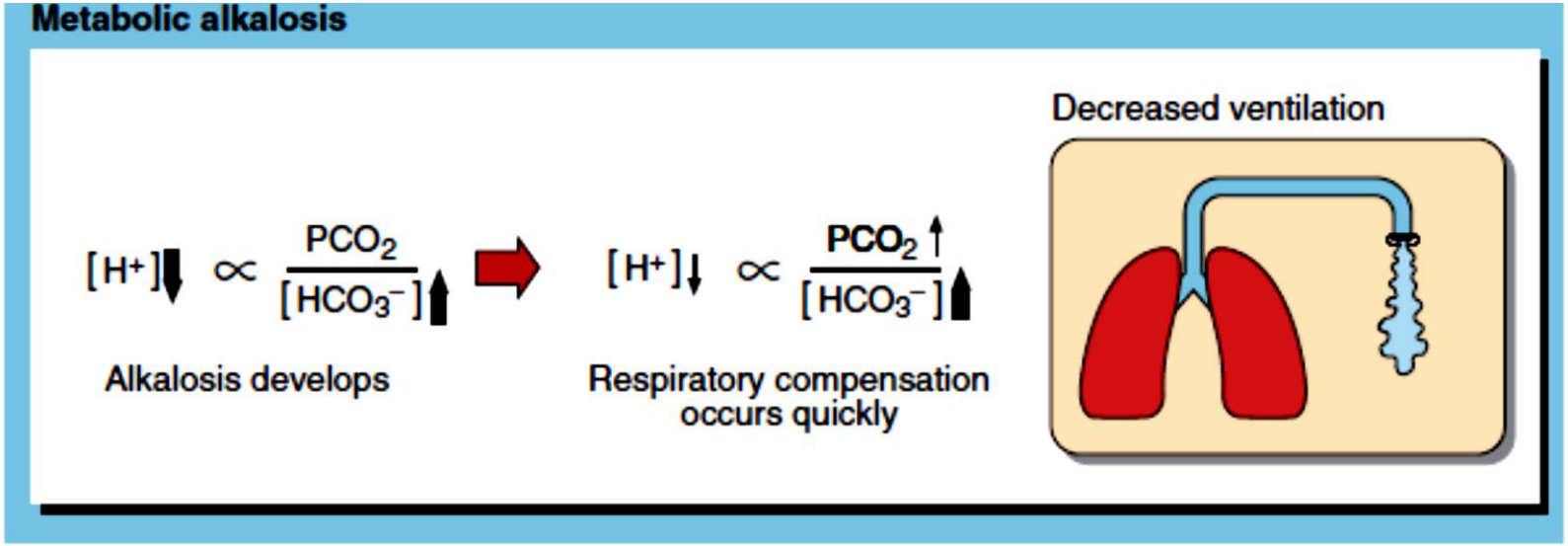
- Depression of consciousness can progress to coma and death

Metabolic alkalosis

- The causes of a metabolic alkalosis may be due to:
  - Loss of hydrogen ion in gastric fluid during **vomiting**. This especially seen when there is pyloric stenosis preventing parallel loss of bicarbonate-rich secretions from the duodenum
  - **Ingestion of absorbable alkali:** such as sodium bicarbonate. Very large doses are required to cause a metabolic alkalosis unless there is renal impairment
  - **Potassium deficiency:** in severe potassium depletion as a consequence of diuretic therapy, hydrogen ion is retained inside cells to replace the missing potassium ions. In the renal tubules more hydrogen ions rather than potassium, are exchanged for reabsorbed sodium. So despite there an alkalosis, the patient passes an acid urine.

Clinical effects of alkalosis

- The clinical effects of alkalosis include:
  - Hypoventilation
  - Confusion and eventually coma
  - Muscle cramps, tetany and paraesthesia may be a consequence of a decrease in the unbound plasma calcium concentration. which is a consequence of the alkalosis.



Respiratory acidosis

- **Lung disease:** in which CO2 is not effectively removed from the blood. In certain patients with chronic obstructive pulmonary disease (COPD, where CO2 is retained in the blood, causing chronic hypercarbia (elevated pCO2)

- In **bronchopneumonia:** gas exchange is impaired because of the secretions. White blood cells, bacteria and fibrin in the alveoli

- **Hypoventilation** caused by drugs such barbiturates, morphine, or alcohol will increase blood pCO2 levels

- **Mechanical obstruction** or asphyxiation (strangulation or aspiration).

- **Decreases cardiac output** such as in CHF also will result in less blood to the lungs for gas exchange and an elevated pCO2

- Kidney will compensate for acidosis but it takes time

Respiratory alkalosis

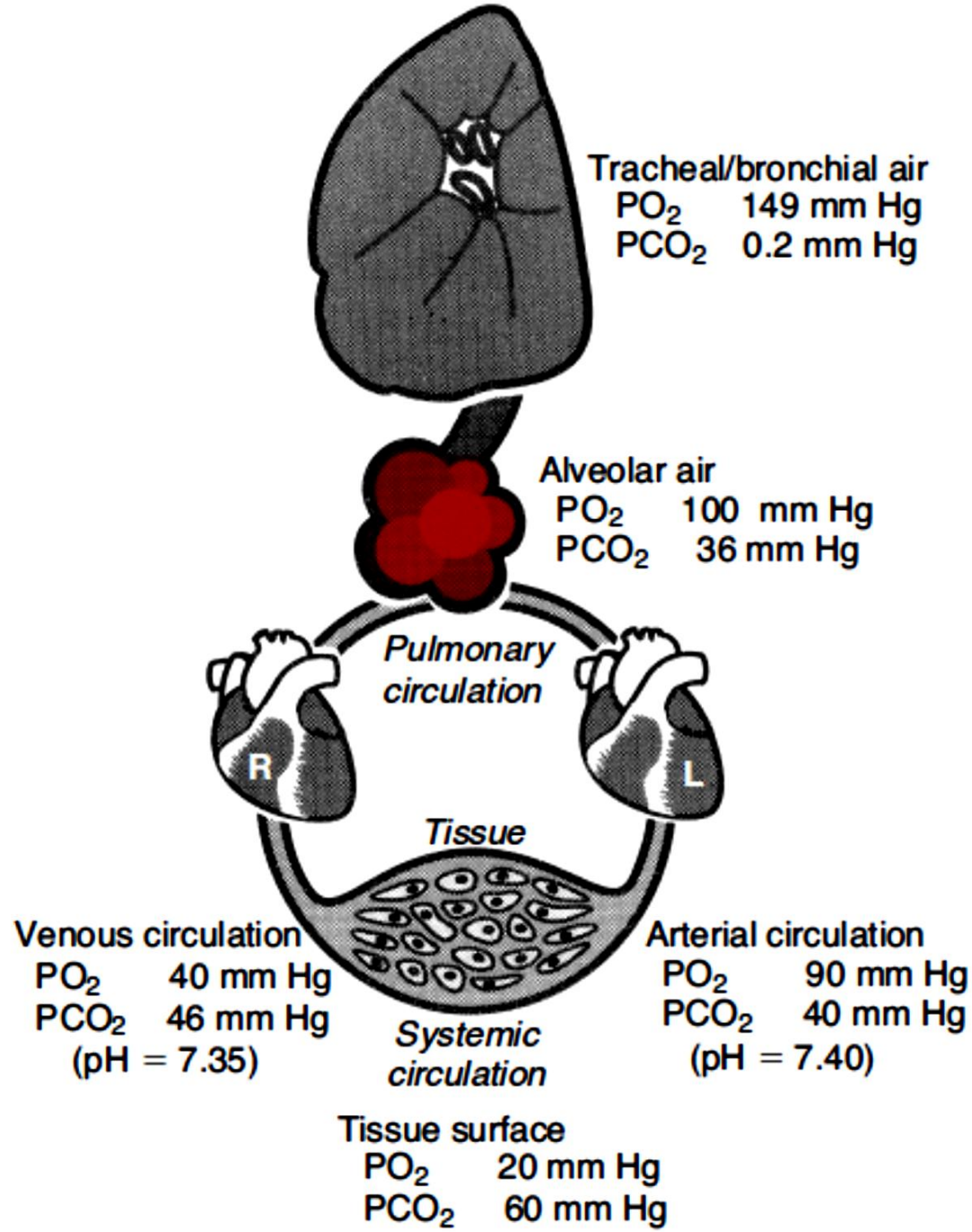
- The causes include:
  - Hypoxemia
  - Chemical stimulation of the respiratory center by drugs, such as salicylate
  - An increase in environmental temperature, fever, hysteria (hyperventilation), Pulmonary emboli and pulmonary fibrosis.

- The kidney compensates by excreting HCO_3^- in the urine and reclaiming H^+ to the blood
- The popular treatment for hysterical hyperventilation, breathing into a paper bag, is self -explanatory

Oxygen and gas exchange
Oxygen and carbon dioxide

- The role of oxygen in metabolism is crucial to all life. In cell mitochondria, electron pairs from the oxidation of NADH and FADH2, are transferred to molecular oxygen
- For adequate tissue oxygenation, the following seven conditions are necessary:
  - (1) available atmospheric oxygen
  - (2) adequate ventilation
  - (3) gas exchange between the lung and arterial blood
  - (4) Loading of O2 onto hemoglobin
  - (5) adequate hemoglobin
  - (6) adequate transport (cardiac output), and
  - (7) release of O2 to the tissue.

  - Any disturbances in these conditions can result in poor tissue oxygenation


Tracheal/bronchial air
PO_2 149 mm Hg
PCO_2 0.2 mm Hg
Alveolar air
PO_2 100 mm Hg
PCO_2 36 mm Hg
Pulmonary circulation
R
L
Tissue
Venous circulation
PO_2 40 mm Hg
PCO_2 46 mm Hg
(pH = 7.35)
Systemic circulation
Arterial circulation
PO_2 90 mm Hg
PCO_2 40 mm Hg
(pH = 7.40)
Tissue surface
PO_2 20 mm Hg
PCO_2 60 mm Hg

Oxygen and carbon dioxide

- Factors that can influence the amount of O2, that moves through the alveoli into the blood and then to the tissue include:
- **Destruction of the alveoli:** the normal surface area of the alveoli is as big as tennis court. When the surface area is destroyed to a critical low value by diseases such as emphysema
- **Pulmonary edema:** Gas diffuses from the alveoli to the capillary through a small space. With pulmonary edema, fluid leaks into the space, increasing the distance between the alveoli and capillary walls
- **Airway blockage.** Airways can be blocked, as in asthma and bronchitis
- **Inadequate blood supply:** As in pulmonary embolism, pulmonary hypertension or a failing heart not enough blood is being carded away to the tissue where it is needed.
- **Diffusion of CO2 and O2.** Because O2 diffuses 20 times slower than CO2, it is more sensitive to problems with diffusion. This type of hypoxemia is generally treated with supplemental O2. 60% or higher O2 concentrations must be used with caution because it can be toxic to lungs

Oxygen transport

- Most O2 in arterial blood is transported to the tissue by hemoglobin.
- Each adult hemoglobin (A1) molecule can combine to four molecules of O2. reversibly with up to four molecules of O2
- The actual amount of O2 loaded depends on:
  - The availability of O2
  - The concentration and type(s) of hemoglobin present
  - The presence of interfering substances, such as (CO)
  - The pH
  - The temperature of the blood
  - The levels of PCO2 and 2,3- DPG.

Oxygen transport

- With adequate atmospheric and alveolar O2 available and with normal diffusion of O2 to the arterial blood, more than 95% of the “functional” hemoglobin will bind O2.

- Increasing the availability of O2 to the blood further saturates the hemoglobin. However, once the hemoglobin is 100% saturated, an increase in O2 to the alveoli serves only to increase the concentration of dissolved O2 (dO2) in the arterial blood. This offers minimal increase in oxygen delivery.

- Prolonged administration of high concentration of O2 may cause oxygen toxicity and in some cases, decreased ventilation that leads to hypercarbia

Oxygen transport

- Normally blood hemoglobin exists in one of four conditions:
  - Oxyhemoglobin (O2Hb), which is O2 reversibly bound to hemoglobin.
  - deoxyhemoglobin (HHb; reduced hemoglobin), which is hemoglobin not bound to O2 but capable of forming a bond when O2 is available
  - Carboxyhemoglobin (COHb), Which is hemoglobin bound to CO. Binding of CO to Hb is reversible but is greater than 200 times as strong as that of O2
  - Methemoglobin (MetHb), which is hemoglobin unable to bind O2, because iron (Fe) is in an oxidized rather than reduced state. The Fe +3 can be reduced by the enzyme methemoglobin reductase, which is found in RBC's
- Co-oximeter are used to determine the relative concentrations (relative to the total hemoglobin) of each of these species of hemoglobin.

Assessing a patient oxygen status

- Four parameters used to assess a patient's oxygen status are:
  - Oxygen saturation (SO2)
  - Measured fractional (percent) oxyhemoglobin (FO2Hb);
  - Transcutaneous pulse oximetry (SpO2) assessments and
  - The amount of O2 dissolved in plasma (PO2)

- Oxygen saturation (SO2) represents the ratio of O2 that is bound to the hemoglobin compared with the total amount of hemoglobin capable of binding O2

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

Oxygen saturation (SO2)

- Software included with the blood gas instruments can calculate SO2 from pO2, pH and temperature of the sample.

- These calculated results can differ from those determined by direct measurement due to the assumption that only adult hemoglobin is present and the oxyhemoglobin dissociation curve has a specific shape and location

- These algorithms for the calculation do not account for the other hemoglobin species, such as COHb and MetHb

- So calculated SO2 should not be used to assess oxygenation status

Fractional oxyhemoglobin

- Fractional (or percent) oxyhemoglobin (FO2Hb) is the ratio of the conc. of oxyhemoglobin to the conc. of total hemoglobin (ctHb)

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

- Where the dysHb represents hemoglobin derivatives, such as COHb, that can't reversibly bind with O2 but are still part of the "total" hemoglobin measurement.

- These two terms SO2 and FO2Hb, can be confused because as the numeric values for SO2 are close to those of FO2Hb (differ in smokers and if dyshemoglobins are present)

Partial pressure of oxygen dissolved in plasma

- Partial pressure of oxygen dissolved in plasma (pO2) accounts for little of the body's O2 stores.

- Noninvasive measurement are attained with pulse oximetry (SpO2). These devices pass light of two or more wavelength through the tissues of the toe, finger or ear.

- The pulse oximeter differentiate between the absorption of light as a result of O2Hb and dysHb in the capillary bed and calculates O2Hb saturation. Because SpO2 does not measure COHb or any other dysHb, it overestimates oxygenation when one or more are present.

- The accuracy of pulse oximetry can be compromised by many factors, including diminished pulse as a result of poor perfusion and severe anemia.

- The maximum amount of O2 that can be carried by hemoglobin in a
- given quantity of blood is the hemoglobin oxygen (binding) capacity. The molecular weight of tetramer hemoglobin is 64,458 g/mol.
- One mole of a perfect gas occupies 22,414 mL. Therefore, each gram of hemoglobin carries 1.39 mL of O2

$$\frac{22{,}414 \text{ mL/mol}_4}{64{,}458 \text{ g/mol}} = 1.39 \text{ mL/g}$$

- When the total hemoglobin (tHb) is 15 g/dL and the hemoglobin is 100% saturated with O2, the O2 capacity is:

$$15 \text{ g/100 mL} \times 1.39 \text{ mL/g}$$
$$= 20.8 \text{ mL } O_2\text{/100 mL of blood}$$

Oxygen content

- Oxygen content is the total O2 in blood and is the sum of the O2 bound to hemoglobin (O2Hb) and the amount dissolved in the plasma (pO2)

- Because pO2 and pCO2 are only indices of gas-exchange efficiency in the lungs, they do not reveal the content of either gas in the blood.

- If the pO2 is 100 mmHg, 0.3 ml of O2 will be dissolved in every 100 ml of blood plasma.

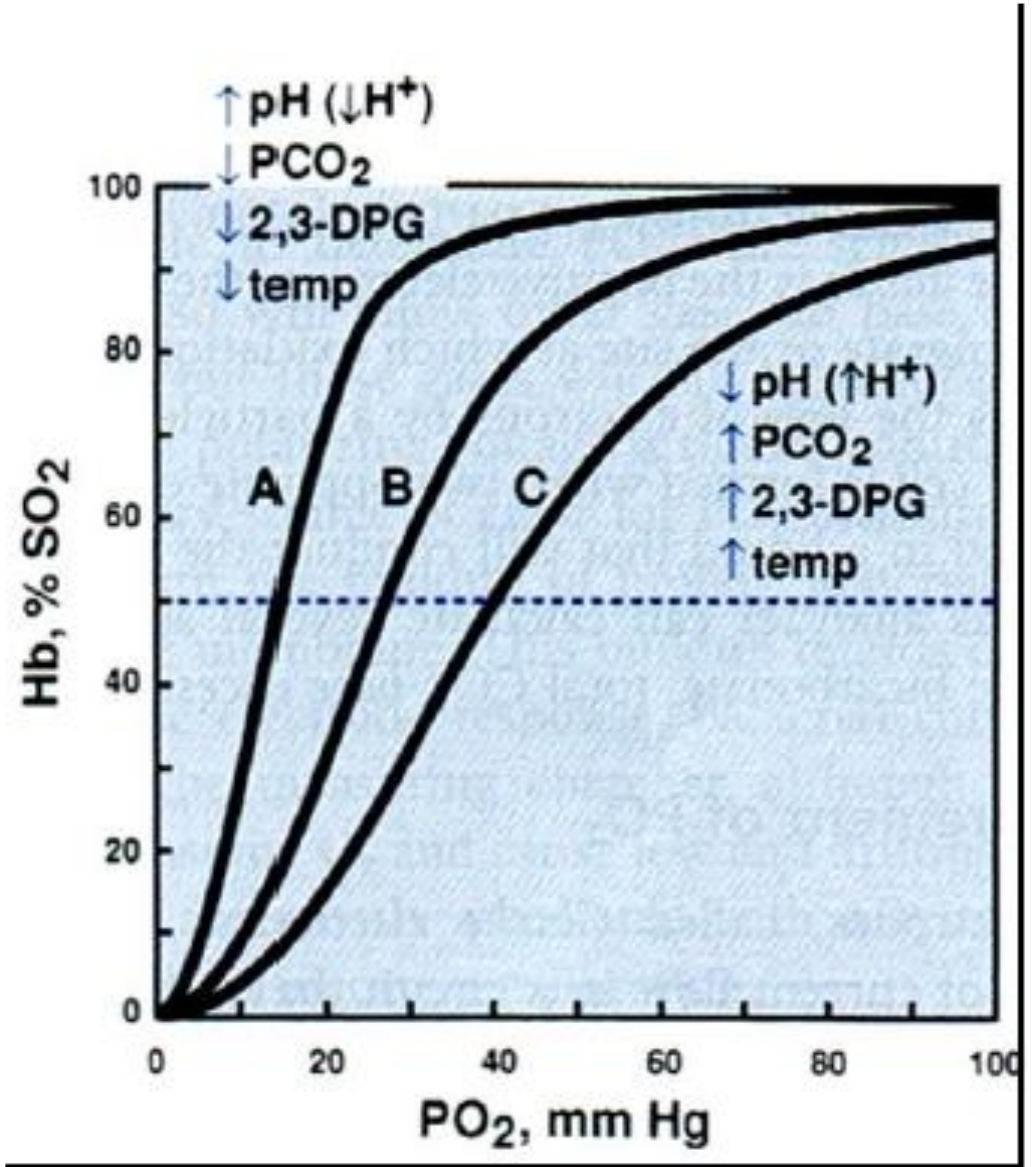
- The amount of dissolved O2 is usually not clinically significant. However, with low tHb or at hyperbolic conditions, it may become a significant source of O2 to the tissue. Normally 98-99% of the available hemoglobin is saturated with O2.

- Assuming a tHb of 15 g/dL, the O2 content for every 100 mL of blood plasma becomes:

$$0.3\ \text{mL} + (20.8\ \text{mL} \times 0.97) = 20.5\ \text{mL}$$

Hemoglobin-oxygen dissociation

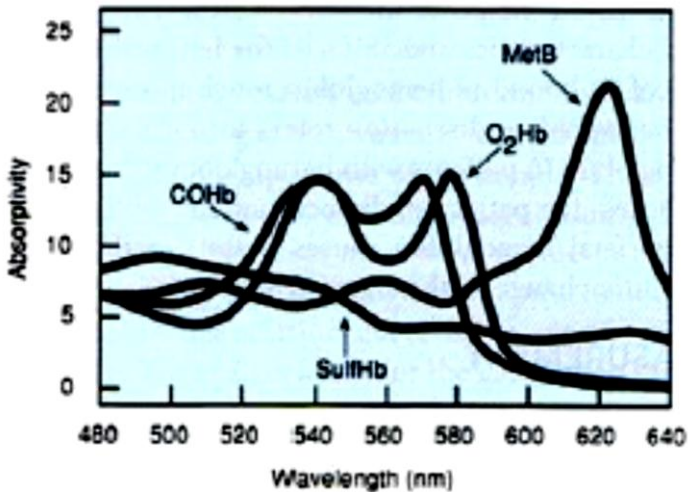
- 2,3-DPG levels increase in patients with extremely low hemoglobin values and as an adaptation to high altitude.



Measurement

Spectrophotometric (Co-oximeter) Determination of oxygen saturation

- The actual determination of oxyhemoglobin (O2HB) can be determined spectrophotometrically using co-oximeter designed to directly measure the various hemoglobin species.
- The number of hemoglobin species measured will depend on the number and specific wavelength incorporated into the instrumentation. For example, two wavelength instrument systems can measure only two hemoglobin species (O2Hb and HHb), which are expressed as a fraction or percentage of the total hemoglobin.



Spectrophotometric (Co-oximeters) Determination of oxygen saturation

- As with any spectrophotometric measurement, potential sources of errors exist, including:
  - Faulty calibration of the instrument
  - Spectral-interfering substances
- The patient's ventilation status should be stabilized before blood sample collection
- An appropriate waiting period before the sample is redrawn should follow changes in supplemental O2 or mechanical ventilation
- All blood samples should be collected under anaerobic conditions and mixed immediately with heparin or other appropriate anticoagulant.
- If the blood gas analysis is not being done on the same sample, EDTA can be used as an anticoagulant
- All samples should be analyzed promptly to avoid changes in saturation resulting from the use of oxygen by metabolizing cells'

Blood gas analyzers (pH, pCO2 and pO2)

- Blood gas analyzers (macroelectrochemical or microelectrochemical sensors) as sensing devices
- The pO2 measurement is amperometric (current flow) related to the amount of O2 being reduced at the cathode
- The PCO2 and pH measurement are potentiometric (change in voltage)
- The blood gas analyzer can calculate several additional parameters, bicarbonate, total CO2, base excess and SO2.

Measurement of pO2

- The primary source of error for pO2 measurement is associated with the buildup of protein material on the surface of the membrane (retards diffusion of O2)
- Bacterial contamination within the measuring chamber, although uncommon, will consume O2 and cause low and drifting values
- It is important not to expose the sample to the room air when collecting, transporting and making O2 measurement.
- Contamination of the sample with room air (pO2, 150 mmHg) can result in significant error
- Even after the sample is drawn, sample should by analyzed immediately as leukocytes continue to metabolize O2 leading to low PO2 values

Measurement of pO2

- Cutaneous measurement for pO2 also are possible using transcutaneous (TC) electrodes placed directly on the skin.

- Measurement depends on oxygen diffusing from the capillary bed through the tissue to the electrode. Although most commonly used with neonates and infants

- Skin thickness and tissue perfusion with arterial blood can significantly affect the results.

- Heating the electrode placed on the skin can enhance diffusion of the O2 to the electrode, however, burns can result unless the electrodes are moved regularly.

Measurement of pH and pCO_2

- Two electrodes (the measuring electrode responsive to the ion of interest and the reference electrode) are needed and voltmeter, which measures the potential difference between the two electrodes.

- The potential difference is related to the concentration of the ion of interest.

- To measure pH, a glass membrane sensitive to H+ is placed around an internal Ag-AgCl electrode to form a measuring electrode

- The potential that develops at the glass membrane as a result of H+ from the unknown solution diffusing into the membrane's surface is proportional to the difference in [H+] between the unknown sample and the buffer solution inside the electrode

pCO2

- An outer semipermeable membrane that allows CO2 to diffuse into a layer of electrolyte, usually bicarbonate buffer, covers the glass pH electrode. The CO2 that diffuses across the membrane reacts with the buffer, forming carbonic acid, which then dissociates into bicarbonate plus H+

- The change in the activity of the H+ is measured by the pH electrode and related to pCO2

- As with the other electrodes, the buildup of protein material on the membrane will affect diffusion and cause errors, pCO2 electrodes are the slowest to respond because of the chemical reaction that must be completed. Other error sources include erroneous calibration caused by incorrect or contaminated calibration materials

Specimen

- Arterial blood specimen is an excellent reference
- Peripheral venous samples can be used if pulmonary function or O2 transport is not being assessed (the source of the specimen must be clearly identified)
- Depending on the patient, capillary blood may need to be used to measure pH and pCO2
- Although the correlation with arterial blood is good for pH and pCO2, capillary pO2 values even with warming of the skin before drawing the sample, do not correlate well with the arterial pO2 values as result of sample exposure to room air
- Sources of error in the collection and handling of blood gas specimens include the collection device, form and concentration of heparin, speed of syringe filling, maintenance of the anaerobic environment, mixing of the sample to ensure dissolution and distribution of the heparin anticoagulant, and transport and storage time before analysis

Interpretation of results

- Laboratory professionals need certain knowledge, attitude and skills for obtaining and analyzing specimens for pH and blood gases.
- Simple evaluation of the data may reveal an instrument problem (possible bubble in the sample chamber or fibrin plug)
- A possible sample handling problem (PO_2 out of line with previous results and current inspired FiO_2 levels)
- The application of knowledge saves time. The ability to correlate data quickly reduces turnaround time and prevents mistakes.