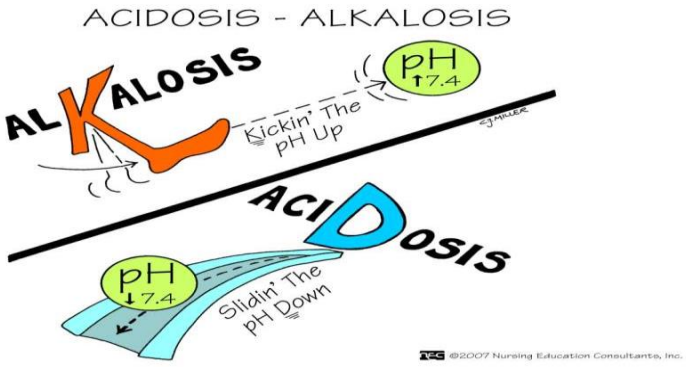
Renal Acid-Base Control Mechanisms:

- **Normal pH :** 7.4 with normal range (7.35-7.45)
- **Acidosis:** A state resulting from abnormally low plasma pH (pH < 7.35)
- **Alkalosis:** A state resulting from abnormally high plasma pH (pH > 7.45)



- The kidneys are the **third line** of defense against wide changes in body fluid pH as their action is *much slower* in regulation of acid – base balance. They take hours to days for correction. However they are the ***most powerful*** and most ***efficient*** buffering mechanism.
- The kidneys control acid-base balance by **excreting** either **acidic** or **basic urine.**
  - Excreting acidic urine reduces the amount of acid in extracellular fluid
  - Excreting basic urine removes base from the extracellular fluid
- Because of the daily production of metabolic acids, urinary excretion of **ammonium** (**NH3**), **phosphate**, **sulfate**, and $\mathbf{H^+}$ is an essential process, and, as a result, the **urine pH** is slightly **acidic**.

- **The kidneys regulate blood pH through three fundamental mechanisms:**
  (1) secretion of H^+
  (2) reabsorption of filtered HCO_3^-
  (3) production of new HCO_3^-

• ***In acidosis,*** the kidneys reabsorb all the filtered HCO_3^- and produce new HCO_3^- which is added back to the extracellular fluid. This reduces the extracellular fluid H^+ concentration back toward normal.

• ***In alkalosis*** the kidneys don't reabsorb all the filtered HCO_3^- thus increasing the excretion of HCO_3^-, this raises the extracellular fluid H^+ concentration back towards normal.

Mechanism of Hydrogen ion secretion and Bicarbonate Reabsorption in renal tubules:

Hydrogen ions are secreted into tubular fluid along:

- Proximal convoluted tubule (PCT)
- Thick ascending limb of LH
- Distal convoluted tubule (DCT)
- Collecting system

Renal reabsorption of bicarbonate

- Proximal convoluted tubule: 70-90%
- Loop of Henle: 10-20%
- Distal convoluted tubule and collecting ducts: 4-7%

Renal reabsorption of bicarbonate and secretion of H^+ in the PCT:

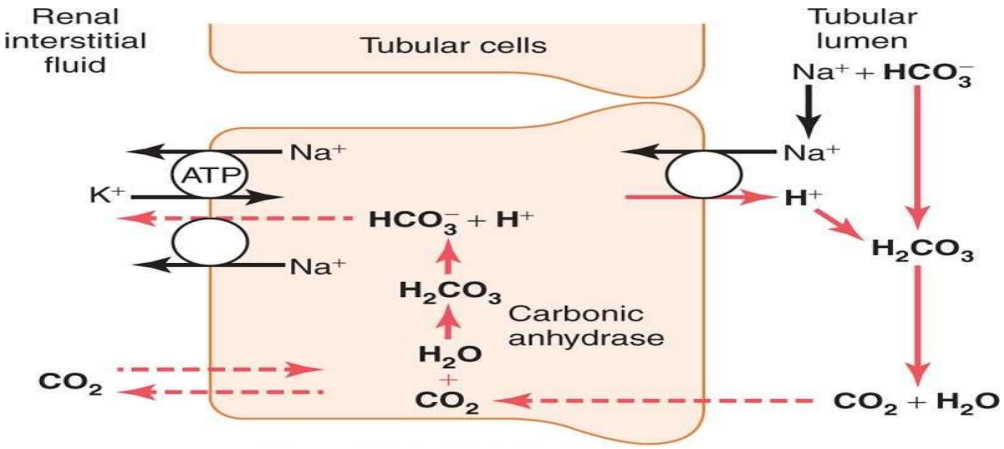


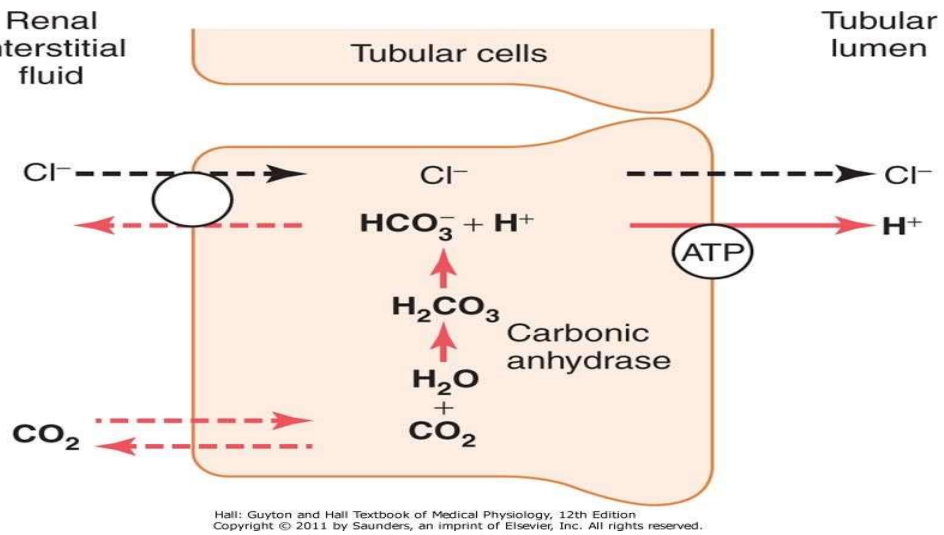
Fig. 2

N.B.

- The antiport utilized in PCTs can transport either Na+ or K+ in exchange for H+ secretion. But in distal segments, Na+ only is transported.
- In DCTs and CDs, H+ and K+ compete for secretion.
- In PCTs, H+ can be secreted till the pH drops to about 6.9, while in the DCTs and CDs, it can be secreted till the pH drops to 4.5

This pattern of hydrogen ion secretion occurs in the proximal tubule, the thick ascending segment of the loop of Henle, and the early distal tubule.

Primary Active Secretion of H^+ in the Intercalated Cells of Late Distal and Collecting Tubules:



Note that one bicarbonate ion is reabsorbed for each hydrogen ion secreted, and a chloride ion is passively secreted along with the hydrogen

Factors that affect renal secretion:

1. *Arterial CO_2 tension:* When this increases, the C02 content in the renal tubular cells also increases leading to more formation of H_2C0_3 which, in turn, leads to more H^+ secretion.

2. *K^+ concentration*: When this increases, H^+ secretion is decreased (and vice versa) since both compete for secretion in the DCTs &. CCDs.

3. *Carbonic anhydrase activity:* Blocking of this enzyme by drugs e.g. acetazolamide (diamox) inhibits H^+ secretion.

4. *Aldosterone:* This hormone increases both H+ and K+ secretion in exchange for Na reabsorption in the DCTs and CCDs.

5. *The tubular fluid pH:* If this decreases below 4.5, H+ secretion stops.

Acid – base regulation during normal metabolism:

The products of normal metabolism are *mainly acidic* and include:

(a) *$C0_2$* (about *12500 mEq /day),* which is mostly **excreted at the lungs**.

(b) *Fixed acids:* These are mostly derived from amino acid metabolism (e.g. sulphuric and phosphoric acids), and they are the only source of excess *H^+* during normal metabolism *(50-60 mEq* day).

- They are immediately buffered *mainly by the bicarbonate buffer* in the blood.

- *$C0_2$* is mostly excreted at the lungs *but it is also increased in the renal tubular cells* leading to *H+* secretion, which is accompanied by *$HC0_3^-$* reabsorption.

Normally, the amount of H^+ secreted in the renal tubules slightly **exceeds** that of the filtered HCO_3^-, and about *90 % of H^+ secretion occurs in the PCTs.* This amount is buffered by the filtered HCO_3^- (figure 2), resulting in complete reabsorption of the latter which *conserves the alkali reserve of the body.*

On the other hand, the *remaining 10* % of H^+ *secretion occurs in the distal renal segments, and is buffered by phosphate and ammonia* (figures 3, 4) resulting in 2 effects :

(1) ***Formation & reabsorption of a new amount of HCO_3^-*** which compensates what has been used during the buffering process. Accordingly, the blood HCO_3^- content increases up to normal, so the ratio (R) rises to its normal value (about 20) and the blood pH will thus be corrected and kept close to 7.4.

(2) *Formation and excretion of acid phosphate & ammonium salts* leading to urine acidification (so the normal urine pH is about 6)

Buffering of Secreted Hydrogen Ions by Filtered Phosphate

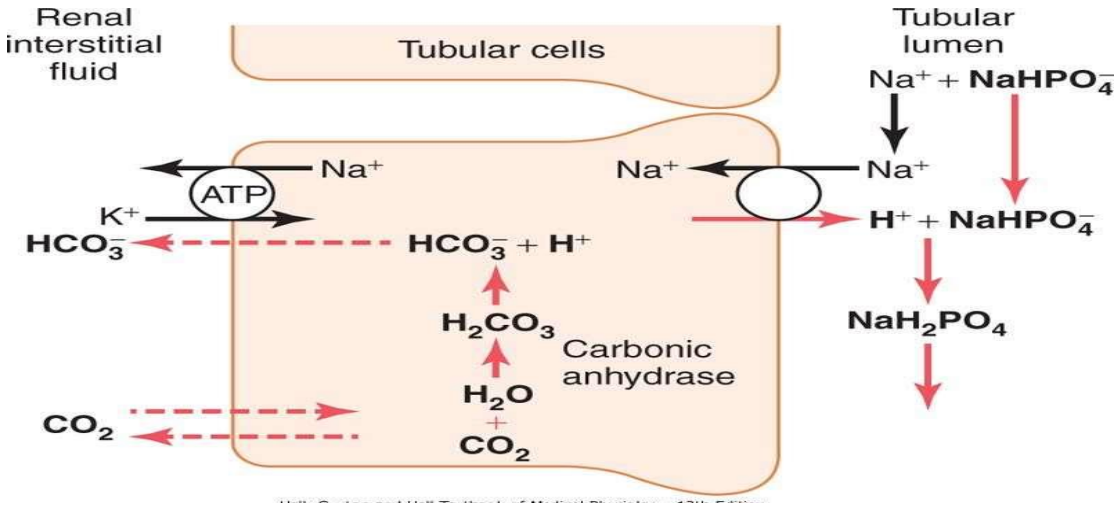


Fig. 3

Buffering of hydrogen ion secretion by ammonia (NH_3) in the collecting tubules:

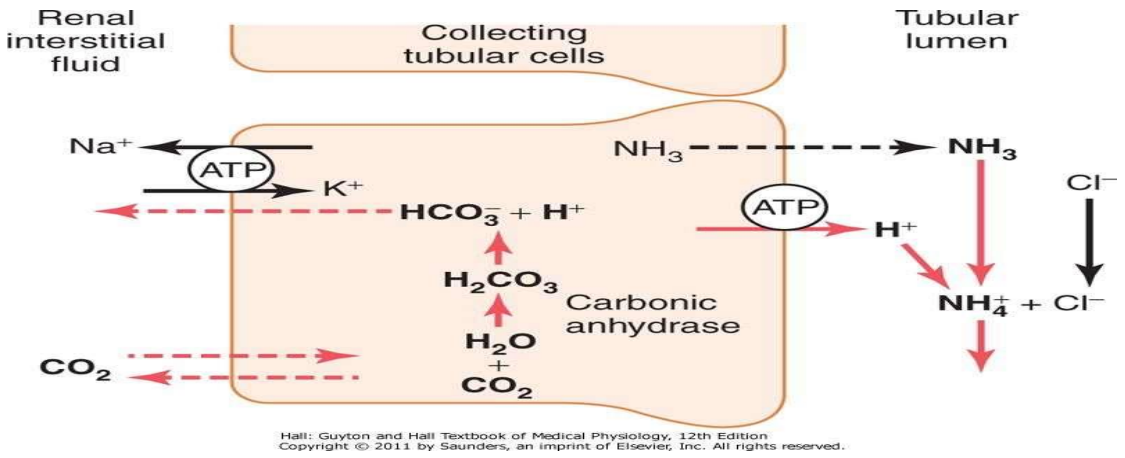


Fig. 4

Four Basic Types of acid – base imbalance:

- **Respiratory acidosis**
- **Metabolic acidosis**:
- **Respiratory alkalosis**
- **Metabolic alkalosis**

Respiratory acidosis:

PH < 7.35, there is much CO_2

Correction by:

1- Chemical buffers

2- Renal correction (since the cause is a respiratory disorder).

Metabolic acidosis:

There is addition of H^+ (not of CO_2 origin) and/or loss of bicarbonate from the body. It is characterized by low pH and HCO_3^-.

Correction by:

1- Chemical buffers

2- The lung: The drop in pH stimulates ventilation via peripheral chemoreceptors.

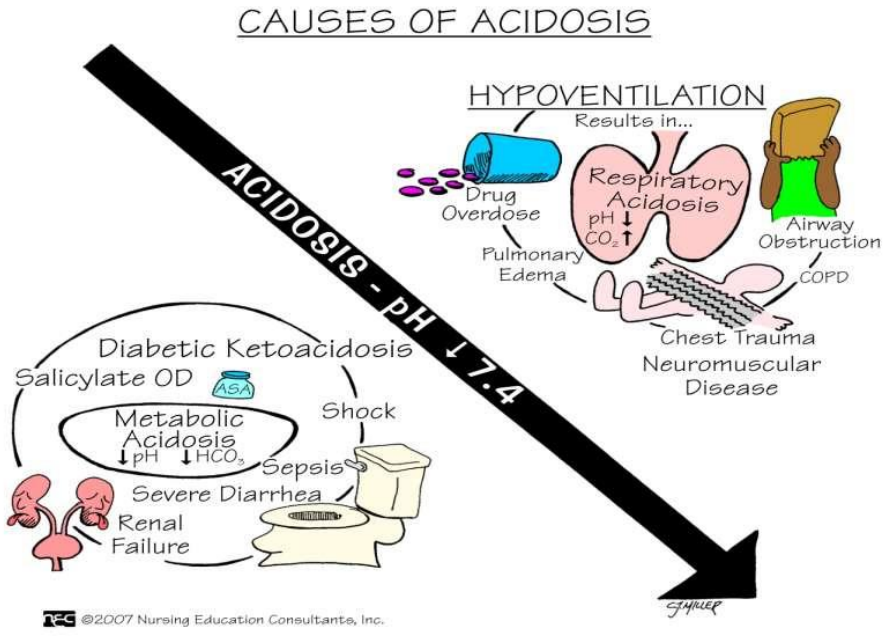
3- The kidney in metabolic acidosis of non renal causes.

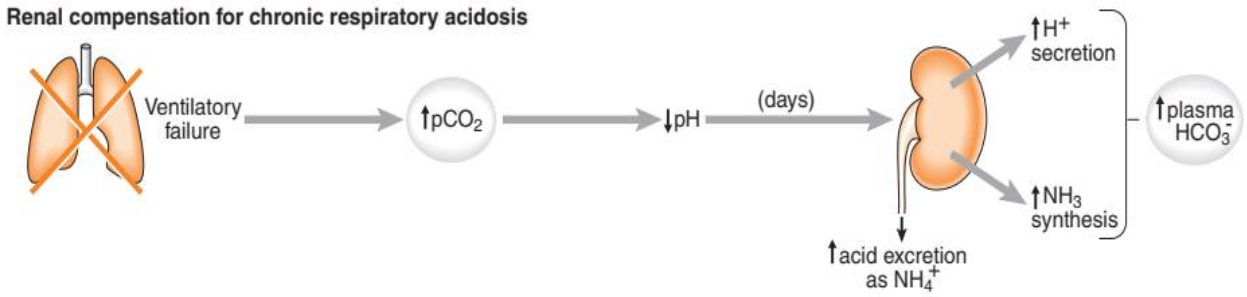
Renal Correction of Acidosis (Increased Excretion of H^+ and Addition of Bicarbonate to the ECF)

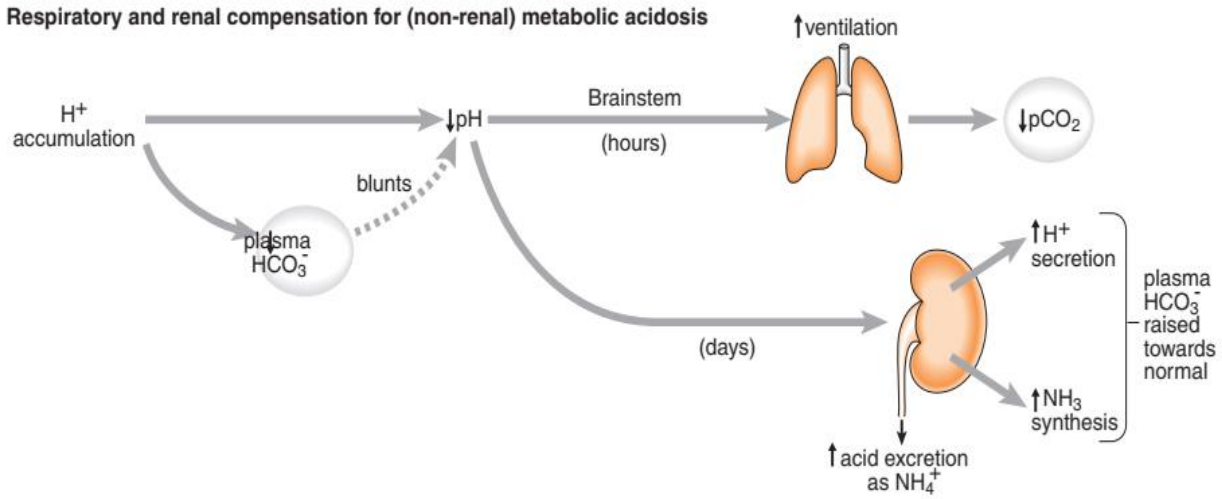
- Acidosis decreases the ratio of Bicarbonate/Hydrogen ion in Renal Tubular Fluid

  • As a result, there is excess H^+ in the renal tubules, causing complete reabsorption of bicarbonate and still leaving additional H^+ available to combine with the urinary buffers (phosphate and ammonia)

Thus, in acidosis, the kidneys reabsorb all the filtered bicarbonate and contribute new bicarbonate through the formation of ammonium ions and titratable acid







Respiratory alkalosis

- Characterized by pH > 7.45 and PaCO2 <35 mmHg
- Corrected by:
  1- The chemical buffers
  2- The kidneys.

Metabolic alkalosis:

Characterized by pH > 7.45 and HCO_3^- > 26 mEq/L

Corrected by:

1- Initial chemical buffering.
2- Respiratory correction: the increased pH acts to inhibit ventilation through the medullary chemoreceptors, such that the pCO2 starts to rise.
3- Renal correction

Renal Correction of Alkalosis (Decreased Tubular Secretion of H^+ and Increased Excretion of Bicarbonate)

In cases of alkalosis, the acid-base balance is regulated by *excreting alkaline urine* as follows:

As a result of buffering the excess alkali by H_2C0_3, the $C0_2$ content in the blood decreases while the HCO_3^- content increases *so the ratio (R) is* increased *above 20* and the *blood pH shifts to the alkaline side.*

Accordingly, more amounts of $HC0_3^-$ than normal are filtered in the renal glomeruli while less H^+ is secreted in the renal tubules. Therefore, the filtered $HC0_3$- is *not completely reabsorbed in the PCTs* and the excess will be excreted in the urine Thus, in alkalosis *urine alkalinization begins in the PCTs* (as urine acidification in acidosis) *and the urine pH may rise up to 8.*

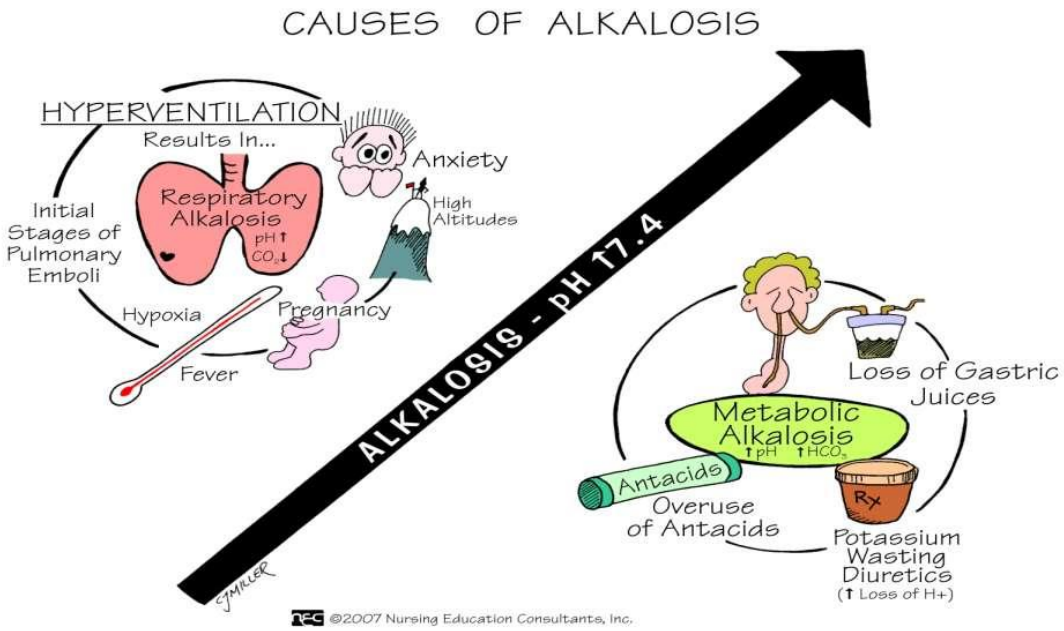
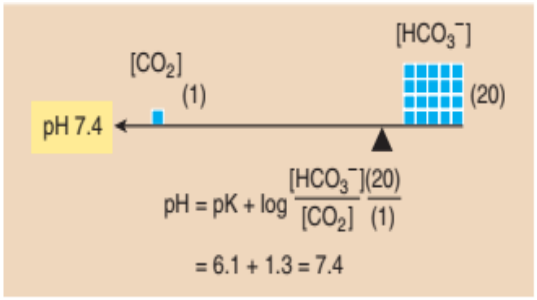
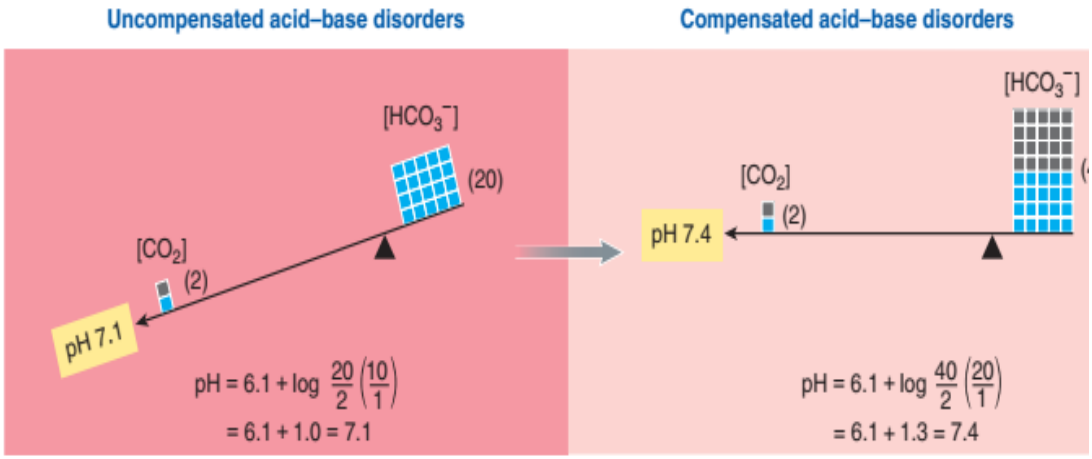


Table 4.3 Summary of 'simple' acid–base disturbances

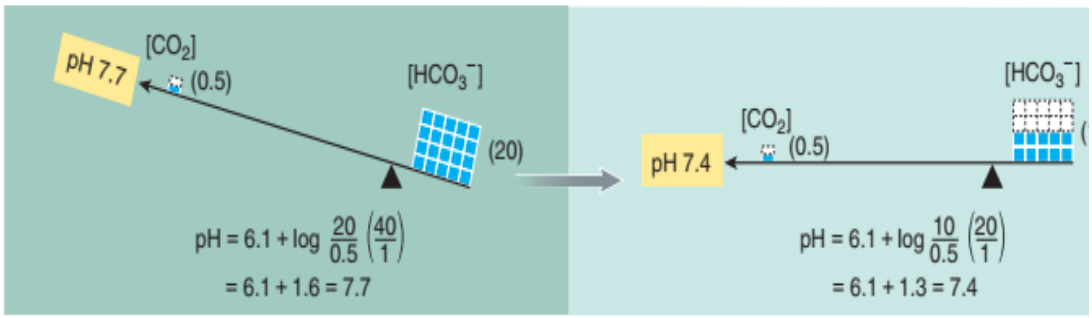
Disorder	*pH*	*Primary change*	*Compensatory response*
Metabolic acidosis	Decreased	Decreased HCO_3	Decreased pCO_2
Metabolic alkalosis	Increased	Increased HCO_3	Increased pCO_2
Respiratory acidosis	Decreased	Increased pCO_2	Increased HCO_3
Respiratory alkalosis	Increased	Decreased pCO_2	Decreased HCO_3



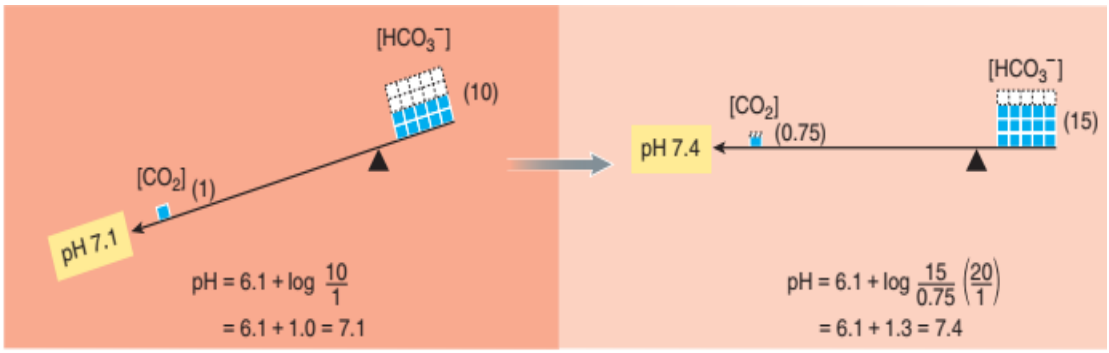
(a) Normal acid-base balance



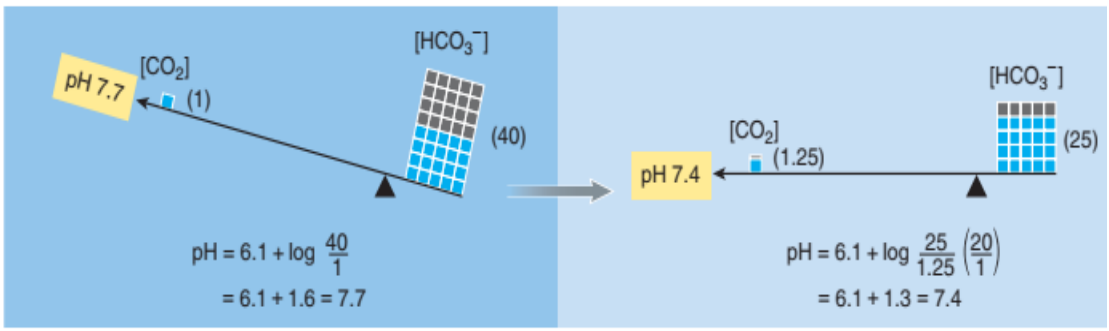
(b) Respiratory acidosis



(c) Respiratory alkalosis



(d) Metabolic acidosis



(e) Metabolic alkalosis

Filling of the U.B:

Urine enters the U.B. without producing much increase in the *intravesical pressure (IVP)* till the bladder becomes well-filled. This is due to:

a. *Plasticity of the detrusor muscle* (when this muscle is slowly stretched, the tension initially produced is not maintained).

b. ***Laplace's law:*** This law states that the pressure *(P)* in a spherical viscus equals twice the wall tension *(2T)* divided by its radius *(r)* i.e. $P = 2T/r$.

As the U.B. fills, the T & r increase together and the IVP rises only slightly, but at a certain volume, the T markedly increases and the IVP rises sharply.

Sensations of the U.B:

1. the *first desire for micturition* is felt at a bladder volume of about *150*

ml, and it can easily be *voluntarily inhibited.*

2. The sense of *bladder fullness* (that normally initiates reflex micturition) is felt at a volume of *300 - 400 ml*, and it can also be *voluntarily inhibited.*

3. A sense of *bladder discomfort* is felt at volumes between *400 - 600 ml,*

but the micturition reflex can still be *voluntarily inhibited.*

4. A sense of *bladder pain* is felt at volumes *exceeding 600 ml*, and it can

hardly be voluntarily inhibited till the volume becomes about *700 ml* (at

which *urination becomes urgent* and *obligatory micturition* occurs).

Mechanism OF micturition (Urination)

(A)In infants:

In infants, urination occurs through a series of *spinal reflexes* called the *micturition reflexes* which are a*utomatic* (i.e. not under voluntary control) because the nerve tracts are *not yet myelinated* in infants.

The micturition reflexes:

These are **a series of <u>6</u>** spinal reflexes that initiate and complete the act of urination. They proceed as follow:

Reflexes	Stimulus	Afferent	Center	Efferent	Response
I	Rise of the IVP	pelvic nerves	the lateral horn cells of 2, 3, 4 sacral	pelvic nerves	contraction of the detrusor muscle
II	Rise of the IVP	pelvic nerves	LHCs of 2, 3, 4 sacral	pelvic nerves	relaxation of the internal urethral sphincter.
III	Rise of the IVP	pelvic nerves	AHCs of 2, 3, 4 sacral	Pudendal nerves	relaxation of the external urethral sphincter.
IV	Flow of urine	Pudendal	LHCs of 2, 3, 4 sacral	pelvic nerves	More contraction of

	through the urethra	nerves			the detrusor muscle
V		Pudendal nerves	LHCs of 2, 3, 4 sacral	pelvic nerves	Further relaxation of the internal urethral sphincter.
VI		Pudendal nerves	AHCs of 2, 3, 4 sacral	Pudendal nerves	Further relaxation of the external urethral sphincter.

(B) In adults:

In adults, the act of micturition occurs *also through the micturition reflexes*, but however, it *can be controlled by the higher centers* in the brain, which include the following:

(1) *Brain stem centres:*

a- *An inhibitozy centre in the midbrain.*

b- *A facilitatozy centre in the pons.*

(2) *Cerebral cortical centre :* It exerts 2 main functions :

a- *Feeling the desire for micturition*

b- *Voluntary control of micturition.*

1- *If the* condition is suitable as regards time and place), the normal inhibitory effect disappears and instead, it facilitates micturition.

2. *If the condition is not suitable,* the normal inhibitory effect increased, which prevents micturition.