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## PHYSIOLOGY OF ACID BASE BALANCE

Awati M. N[1], Vandana Mudda[2], Minal Chandra[3], Samudyatha T. J[4]

**ABSTRACT:** Acid-base, electrolyte, and metabolic disturbances are common in the intensive care unit. Almost all critically ill patients often suffer from compound acid-base and electrolyte disorders. Successful evaluation and management of such patients requires recognition of common patterns (e.g., metabolic acidosis) and the ability to dissect one disorder from another. The intensivists needs to identify and correct these condition with the easiest available tools as they are the associated with multiorgan failure. Understanding the elements of normal physiology in these areas is very important so as to diagnose the pathological condition and take adequate measures as early as possible. Arterial blood gas analysis is one such tool for early detection of acid base disorder. Physiology of acid base is complex and here is the attempt to simplify it in our day to day application for the benefit of critically ill patients.
**KEYWORDS:** PH, Pka, Buffer.

**INTRODUCTION:** Under normal conditions PH of ECF is maintained between 7.35-7.45.[1] Maintenance of this constant blood PH is prime requisites of life and any material variation on either side, disturbs the vital process and may lead to death. The mechanisms of neutrality regulations are concerned with maintaining a state of equilibrium b/w production & removal of H+ ions.

There are multiple acid-base buffering mechanisms involving the blood, cells and lungs that are essential in maintaining normal H+ concentrations in both the extracellular and the intracellular fluid.[2]

**This is achieved through three lines of defense:**
1. physico-chemical buffering,
2. rapid respiratory changes in pCO2,
3. slow renal changes in H+ excretion and HCO3− reabsorption and production.

**DISCUSSION: HYDROGEN ION CONCENTRATION IS REGULATED BY;**
- Precise $H^+$ regulation is essential because the activities of almost all enzyme systems in the body are influenced by H+ concentration.[3]
- Changes in hydrogen concentration alter virtually all cell and body functions.
- Normal concentration of $H^+$ is only 0.00004 mEq/L.
- The precision with which $H^+$ is regulated emphasizes its importance to the various cell functions.

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**DEFINITIONS:**

- **ACID**[4]- Molecules containing hydrogen atoms that can release hydrogen ions in solutions are referred to as acids. Eg: HCl, $H_2CO_3$.
- A strong acid is one that rapidly dissociates and releases especially large amounts of H+ in solution.
- Eg: HCl.
- Weak acids have less tendency to dissociate their ions and, therefore, release $H^+$ with less vigor.
- Eg: $H_2CO_3$.
- A strong base is one that reacts rapidly and strongly with H+. Eg: $OH^-$
- Weak base binds with H+ much more weakly. Eg: $HCO3^-$

**BASE**[5]- A base is an ion or a molecule that can accept a hydrogen ion. Eg: HCO3 $^-$
pH/ Pka The dissociation of a weak acid is a reversible reaction and hence is at equilibrium.
Ka is the dissociation constant.

$$HA \xleftrightarrow{} [H^+] [A^-] \quad OR \quad Ka = \frac{[H^+] [A^-]}{[HA]}$$
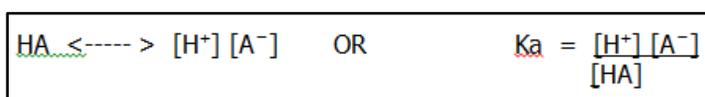
Because H+ concentration normally is low it is customary to express H+ concentration on a logarithm scale, using pH unit.

$$pH = -\log [H^+] = \frac{1}{\log [H^+]}$$

- Lower the pH, higher the acidity, i.e. $[H^+]$.
- With each point increase in the pH value, $[H^+]$ decreases by 10 times. (logarthmic)
- PKA is the pH at which an acid is half ionized and it is constant at a particular temp. and pressure.
- Strong acids have low PKA and vice versa.
- Intracellular pH is more acidic than plasma, averaging approximately 7.05. But it is not same in all tissues and differs in accordance with the functional activity of the cells.

It is generally accepted that changes in blood H +concentration occur as the result of changes in volatile [partial carbon dioxide tension (pCO2)] and nonvolatile acids (hydrochloric, sulfuric, lactic, etc). Clinically, refer to changes in volatile acids as 'respiratory' and changes in nonvolatile acids as 'metabolic'.

Three methods quantify the metabolic component either by using HCO3 - (in the context of pCO2), the standard base excess (SBE), or the strong ion difference. (SID)

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**THE HENDERSON-HASSELBALCH EQUATION (H-H)[6]:**
- H-H equation mathematically illustrates how the pH of a solution is influenced by the HCO3– to H2CO3 ratio (the bicarbonate buffer system); the base to acid ratio.

**H-H equation is written as follows:**
- PH = PK + log [ $HCO_3^-$ ]/ [$H_2CO_3$]
- pK is derived from the dissociation constant of the acid portion of the buffer combination.
- pK is 6:1 and, under normal conditions, the $HCO_3^-$ to $H_2CO_3$ ratio is 20:1.
- Clinically, the dissolved $CO_2$ ($PCO_2$ x 0.03) can be used for the denominator of the H-H equations, instead of the $H_2CO_3$.
- This is possible since the dissolved carbon dioxide is in equilibrium with, and directly proportional to, the blood [H2CO3], the PaCO2 is easily measured via blood gas analysis and can easily be converted to mmol/L (same as mEq/L).

**THUS, THE H-H EQUATION CAN BE WRITTEN AS FOLLOWS:** When the HCO3$^-$ is 24 mEq/L, and the PaCO2 is 40 mm Hg, the base to acid ratio is 20:1 and the pH is 7.4 (normal).

**H-H equation confirms the 20:1 ratio and pH of 7.4 as follows:**
- PH = PK + log [HCO3$^-$]/($PCO_2$×0.03)
- H -H Equation Applied During Normal Conditions
- PH = PK + LOG(HCO3$^-$) / ($PCO_2$× 0.03)
    = 6.1 + LOG 24/ 40×0.03
    = 6.1 + LOG 24/1.2
    = 6.1 + LOG 20/1
    = 6.1+ 1.3 =7.4

**BASE EXCESS APPROACH TO ACID/BASE PHYSIOLOGY:** The nonlinearity of Henderson-Hasselbalch prevents from quantifying the exact amount of bicarbonate deficit in a metabolic acidosis. This observation led to the development of a semi quantitative approach, base excess (BE).

BE = (HCO3 − 24.4 + [2.3 X Hgb + 7.7] X [pH − 7.4]) X (1 − 0.023 X Hgb)

Base excess attempts to give a quantitative amount of bicarbonate (mmol) that is required to be added or subtracted to restore 1 L of whole blood to a pH of 7.4 at a pCO2 of 40 mm Hg. To standardize BE for haemoglobin, the following formula was developed with improved in vivo accuracy, the standardized base excess (SBE):

SBE = 0.9287 X (HCO3 − 24.4 + 14.83 X [pH − 7.4])

**STRONG ION DIFFERENCE[7]:** Dr. Peter Stewart developed an acid/base theory (Strong Ion) using quantitative chemistry, which accounted for fluctuations of all the ions dissolved in plasma. Based on the requirements for electrical neutrality in any solution as any one of the concentrations of these ions changes, water must dissociate into H+ or OH- to balance the charge.

SID = [Na+ + K+ + Ca2+ + Mg2+] – [Cl- + Lactate-]

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Buffer system[8]: A buffer is defined as a solution which resists change in PH upon addition of acid or base to the solution.

Buffers consist of mixture of weak acid and its salt /weak base and its salt.

**MECHANISM OF BUFFER ACTION:** When a strong acid is added to a solution, it forms a weak acid and its salt.

$$HCl + CH_3COONa \longrightarrow CH_3COOH + NaCl$$
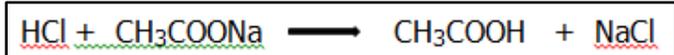
Similarly, when a strong base is added, it reacts with the weak acid of buffer and forms a salt.

$$NaOH + CH_3COOH \longrightarrow CH_3COONa + H_2O$$
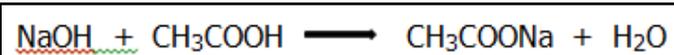
Thus changes in pH are minimized.

Normally a number of acids are constantly produced in the body during various metabolic processes

Volatile acids: $H_2CO_3$

Fixed acids: Lactic acid, keto acids, $H_2SO_4$, $H_3PO_4$

The body regulatory mechanisms promptly and effectively remove the excess acid and maintain body pH within a normal range

**SOURCES OF ACID TO BODY:**
1) Carbonic acid: chief acid, from oxidation of carbon compounds
   -Cellular metabolism produces $CO_2$

$$CO_2 + H_2O \longrightarrow H_2CO_3 \longrightarrow H^+ + HCO3^-$$
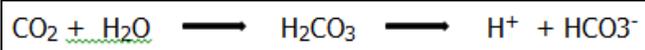
2) $H_2SO_4$: Strong acid, from sulphur containing amino acids.
3) $H_3PO_4$: From dietary phospho-proteins.
4) Organic acids: from oxidation of major food stuffs.
5) Iatrogenic: certain drugs.

**DEFENCE AGAINST CHANGES IN H+ ION IN BODY-** There is three primary systems that regulate the H+ concentration in the body fluids to prevent acidosis or alkalosis:
1) The chemical acid-base buffer systems of the body fluids.
2) The respiratory system, which regulates the removal of CO2.
3) The kidneys, which can excrete either acid or alkaline urine.

When there is a change in H+ concentration, the buffer systems of the body fluids react within a fraction of a second to minimize these changes.

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First two lines of defense keep the H+ concentration from changing too much until the more slowly responding third line of defense, the kidneys, can eliminate the excess acid or base from the body.

Although the kidneys are relatively slow to respond compared with the other defenses, they are by far the most powerful of the acid-base regulatory systems.

## 1) BICARBONATE BUFFER SYSTEM:

- The major buffer system in the ECF is the CO2-bicarbonate buffer system.
- This is responsible for about 80% of extracellular buffering.
- The bicarbonate buffer system consists of a water solution that contains two ingredients:
  1. a weak acid, $H_2CO_3$, and
  2. a bicarbonate salt, such as $NaHCO_3$.
- Normal ratio in blood = NaHCO3 / $HCO_3$ = 20/1.
- They are the chief buffers of blood & constitutes–alkali reserve.
- Mechanism of action.
- When a strong and non-volatile acid, Eg. Lactic acid is added.

$$NaHCO_3 + H+ L- \longrightarrow \underset{\text{(weak acid)}}{H_2CO_3} + \underset{\text{(salt)}}{Na\text{-}Lactate}$$

$$H_2CO_3 \overset{}{\underset{CA}{\longrightarrow}} CO_2 + H_2O \text{ (CO}_2 \text{ eliminated through lungs)}$$
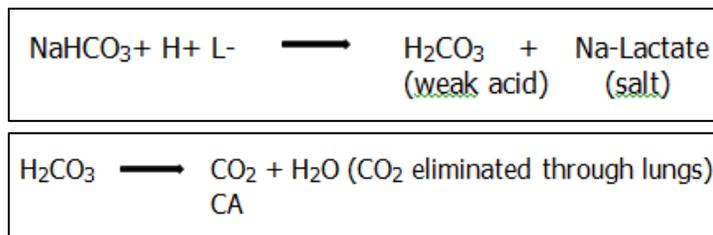
Thus, a strong and non-volatile acid is converted into a weak and volatile acid at the expense of NaHCO3 (salt component of the buffer) – bicarbonate buffer system is directly linked to respiration.

When an alkaline substance enters (Eg. NaOH)

$$CO_2 + H_2O \overset{}{\underset{CA}{\longrightarrow}} H_2CO_3$$

$$H_2CO_3 + NaOH \longrightarrow H_2O + NaHCO_3$$

(-HCO3 eliminated through kidney)
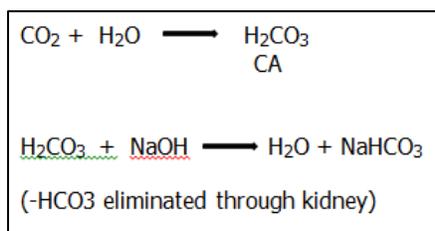
**Alkali reserve**: Represented by NaHCO3 concentration in blood The Henderson–Hasselbalch equation for bicarbonate can be written as follows:

pH = Pka + log $(HCO_3\text{-})/(.03x\ PCO_2)$ where pk is 6.1

It is apparent that an increase in HCO3$^-$ concentration causes the pH to rise, shifting the acid-base balance toward alkalosis.

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An increase in PCO2 causes the pH to decrease, shifting the acid-base balance toward acidosis. According to HENDERSON - HASSELBALCH'S equation.

pH = pKa + log (HCO3-) / [0.03×PCO2]

= 6.1 + log (hco3-)[0.03×PC02]

= 6.1 + log 24 / 1.2

= 6.1 +log 20 = 6.1 + 1.3 = 7.4

The Henderson-Hasselbalch equation, in addition to defining the determinants of normal pH regulation and acid-base balance in the extracellular fluid, provides insight into the physiologic control of acid and base composition of the extracellular fluid.

Normal physiologic acid-base homeostasis results from the coordinated efforts of kidneys and lungs

**ADVANTAGES**: Bicarbonate is an efficient buffer due to high alkali reserve and a weak and volatile acid, exhaled as $CO_2$.

**DISADVANTAGE**: As a chemical buffer, it is rather weak, pK which is farther away from physiological pH.
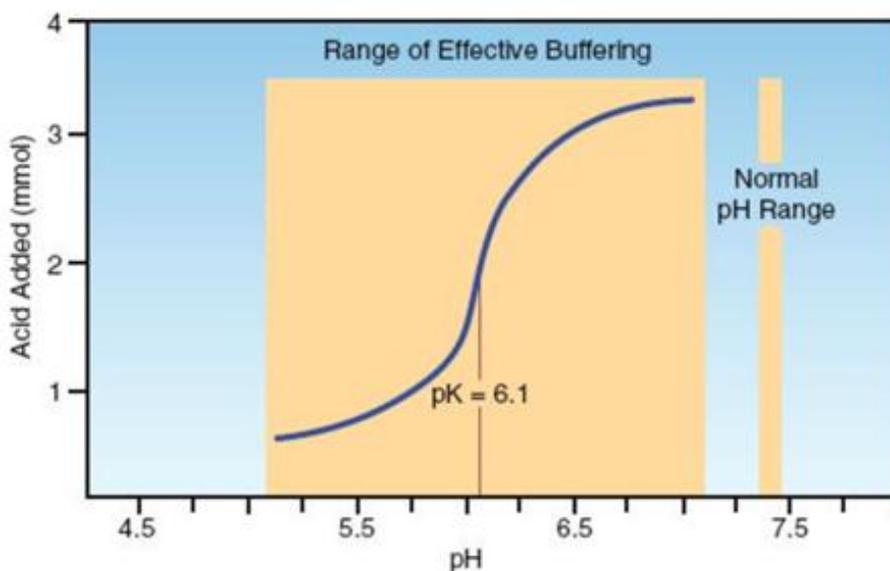


Buffer Power" Is Determined by the Amount and Relative Concentrations of the Buffer Components.

The buffer system is still reasonably effective for 1.0 pH unit on either side of the pK(5.1 – 7.1) Beyond these limits, the buffering power rapidly diminishes.

The two elements of the buffer system, HCO3– and CO2, are regulated, respectively, by the kidneys and the lungs.

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As a result of this regulation, the pH of the extracellular fluid can be precisely controlled by the relative rate of removal and addition of HCO3– by the kidneys and the rate of removal of CO2 by the lungs. It plays a major role in buffering renal tubular fluid and intracellular fluids.

## 2) The phosphate buffer system[10]:

The phosphate buffer system has a pK of 6.8, which is not far from the normal pH of 7.4 in the body fluids; Present in low concentration in plasma ratio of $Na_2HPO_4$: $NaH_2PO_4$ = 4:1. Ratio is kept constant by kidneys and normally functioning kidneys required for its action.

**The phosphate buffer is especially important in the tubular fluids of the kidneys, for two reasons:**
1) Phosphate usually becomes greatly concentrated in the tubules, thereby increasing the buffering power of the phosphate system.
2) The tubular fluid usually has a considerably lower pH than the extracellular fluid, bringing the operating range of the buffer closer to the pK (6.8) of the system.

The phosphate buffer system is also important in buffering intracellular fluid.

**DISADVANTAGES:** Low concentration (1mmol/L) and hence less efficient as a physiological buffer.

## 3) PROTEIN BUFFER[11]: Protein buffers in the body include:
- plasma protein buffer system.
- Hemoglobin buffer system (RBC).
- Buffering capacity of plasma proteins is less than hemoglobin.
- Buffering capacity depends on the pKa of the ionisable groups of amino acids.
- Histidine with its imidazole group – most effective.

**MECHANISM OF ACTION**: The acidic group COOH dissociates to COO- and H+, The H+ reacts with OH- of alkali and forms $H_2O$ and the protein becomes negatively charged (anion).

Sodium proteinate, the salt component combines with strong acids and produces weak acid, HPr

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Na+ Pr - + H+L -          ⟶          NaL  +  HPr
( strong acid)                        (salt)  (weak acid)
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**PROTEINS:** Proteins are among the most plentiful buffers in the body because of their high concentrations, especially within the cells.

Proteins contain – COO- groups, which, like acetate ions ($CH_3COO-$), can act as proton acceptors, also contain – $NH_3+$ groups, which, like ammonium ions ($NH_4+$), can donate protons. If acid comes into blood, hydronium ions can be neutralized by the – COO- group.

$$-COO^- + H_3O^+ \longrightarrow -COOH + H_2O$$

If base is added, it can be neutralized by the – NH3+ groups

$$NH3^+ + OH- \longrightarrow -NH2 + H2O$$
$$\text{(salt)} \qquad \text{(weak acid)}$$

Approximately 60 to 70 per cent of the total chemical buffering of the body fluids is inside the cells, and most of this results from the intracellular proteins.

**Factor that contributes to their buffering power;**
1) The high concentration of proteins in the cells,
2) The pKs of many of these protein systems are fairly close to 7.4.

**HAEMOGLOBIN:**
- Haemoglobin is an important blood buffer particularly for buffering $CO_2$.
- Protein buffers in blood include haemoglobin (150g/l) and plasma proteins (70g/l).
- Buffering is by the imidazole group of the histidine residues which has a pKa of about 6.8.
- This is suitable for effective buffering at physiological pH.
- Haemoglobin is quantitatively about 6 times more important then the plasma proteins as it is present in about twice the concentration and contains about three times the number of histidine residues per molecule.
- Hemoglobin is rich in histidine, which is an effective buffer from pH 5.7 to 7.7.
- Hemoglobin is the most important non-carbonic buffer in extracellular fluid.
- oxyHb – is strong acid, imidazole group donates $H^+$.
- Deoxy Hb – less acidic, $N_2$ group acts as base & takes up $H^+$ ions.

**IN TISSUE:**
1. Due to the low $O_2$ tension, acidity of medium and $CO_2$ bohr effect, oxy-Hb ($HbO_2$) dissociates delivering $O_2$ to tissues, forming deoxygenated Hb.
2. $CO_2$ formed in the cells is hydrated to form $H_2CO3$, which ionises to H+ and HCO3-
3. Deoxy Hb acts as anion and accepts the H+ forming HHb (reduced Hb).

When a tissue's metabolic rate increases, its carbon dioxide production increases. This causes the pH of tissues to decrease - promotes the dissociation of oxygen from haemoglobin. Conversely, binding of oxygen causes hemoglobin to release protons, which combine with bicarbonate to drive off carbon dioxide in exhalation.
Since these two reactions are closely matched, there is little change in pH.

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**Respiratory regulation of acid base balance[13]:**
- The second line of defence against acid-base disturbances is control of extracellular fluid CO2 concentration by the lungs.
- An increase in ventilation eliminates CO2 from extracellular fluid, which, by mass action, reduces the H+ concentration
- About 1.2 mol/ L of dissolved CO2 normally is in the extracellular fluid, corresponding to a Pco2 of 40 mm Hg.
- Changes in either pulmonary ventilation or the rate of CO2 formation by the tissues can change the extracellular fluid Pco2.
- Changes in alveolar ventilation responsible for pulmonary compensation of PaCO2 are mediated by chemoreceptors within the brain stem.
- These receptors respond to changes in cerebrospinal spinal fluid pH.
- Minute ventilation increases 1–4 L/min for every 1 mm Hg increase in PaCO2.
- the lungs are responsible for eliminating the approximately 15 mEq of carbon dioxide produced every day as a byproduct of carbohydrate and fat metabolism.
- Pulmonary compensatory responses are also important in defending against marked changes in pH during metabolic disturbances
- Feedback control of H+ ION concentration by respiratory system
- Because increased H+ concentration stimulates respiration, and because increased alveolar ventilation decreases the H+ concentration, the respiratory system acts as a typical negative feedback controller of H+ concentration.
- That is, whenever the H+ concentration increases above normal, the respiratory system is stimulated, and alveolar ventilation increases
- This decreases the PCO2 in extracellular fluid and reduces H+ concentration back toward normal.

## PULMONARY COMPENSATION DURING METABOLIC ACIDOSIS:
- Decreases in arterial blood pH stimulate medullary respiratory centers.
- The resulting increase in alveolar ventilation lowers PaCO2 and tends to restore arterial pH toward normal.
- The pulmonary response to lower PaCO2 occurs rapidly but may not reach a predictably steady state until 12–24 h; pH is never completely restored to normal.
- PaCO2 normally decreases 1–1.5 mm Hg below 40 mm Hg for every 1 mEq/L decrease in plasma [HCO3–].

## PULMONARY COMPENSATION DURING METABOLIC ALKALOSIS:
- Increases in arterial blood pH depress respiratory centers.
- The resulting alveolar hypoventilation tends to elevate $PaCO_2$ and restore arterial pH toward normal.
- The pulmonary response to metabolic alkalosis is generally less predictable than the response to metabolic acidosis. Hypoxemia, as a result of progressive hypoventilation,

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eventually activates oxygen-sensitive chemoreceptors; the latter stimulates ventilation and limits the compensatory pulmonary response.

- As a general rule, $PaCO_2$ can be expected to increase 0.25–1 mm Hg for each 1 mEq/L increase in [HCO3–].

**Efficiency of Respiratory Control of Hydrogen Ion Concentration:** Respiratory control cannot return the H+ concentration all the way back to normal when a disturbance outside the respiratory system has altered pH.

**BUFFERING POWER OF THE RESPIRATORY SYSTEM:** Respiratory regulation of acid-base balance is a physiologic type of buffer system because it acts rapidly and keeps the H+ concentration from changing too much until the slowly responding kidneys can eliminate the imbalance.

Renal control of acid base balance.[14] The kidneys control acid-base balance by excreting either an acidic or a basic urine. Large numbers of $HCO3^-$ are filtered continuously into the tubules, and they are excreted into the urine, this removes base from the blood.

Large numbers of $H^+$ are also secreted into the tubular lumen by the tubular epithelial cells, thus removing acid from the blood.

**Renal compensation[15,16,17]:** The ability of the kidneys to control the amount of $HCO3^-$ reabsorbed from filtered tubular fluid, form new $HCO3^-$, and eliminate H+ in the form of titratable acids and ammonium ions allows them to exert a major influence on pH during both metabolic and respiratory acid–base disturbances.

Kidneys are responsible for eliminating the approximately 1 mEq/kg per day of sulphuric acid, phosphoric acid, and incompletely oxidized organic acids that are normally produced by the metabolism of dietary and endogenous proteins, nucleoproteins, and organic phosphates from phosphoproteins and phospholipids.

Metabolism of nucleoproteins also produces uric acid. Incomplete combustion of fatty acids and glucose produces keto acids and lactic acid.

Endogenous alkali are produced during the metabolism of some anionic amino acids (glutamate and aspartate) and other organic compounds (citrate, acetate, and lactate), but the quantity is insufficient to offset the endogenous acid production

**RENAL COMPENSATION DURING ACIDOSIS:** The renal response to acidemia is 3-fold:
1. Increased reabsorption of the filtered $HCO3^-$.
2. Increased excretion of titratable acids
3. Increased production of ammonia.

These mechanisms are probably activated immediately, but their effects are generally not appreciable for 12–24 hrs and may not be maximal for up to 5 days.

**INCREASED REABSORBTION OF HCO3⁻:** $CO_2$ within renal tubular cells combines with water in the presence of carbonic anhydrase.

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The carbonic acid (H2CO3) formed rapidly dissociates into H+ and HCO3$^-$. Bicarbonate ion then enters the bloodstream while the H+ is secreted into the renal tubule, where it reacts with filtered HCO3$^-$ to form $H_2CO_3$.

Carbonic anhydrase associated with the luminal brush border catalyzes the dissociation of $H_2CO_3$ into $CO_2$ and $H_2O$. $CO_2$ thus formed can diffuse back into the renal tubular cell to replace the $CO_2$ originally consumed. The proximal tubules normally reabsorb 80–90% of the filtered bicarbonate load along with sodium, whereas the distal tubules are responsible for the remaining 10–20%.

Increased Excretion of Titratable Acids: After all the HCO3$^-$ in tubular fluid is reclaimed, the H+ secreted into the tubular lumen can combine with $HPO4^{2-}$ to form $H_2PO_4^+$. The latter is not readily reabsorbed because of its charge and is eliminated in urine. The net result is that H+ is excreted from the body as $H_2PO4^-$, and the HCO3$^-$ that is generated in the process can enter the bloodstream.

The $H_2PO4^-$/$HPO4^{2-}$ pair is normally an ideal urinary buffer.

**INCREASED FORMATION OF AMMONIA:** After complete reabsorption of HCO3$^-$ and consumption of the phosphate buffer, the $NH_3$/$NH_4^+$ pair becomes the most important urinary buffer.

Deamination of glutamine within the mitochondria of proximal tubular cells is the principal source of $NH_3$ production in the kidneys.

Acidemia markedly increases renal $NH_3$ production.

The ammonia formed is then able to passively cross the cell's luminal membrane, enter the tubular fluid, and react with $H^+$ to form $NH_4^+$.

Unlike $NH_3$, $NH_4$+ does not readily penetrate the luminal membrane and is therefore trapped within the tubules. Thus, excretion of $NH_4$+ in urine effectively eliminates $H^+$.

**RENAL CORRECTION OF ALKALOSIS:** In alkalosis, the ratio of $HCO_3$ $^-$ to $CO_2$ in the extracellular fluid increases, causing a rise in pH.

Regardless of whether the alkalosis is caused by metabolic or respiratory abnormalities, there is still an increase in the ratio of HCO3 $^-$ to $H^+$ in the renal tubular fluid.

The net effect of this is an excess of HCO3 $^-$ that cannot be reabsorbed from the tubules and is, therefore, excreted in the urine.

**BONE AS BUFFER[18]:** Bone is an important source of buffer in chronic metabolic acidosis, (renal tubular acidosis & uraemic acidosis). The carbonate and phosphate salts in bone act as a long term supply of buffer especially during prolonged metabolic acidosis.

Bone consists of matrix within which specialised cells are dispersed. The matrix is composed of organic [collagen and other proteins in ground substance] and inorganic (hydroxyapatite crystals).

Bone is the major CO2 reservoir in the body and contains carbonate and bicarbonate equivalent to 5 moles of CO2 out of a total body CO2 store of 6 moles.

CO2 in bone is in two forms: bicarbonate (HCO3-) and carbonate (CO3$^-$).

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The bicarbonate makes up a readily exchangeable pool because it is present in the bone water which makes up the 'hydration shell' around each of the hydroxyapatite crystals.

The carbonate is present in the crystals and its release requires dissolution of the crystals. This is a much slower process.

**BONE ACT AS BUFFER BY TWO PROCESSES:**
1. Ionic exchange.
2. Dissolution of bone crystal.

Bone can take up H+ in exchange for Ca++, Na+ and K+ (ionic exchange) or release of HCO3-, CO3- or $HPO4^{-2}$.

In acute metabolic acidosis uptake of H+ by bone in exchange for $Na^+$ and $K^+$ is involved in buffering as this can occur rapidly without any bone breakdown.

This 'intracellular buffering' of acute metabolic disorders may represent some of the acute buffering by bone, it is probably involved in providing some buffering (mostly by ionic exchange) in most acute acid-base disorders but this has been little studied.

In chronic metabolic acidosis, the major buffering mechanism by far is release of calcium carbonate from bone.

**The mechanism by which this dissolution of bone crystal occurs involves two processes:**
1. Direct physicochemical breakdown of crystals in response to [H+].
2. Osteoclastic reabsorption of bone.

Release of calcium carbonate from bone is the most important buffering mechanism involved in chronic metabolic acidosis.

**CONCLUSION**: Thus understanding of physiology of acid base balance makes it easy to understand the deviation of normal acid base balance and this knowledge will guide us in early detection of acid base disorder.

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**AUTHORS:**
1.  Awati M. N.
2.  Vandana Mudda
3.  Minal Chandra
4.  Samudyatha T. J.

**PARTICULARS OF CONTRIBUTORS:**
1.  Professor & HOD, Department of Anaesthesia, M. R. Medical College, Gulbarga.
2.  Associate Professor, Department of Forensic Medicine, M. R. Medical College, Gulbarga.
3.  Post Graduate, Department of Anaesthesiology, M. R. Medical College, Gulbarga.
4.  Post Graduate, Department of Anaesthesiology, M. R. Medical College, Gulbarga.

**NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. Minal Chandra,
# 10-105/39,
Sharana Nagar, Gulbarga,
Karnataka.
E-mail: mnawati@gmail.com