3/Regulation of Reaction of Blood and Disturbances in Acid-Base Regulation

REGULATION OF REACTION OF BLOOD

Although, large quantities of acids and alkalies—derived from food and metabolites, are constantly entering the blood stream, yet the reaction of blood remains rigidly constant with limits of pH varying from 7·36 to 7·44, the H^+ concentration ranging between 44 nMols and 36 nMols per litre. This constant blood reaction is one of the essential requisites of life and any material variation on either side, seriously disturbs the vital processes and may lead to death.

This constant blood reaction is the result of a dynamic process by which an equilibrium between the production and excretion of hydrogen ions is maintained. Major sources of hydrogen ion production in the human body may be conveniently and arbitrarily be devided into two categories, viz.,

(1) **Respiratory H^+**

Source: $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$

In alveolar hypoventilation CO_2 is retained and so H_2CO_3 and H^+ are increased in the blood (*Respiratory acidosis*). The reaction moves to the right. In hyperventilation the reaction shifts to the left and H^+ is eliminated from the blood.

(2) **Metabolic H^+**

Sources:

(a) Oxidation of 'S' and 'P' of proteins to nonvolatile acids.

(b) Incomplete oxidation of organic food stuff leading to the formation of organic acids, e.g. lactic acid.

(c) Abnormal production of organic acids, e.g. acetoacetic acid in metabolic disorders.

(4) Drugs like NH_4Cl and mandelic acid.

Channels of elimination of H^+ ion from the body are two, viz.:

(1) **Lungs**—15,000 mMols of CO_2 are eliminated daily by this route.

(2) **Kidney**—50 mEquivalent. of metabolic H^+ are eliminated daily by this route.

Mechanism of regulation of blood reaction

Factors responsible for maintaining blood reaction within narrow limits of H^+ concentration are three, viz.:

I. **Buffers of the blood;**

II. **Respiration;**

III. **Kidneys.**

These are discussed below in greater details.

I. **Buffers** are substances which fix up the H^+ or OH^- as soon as they are formed, till they are disposed off by the lung or the kidney. They are formed by a weak acid and its salt with a strong base.

Example: $H^+ + HCO_3^- \rightleftharpoons H_2CO_3 \rightleftharpoons H_2O + CO_2$ (eliminated by lungs).

$HL + Na_2HPO_4 \rightleftharpoons NaL + NaH_2PO_4$ (excreted by kidney) (Lactic acid).

The buffers (Fig. 3.1) may be classified as follows:

(*i*) **Bicarbonate buffers** [(HCO_3^-/H_2CO_3) = (salt/acid)]. This consists of carbonic acid and its salt with strong base, sodium bicarbonate. Normal [sodium bicarbonate/carbonic acid] ratio in plasma is 20 : 1. They are the chief buffers of blood and constitute the so-called "alkali reserve" of plasma. They help in the following way:

Lactic acid + $NaHCO_3$ = Na-lactate + H_2CO_3. The H_2CO_3, thus formed, is eliminated through diffusion of CO_2 into the alveolar air in the lungs.

$$H_2CO_3 \underset{\text{anhydrase}}{\overset{\text{carbonic}}{\rightleftharpoons}} H_2O + CO_2\uparrow$$

(exhaled)

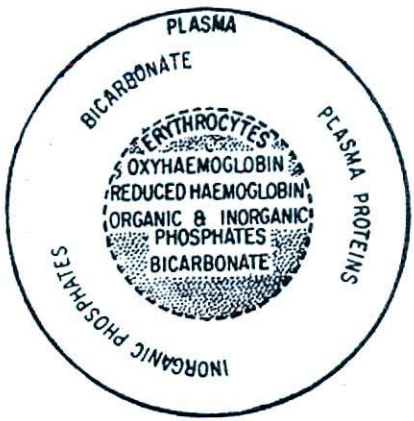


Fig. 3.1. In whole blood four principal buffer systems are present. In the plasma—bicarbonate, plasma proteins and phosphates. In the erythrocytes—haemoglobin, phosphates and bicarbonate.

Thus the bicarbonate buffer system is directly linked up with respiration. Similarly if a strong base NaOH is added, the reaction is $NaOH + H_2CO_3 \rightleftharpoons NaHCO_3 + H_2O$

Alkali reserve. The alkali reserve is represented by the sodium bicarbonate concentration in the blood that has not yet combined with non-volatile acids. Normally all acids except carbonic acid react with CO_2 of bicarbonate forming $H_2 + CO_3$.

$$\left[\begin{array}{l}\text{Fixed acid}\\ H_2SO_4\\ \text{lactic}\\ H_3PO_4\\ HCl\end{array}\right] + NaHCO_3 \rightarrow \text{Na salt of the acid} + H_2CO_3$$

(*ii*) **Phosphate buffers** [(Na_2HPO_4/NaH_2PO_4) = (salt/acid)]. Two varieties of phosphates are present in blood—alkaline and acid. In the plasma, they remain in the ratio of 4 : 1. This ratio is kept constant with the help of the kidneys. For instance, when an acid enters the blood, it is fixed up by the alkaline phosphates which becomes converted into acid phosphates in the following way:

Lactic acid + Na_2HPO_4 = Na-lactate + NaH_2PO_4.

The acid phosphates, thus produced, are excreted by the kidneys and hence urine becomes more acid. Similarly, when an alkali enters, it is buffered by the acid phosphates which, during the reaction, become converted into alkaline phosphates. The excess alkaline phosphates are eliminated by the kidneys and urine becomes alkaline. In this way, the

phosphate buffers work in co-operation with the kidneys and help to maintain the blood reaction constant.

(*iii*) **Haemoglobin.** Haemoglobin is one of the most important buffers of the blood. Each molecule of haemoglobin contains 38 molecules of histidine. Histidine in haemoglobin molecule contains imidazole, which contains two groups: iron-containing group concerned with carriage of oxygen and imidazole nitrogen group, which is responsible for (Fig. 3.2) buffering property of haemoglobin since it remains dissociated in acid and conjugate base forms.

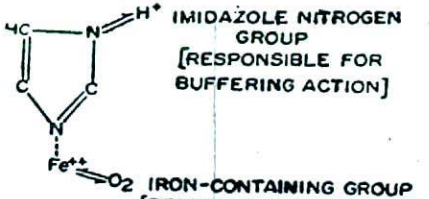


Fig. 3.2.

1 mMol of reduced Hb can accept 0·7 mMol of H^+ without any change of blood reaction.

Carbamino-compounds formed by direct union of CO_2 with NH_2 part of protein molecule, confers upon the proteins the ability to act as buffers, since the reaction is reversible.

(*iv*) **Plasma proteins**

Plasma proteins (Na^+proteinate/HPr) = (salt/acid). Buffering capacity of the plasma proteins is weaker than haemoglobin. Proteins contain a large number of acidic and basic groups due to presence COOH and NH_2 groups respectively in their structure. In acid solution they act as a buffer in that the basic amino group takes up excess H^+ ions forming (NH_3^+), whereas in basic solutions, the acidic COOH groups give up hydrogen ion forming COO^-. They remain mostly combined with Na and help in two ways:

(a) As Na-proteinate: NaPr + Lactic acid = Na–lactate + HPr.

(b) Forming carbamino-compounds and thus directly fixing CO_2 (vide Volume I).

For simplicity the 'Buffers' of the blood may be classified into groups:

1. **Bicarbonate system**—located principally in the plasma:
$H^+ + HCO_3^- \rightleftharpoons H_2CO_3$

2. **Non-bicarbonate system**—consisting of haemoglobin and other buffers noted above which may be symbolised as Buf indicating all Buffer Anions excepting HCO_3^-.
Thus $H^+ + Buf^- \rightleftharpoons HBuf$.

3. Total Buffer Base (B.B.) of the blood:

B.B. = $Buf^- + HCO^-$ = 48 m Eq/litre at pCO_2 40 mm Hg and pH 7·4 and Hb 15 g%.

II. **Respiration**—Under normal conditions the alveolar ventilation is adjusted so as to maintain an arterial pCO_2 of 40 mm Hg and blood pH 7·4.

Respiratory regulation of blood pH is effected by rapid alteration of the volume of alveolar ventilation according to increase or decrease of $[H^+]$ of blood. Thus as a compensatory response to acidaemia—the respiratory centre is stimulated and the reaction:

$H^+ + HCO_3^- \rightleftharpoons H_2CO_3 \rightleftharpoons H_2O + CO_2$ moves to the right while the CO_2 is eliminated and H^+ is converted to H_2O. Likewise, in alkalaemia the reaction moves in the opposite direction and CO_2 is retained in blood when the concentration of H_2CO_3 increases, as a compensatory measure (Fig. 3.3).

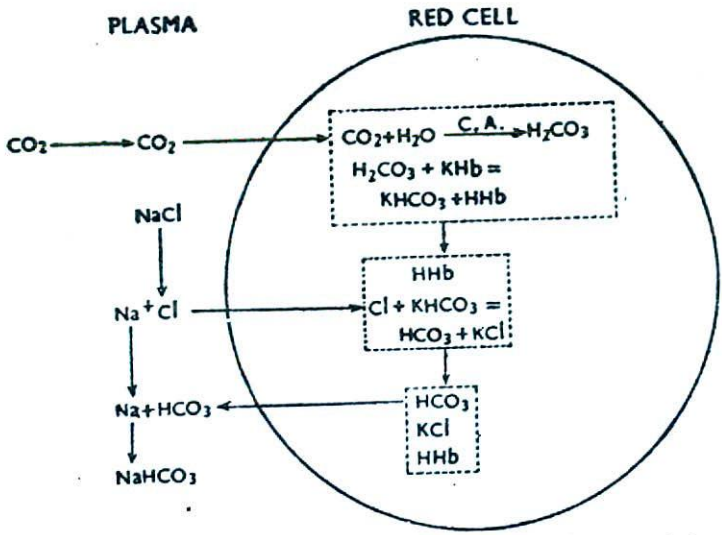


Fig. 3.3. Scnem showing the steps of chloride shift. C.A. = *carbonic anhydrase.*

III. **Kidneys** play an important role in maintaining a constant blood reaction by the mechanisms described below:

(1) **Absorption of filtered** $NaHCO_3$. Under normal conditions urine is almost free of bicarbonate. This helps in maintaining the 'alkali reserve' of the blood. In other words it helps to preserve the HCO_3 buffers of the blood.

(2) **Manufacturing of** H^+ by the renal tubular epithelium from H_2CO_3 and utilisation of the H^+ for

(a) **Formation of titrable acid** (24 to 28 mM/litre)

$Na_2HPO_4 = Na^+ + Na^+ + HPO_4^- + H^+ \rightleftharpoons$

NaH_2PO_4 (excreted) + Na^+ (reabsorbed as $NaHCO_3$) (Fig. 3.4)

(b) **Under conditions of acidosis** some of the H^+ manufactured may combine directly with the acid radical releasing the Na^+ to be reabsorbed as $NaHCO_3$.

Na-lactate + $H^+ \rightleftharpoons$ Lactic acid + Na^+ (reabsorbed as $NaHCO_3$)

(c) **Formation** of (NH_4^+)

About 30 to 50 mEquiv. of NH_4 salts are excreted daily in urine. The kidneys manufacture NH_3 from glutamine and some other amin acids. The H^+ manufactured by the kidney combines with NH_3 to form

(NH_4^+) radical (Fig. 3.5) which is exchanged for Na^+ in the glomerular filtrate in combination with nonvolatile acids, e.g., say aceto-acetic acid (AAA) in Diabetic Ketosis: $NaAA+(NH_4)^+ \quad NH_4AA+Na^+$ (reabsorbed as $NaHCO_3$)

Note: Mechanism of formation of H^+ by kidney:

$$H_2O+CO_2 \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

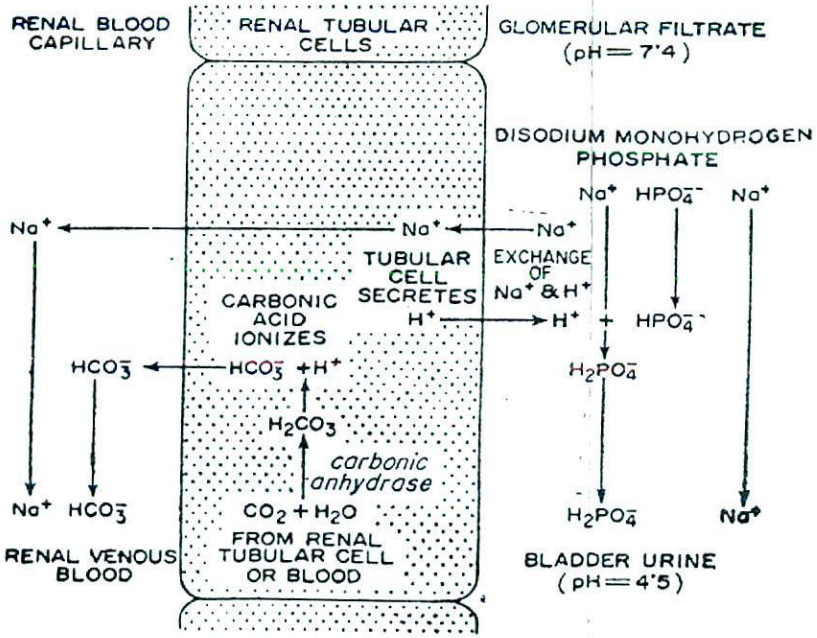


Fig. 3.4 Schematic representation of acid-base equilibrium by the kidneys by the armmonia mechanism.

Points to note :

(*i*) HCO_3^- is always available to combine with Na^+ released by H^+ from its combination with non-volatile acids.

(*ii*) This reaction is pCO_2 dependant. Higher the pCO_2 greater will be availability of H_2CO_3 and H^+ in the kidneys.

(*iii*) The reaction $H_2O+CO_2 \rightleftharpoons H_2CO_3$ is catalysed by the enzyme carbonic anhydrase (Fig. 3.3).

Under physiological conditions H_2SO_4 formed from oxidation of 'S' in methionine and cystine is excreted as Na_2SO_4. The reactions in the kidney may be briefly formulated as

$$Na_2SO_4+2H_2CO_3+2NH_3 \longrightarrow \underset{\downarrow \text{ excreted}}{(NH_4)_2SO_4} + \underset{\text{reabsorbed}}{2NaHCO_3}$$

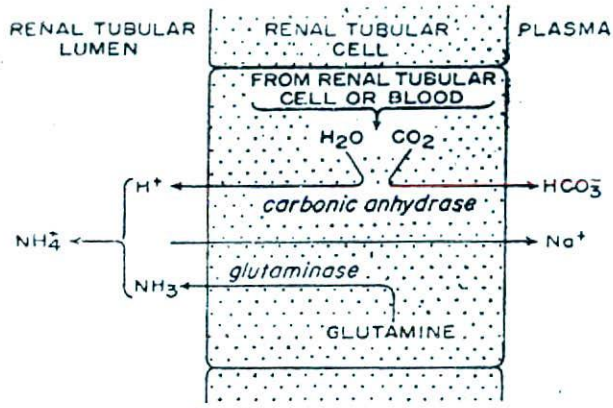


Fig. 3.5. Schematic representation of acid-base equilibrium by the kidneys by the ammonia mechanism.

The role of intestine in the regulation of blood reaction is not yet fully known. It is claimed that excess alkaline phosphates taken by the animal are excreted through the bowel, but in *acidaemia* these are absorbed and retained only to maintain the blood reaction constant. Furthermore, if an excess $CaCl_2$ is taken, then Ca^{++} is excreted in great parts through the bowel but the Cl^- is absorbed. The exces C^-thus takes away Na^+ from the Na-bicarbonate *(alkali reserve)* only to maintain the blood reaction constant. For this reaction alkali reserve is diminished in case of excess $CaCl_2$ taken.

DISTURBANCES IN ACID-BASE REGULATION

Alteration of hydrogen ion concentration of blood may lead to two main patho-chemical conditions:

1. **Acidosis,** 2. **Alkalosis.**

Acidosis is defined as a patho-chemical condition with lowering of blood pH below 7·36 resulting from primary accumulation of acid or primary loss of base from the body or from some specific fluid compartment of the body.

Alkalosis is a patho-chemical condition with increase of blood pH above 7·44 resulting from primary accumulation of base or primary loss of acid from the body or some specific fluid comportment of the body.

Before we proceed to learn the clinical status affecting acid-base balance it is worthwhile to be acquainted with certain recent terminology.

We have seen that

$$\text{Buffer Base} = Buf^- + HCO_3^-$$

where Buf^- represents all the acid anions capable of accepting H^+ including Hb. but excluding HCO_3^-. It amounts to 48 mEq./litre. at pCO_2 40 mm and pH 7·4. Obviously, B. B. value depends on the quantity of Hb.

"Base excess" is a condition where the B. B. value of the patient deviates from the normal value by a quantity which may be 'positive' (+) or 'negative' (—). Thus, if in a patient it is observed that the B. B. value is 20 the "base-excess" value is "—28".

The relationship is simple:

observed B.B.—normal B. B. = Base excess

20 —48 = —28

Base excess actually means either a deficit of 28 mEq./litre of 'Base' or an excess of 20 mEq./litre of 'Acid'.

(hypobasaemia or hyperacidaemia in blood)

Standard Bicarbonate—normal value 22 to 26 mEq/litre. It is the amount of HCO_3^- in the plasma at pCO_2 40 and fully orygenated Hb at 37°C.

Values of standard bicabonate outside the normal range indicates metabolic disequilibrium of acid-base balance the respiratory factor being eliminated by fixing the pCO_2 to 40 mm Hg.

Clinically 'acidosis' may be primarily due to either (i) Respiratory causes or (ii) Metabolic causes.

Since reaction of the blood depends primarily upon the ratio $H_2CO_3/NaHCO_3 = 1/20$, the simplest way of understanding the difference between the two types of acidosis is to understand that anything which lead to increase in H_2CO_3 (alveolar hypoventilation from any cause) will alter the ratio in such a way that excessive H^+ will accumulate in the blood (Respiratory acidosis). Whereas in metabolic acidosis too much of acid metabolites are formed and are buffered by $NaHCO_3$ (and other buffers) so that again there occurs "Base deficit" associated with increase in H^+ concentration.

Thus in respiratory acidosis the increase in H^+ is due primarily to increase in the numerator of the ratio $\frac{H_2CO_3}{NaHCO_3}$. In metabolic acidosis—the increase in H^+ is due primarily to decrease in the denominator of the ratio.

Respiratory acidosis—Definition: Acidosis is due to respiratory failure.

Causes: I. Alveolar hypoventilation from any cause, e.g. (i) Emphysema; (ii) Morphin or Barbiturate poisonistg; (iii) obruction to air-passage; (iv) Bulbar poliomyelitis; etc.

II. If there is too much of CO_2 in the inspired air.

The body response to respiratory acidosis may now be considered in greater details.

Alveolar hypoventilation $\rightarrow$rise in alveolar pCO_2 $\rightarrow$Rise in arterial pCO_2 $\rightarrow$increased H_2CO_3 $\rightarrow H^+ + HCO_3^- + H^+$ is buffered, so that, $H^+ Buf^- + H Buf$.

(1) There is rise in HCO_3^-.
(2) Corresponding diminution of Buf^-.
(3) Total Buffer Base ($HCO_3^- + Buf^-$) is unaltered.
(4) Therefore, there is no Base Excess (B.E.).
(5) pCO_2 is elevated and blood pH is low.

Compensatory Mechanisms

(1) Increased HCO_3^- is filtered by the kidney due to raised HCO_3^- in plasma. The whole of it is reabsorbed and sent back to the blood. This elevates the B. B. of the blood.

(2) Increased pCO_2 of blood means increased secretion of H^+ by the kidney. This excess 'H^+' is available for formation of 'titrable acid' and (NH_4^+) by the kidney so that base is conserved. This further elevates the Buffer of the blood.

So, after renal compensation both plasma HCO_3^- and other buffer bases (Buf^-) are elevated in the blood. There is 'positive Base Excess' and the blood pH is elevated and brought back near normal level in spite of the high pCO_2.

Causes of acidosis

It may be caused by either (1) *diminished bicarbonates* or primary accumulation of acids (metabolic acidosis) or (2) *increased H_2CO_3 in the plasma* (respiratory acidosis).

I. *Bicarbonates are diminished* or *accumulation of acids* occurs in the following conditions:

1. In **diabetes mellitus,** starvation and severe muscular exercise due to excessive production of non-volatile metabolic acids.
2. In **renal failure**—due to retention of acid metabolites.
3. **Diarrhoea** may lead to acidosis. It is caused by (*a*) Dehydration, impaired renal circulation and thereby low kidney function. (*b*) Anoxia—from impaired circulation leads to lactic acid accumulation in the tissues. (*c*) Acidosis and ketosis due to starvation. (*d*) Loss of bases in the faeces.
4. Intake of **acidifying agents** like ammonium chloride, NaH_2PO_4, salicylates and methyl alcohol.

NH_4Cl is split off in the liver cells and HCl is formed which enters the blood stream.

In the stage of acute *salicylate intoxication,* there is marked metabolic acidosis. In this condition excessive H^+ ions are produced as a result of interference with pathways in Krebs tricarboxylic acid cycle.

Methyl alcohol even in small amount may cause profound metabolic acidosis due to its conversion to strong formic acid.

5. Severe and prolonged **hypotension** leading to poor tissue perfusion and tissue anoxia.
6. **Cardiac arrest.**
7. **Hyperchloraemic acidosis** following implantation of the ureter into a segment of colon (*ureterosigmoidostomy*) as in carcinoma of the urinary bladder.
8. Infusion or retention of a large amount of fluids in the body may produce acidosis due to reduction of bicarbonate concentration (*dilutional acidosis*).

Patients suffering from acidosis due to diminished bicarbonate (metabolic acidosis) usually present with hurried shallow respiration, low blood pressure not responding to vasopressor drugs and sweating. Diagnosis of the acidosis and its correction is urgently needed to save the patient.

II. *Excess H_2CO_3 occurs* in the following conditions:

1. Diseases of lungs, viz., emphysema, etc.
2. Depressed respiration—from barbiturates, morphin, after anaesthesia, etc.
3. Obstruction to air-passages.
4. Operations on the chest or chest injuries.
5. Heart failure.
6. Sleep—causing depressed respiration.
7. Some forms of congenital heart disease.
8. Bulbar poliomyelitis.
9. Inspired air containing excess CO_2 (experimental).

Causes of alkalosis

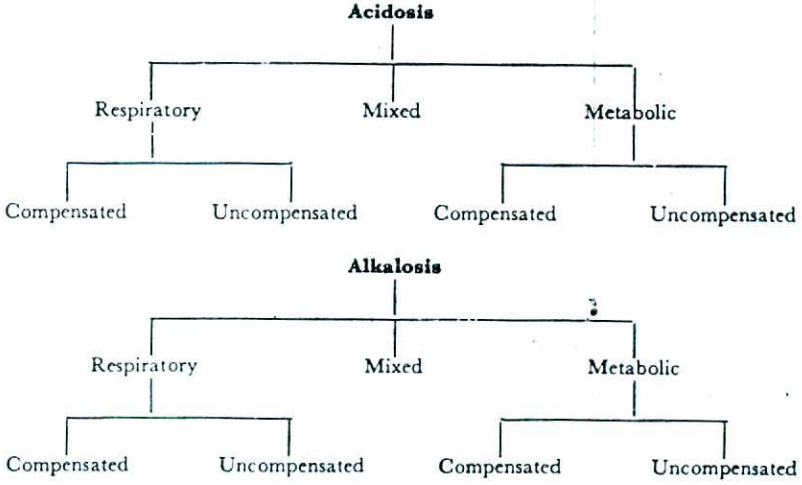
It may occur under the two general conditions:

I. *Accumulation of bicarbonate content of plasma* or primary loss of acids occurs in the following conditions: (*a*) **Excess of alkali intake**—as in the treatment of peptic ulcer (*milk-alkali syndrome*). (*b*) **Vomiting** specially in the early stages (in the late stages of vomiting acidosis and ketosis occur due to starvation), viz. (*i*) in pyloric stenosis, (*ii*) in high intestinal obstruction. (*c*) **Over zealous treatment of acidosis** without repeated assessment for the acid-base status. (*d*) **Potassium deficiency** leads to intracellular migration of H^+ ion in exchange of potassium lost from the cell. Unlike other types of alkalosis, there occurs aciduri in alkalosis following potassium deficiency (*paradoxical aciduria*).

II. *Fall of pCO_2 of blood* occurs in the following conditions: (*a*) Voluntary **hyperpnoea.** (*b*) **High external temperature** with moist air, causing increased pulmonary ventilation to help heat loss. Excess CO_2 is also lost, hence, alkalosis. (*c*) **Anoxia.** (*d*) **High altitude,** etc.

Patients with alkalosis suffer from lethargy, muscular weakness and mental confusion.

Acidosis and alkalosis are classified as follows:



Henderson-Hasselbalch equation states that :

$$pH = pK + \log \frac{[HCO_3^-] = [\text{Bicarbonate}]}{[H_2CO_3] = [\text{Carbonic Acid}]}$$

$$= 6{\cdot}1 + \log \frac{[HCO_3^-]}{0{\cdot}0301 \times \text{partial pressure of } CO_2\ (pCO_2)}$$

It is evident from the above equation that pH of a sample of blood depends on the $[HCO_3^-]/[pCO_2]$ ratio. When this ratio is increased, pH will be elevated resulting in alkalosis. The ratio is increased either by rise of the numerator (bicarbonate) or by decrease of the denominator (partial pressure of CO_2). Similarly acidosis, i.e., lowering of pH will occur when $[HCO^-]/[pCO_2]$ ratio is decreased. The decrease of the ratio may be due

to the decrease of the numerator (bicarbonate) or due to the increase of the denominator (partial pressure of CO_2). In either case, acidosis or alkalosis, when the alteration of the pH is primarily due to bicarbonate concentration of blood, the condition is designated as metabolic or non-respiratory. Similarly, the alteration of pH resulting in acidosis or alkalosis primarily due to carbon dioxide tension of the blood, is designated as respiratory or gaseous.

Metabolic acidosis

The excess metabolic H^+ are buffered both by—HCO and by non-bicarbonate buffer system. Thus

(1) $H^+ + HCO_3^- \rightarrow H_2CO_3 \rightarrow H_2O + CO_2$

(2) $H^+ + Buf^- \rightarrow H\ Buf$

In contradistinction to Respiratory Acidosis, therefore, the Metabolic Acidosis is accompanied by diminished total Buffer Base (i.e., negative Base Excess value) as well as by diminution in Standard Bicarbonate.

Compensation—(1) Partial compensation is effected by hyperventilation caused by acidosis. This results in fall in pCO_2 and the amount of H_2CO_3 in the blood.

(2) Renal compensation—takes longer time to be established but is more effective.

The kidneys reabsorb all the $-HCO_3^-$ that is filtered and continue to excrete H^+ in the form of titrable acidity and NH_4^+ salts.

If the metabolic defects are rectified in the mean time, e.g., by insulin in diabetic acidosis—the HCO^- concentration of the blood increases (due to continued reabsorption by the kidney) and the B. B. are restored to normal:

$H\ Buf + HCO_3^- \rightarrow Buf^- + H_2CO_3$

Respiratory alkalosis—Causes, (1) Anoxia leading to hyperventilation; (2) some lungs disease; (3) some cerebral disease; (4) hepatic failure.

Any condition which leads to hyperventilation will drive out CO_2 from the body and the concentration of H_2CO_3 in the blood will fall with relative excess of HCO_3^-, which is responsible for alkalosis.

The excess HCO_3^- is buffered as follows:

$$HCO_3^- + HBuf \rightleftharpoons Buf^- + H_2O + CO_2 \text{ (expired)}.$$

This tends to diminish HCO_3^- with corresponding increase in Buf^- so that the total B. B. and base excess remains unaltered.

In a typical case the biochemical data may be as follows:

pH=7·52, pCO_2=22 mm Hg (due to hyperventilation).

Plasma bicarbonates 16 mEq/litre (due to buffers as noted above).

B.E=0.

Renal compensation—The amount of HCO_3^- filtered by the kidneys is not reabsorbed by the renal tubule and is excretedin the urine. H^+ is secreted by the tubule is pCO_2 dependent and since pCO_2 is low H^+ secreted by the renal tubules is low. Therefore, the titrable acidity and the NH_3 coefficient of the urine are both decreased and the kidney secretes an alkaline urine to correct the alkalosis.

Metabolic Alkalosis

Causes:—(1) Loss of any acid from the body excepting H_2CO_3 e.g., loss of HCl in repeated vomiting

(2) Intravenous infusions of Na-lactate or Na-salt of other organic acids which are oxidised to $NaHCO_3$ in the body.

(3) Alkalosis from prolonged treatment of peptic ulcer with anti acids and alkalies.

Alkalosis at once depresses respiration leading to rise in pCO_2 and H_2CO_3 in blood (Respiratory compensation)

$H_2CO_3 \rightarrow H^+ + HCO_3^-$

Some of the HCO_3^- are buffered by nonbicarbonate buffers:

$HCO_3^- + H\ Buf \rightarrow H_2CO_3 + Buf^-$

There thus occurs increase in pCO_2 along with rise in total Buffer Base as well as Bicarbonate in the blood.

Renal compensation is slow to develop and consists mainly in excretion of excess of alkali from the body in the form of alkaline urine. It may be noted that the high pCO_2 favours the formation of H^+ by the kidney and excretion of titrable acid and (NH_4) salts. In this respect the respiratory compensatory effect counteracts to some extent the renal compensatory effects. But nevertheless, if adequate treatment is available—the continued excretion of alkaline urine by the kidney establishes the normal blood pH within a reasonable period.

Assessment of the acid-base status

Precise evaluation of acid-base abnormalities is necessary for instituting proper treatment in many clinical conditions, to indicate the type and severity of the acid-base disturbance, determination of (1) pH, (2) pCO_2 and (3) the base content of arterial blood is necessary.

1. **pH.** Nowadays pH of whole blood is universally determined eletrometrically using a reliable pH metres, equipped with thermostated glass electrode at a temperature of 37°C. This can be done with only 2 to 3 drops of blood with an Astrups apparatus (Fig. 3.6).

2. **pCO_2.** Arterial pCO_2 can be determined directly with the help of a pCO_2 electrode, or computed from Siggaard-Andersen nomogram (Fig. 3·7).

3. **Base content.** Base content of blood may be expressed by any one or combination of the some of the following:

(*i*) **total CO_2 of plasma,**
(*ii*) **CO_2-combining power of plasma,**
(*iii*) **standard bicarbonate of plasma,**
(*iv*) **base excess (BE) of blood,**
(*v*) **buffer base (BB) blood.**

(*i*) **Total CO_2 content of the separated plasma** can be measured by volumetric, manometric or titremetric techniques. The value varies with the pCO_2 and oxygen saturation and hence does not correctly represent the non-respiratory (metabolic) disturbances in presence of respiratory abnormalities.

(*ii*) **CO_2-combining power of plasma** is defined as the CO_2 content of plasma separated at actual pH and then equilibrated with CO_2 at 40 mm Hg. This also does not correctly represent the base content of blood in presence of respiratory disturbances for reasons same as in (i).

(*iii*) **Standard bicarbonate** has already been explained in p. 3-5.

(*iv*) **Base excess (BE) and base deficit** are the measures of the amount of base or acid required to restore 1 litre of blood to normal acid-

base status at pCO_2 40 mm Hg at 37°C. This parameter is also directly read out from the Siggaard-Andersen nomogram. Normal value varies from —2·5 to +2·3 m Eq/litre blood. Positive values above +2·3 indicate metabolic alkalosis and the negative values below —2·5 indicate base deficit, hence, metabolic acidosis. The greatest value of this parameter is that it readily gives the amount of sodium bicarbonate or ammonium chloride in mEq/litre required to correct the metabolic acidosis or alkalosis in clinical practice by applying the formula:

$$a = 0{\cdot}30 \times \text{body weight in kg} \times \text{base excess},$$

where 'a' denotes the amount of sodibicarb or ammonium-chloride required in mEq/litre to correct the acidosis or alkalosis.

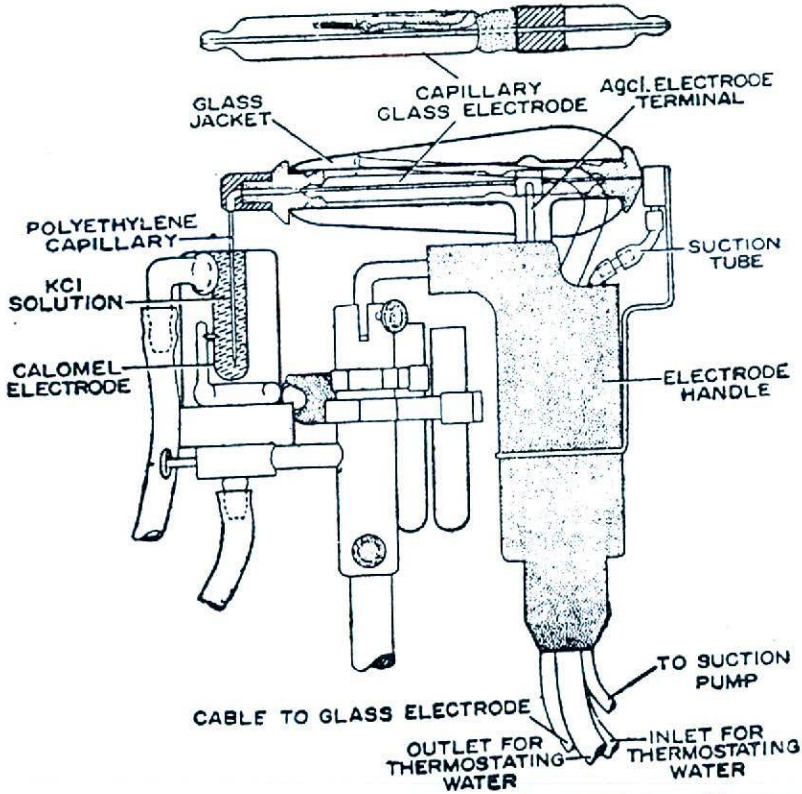


Fig. 3.6 Thermostated micro-electrode unit of Astrup micro-equipments. pH measurements are made by meaus of a thermostated capillary glass electrode and calomel electrode. In order to measure the pH, blood is drnwn anaerobica by into the capillary of the glass electrode by suction.

(*v*) **Buffer base** (BB). This term denotes the sum total of actual concentration of buffer anions ($Prot^-$, Hb^-, etc.) in a sample of blood. This is different from the term normal buffer base (NBB) in that, NBB signifies the concentration of all the buffer anions estimated at 40 mm

Hg pCO_2 at 37°C. It follows that BB—NBB=BE (Singer and Hastings). Normal value for the buffer base in an individual with 15 g of haemoglobin per 100 ml of blood is 50 mEq/litre blood.

Most of the above-mentioned acid-base parameters can be determined with only few drops of arterial or capillary (arterialised) blood using Astrup blood-gas micro-equipments consisting of a pH metre; thermostated micro-electrode unit; a circulating water thermostat with a built-in section device; and a microtonometer for equilibration of blood with two known oxygen-carbon dioxide gas mixtures. From this apparatus three pH values are determined from the sample of blood at°37 C.—(a) actual pH, (b) pH after equilibrating with 4% carbon dioxide and 96% oxygen mixture, and (c) pH after equilibrating with 8% CO_2 and 92% O_2 mixture.

The pH values for (b) and (c) are plotted on the Siggaard-Andersen nomogram (Fig. 3.7). They are shown as Z⊙ and X⊙ respectively

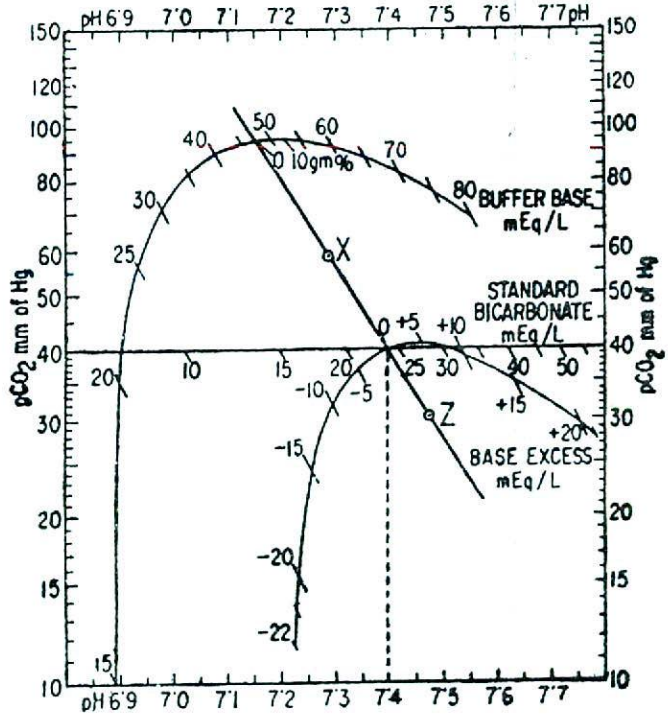


Fig. 3.7. Siggaard-Andersen curve nomogram.

on the nomogram. A log pCO_2/pH line is drawn by joining ⊙Z and ⊙X by a straight line. By interpolating (a) log pCO_2/pH line, the actual-pCO_2 of the sample of blood is determinted. The values for base excess (BE), standard bicarbonate and buffer base (BB) are read out directly from the nomogram where the log pCO_2/pH line intersects the corresponding curves on the nomogram.

⊙X is the pH of the sample after equilibration with 8% CO_2 and 92% O_2. ⊙Z is pH of same sample after equilibration with 4% CO_2 and 96% O_2, X–Z line is the log pCO_2/pH line. $⊙0_2$ is the actual pH of the sample (here 7·4) without equilibration interpolated on X–Z line. pCO_2 is read out from the nomogram by drawing a horizontal line through ⊙O (here 40 mm of Hg).

The B. B, (Buffer Base) value is 48 mEq/litre. and there is no base excess (Base Excess = 0).