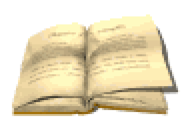
RENAL PHYSIOLOGY

ACID BASE BALANCE



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ACIDS

Acids dissociate in solution to liberate free H+ ions

- STRONG acids (eg. Hydrochloric acid i.e. HCl) completely dissociate (to H+ and Cl-)
- WEAK acids (H2CO3) have more limited dissociation

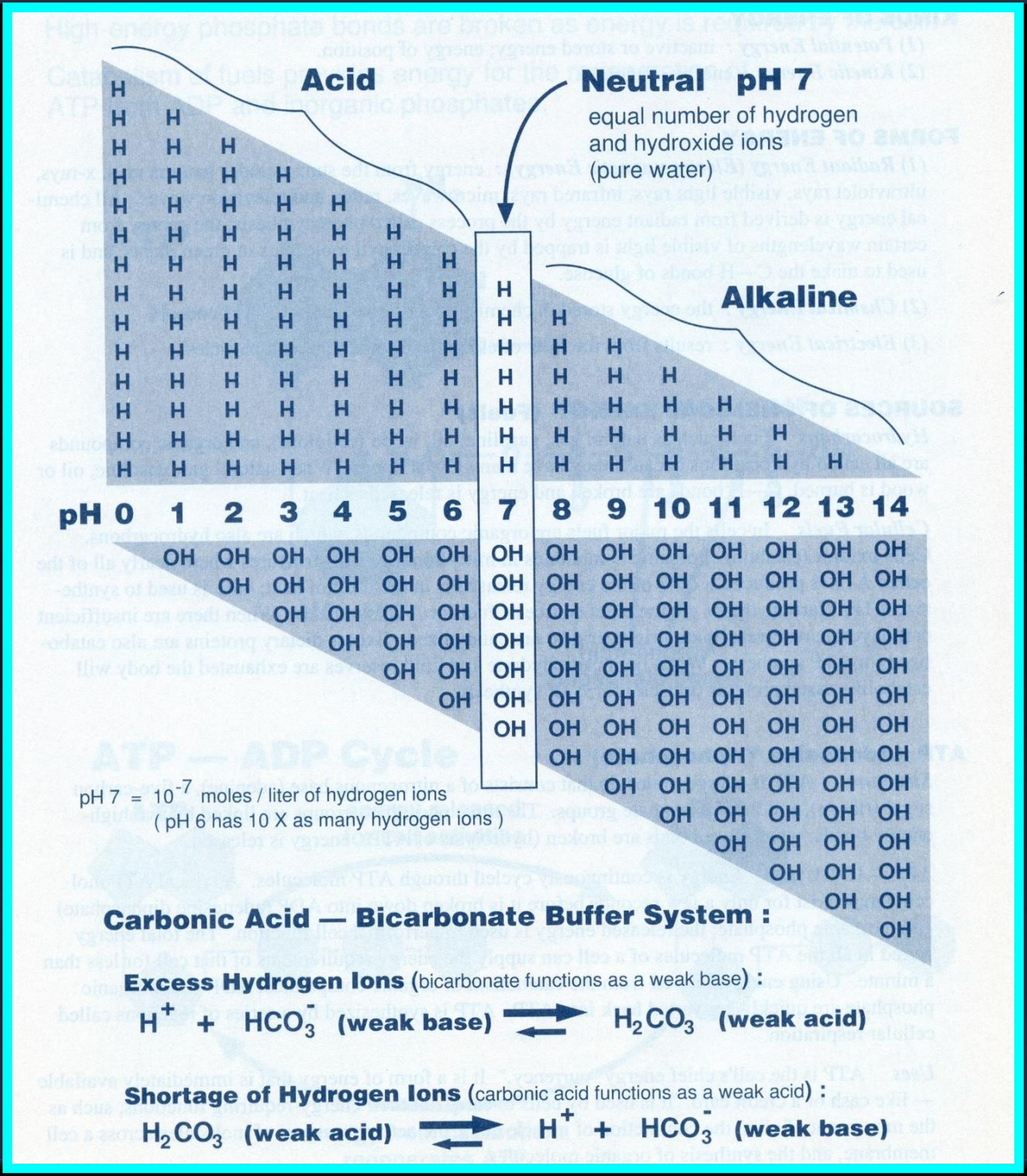
BASES

- Bases are ions or molecules that bind free H+ and remove it from solution

  eg. HCO_3^- combines with H+ to form H_2CO_3

- Alkali is a molecule formed by one of the alkaline metals. (Na, K, Li) with a highly basic ion such as a hydroxyl ion (OH–).

pH SCALE



pH 7 = 10^{-7} moles / liter of hydrogen ions
(pH 6 has 10 X as many hydrogen ions)

Carbonic Acid — Bicarbonate Buffer System :

Excess Hydrogen Ions (bicarbonate functions as a weak base) :

$$H^+ + HCO_3^- \text{ (weak base)} \rightleftarrows H_2CO_3 \text{ (weak acid)}$$

Shortage of Hydrogen Ions (carbonic acid functions as a weak acid) :

$$H_2CO_3 \text{ (weak acid)} \rightleftarrows H^+ + HCO_3^- \text{ (weak base)}$$

pH

- **pH is the log of the reciprocal of the H+ ion concentration**

$$pH = \log (1 / [H^+])$$

OR

$$pH = - \log([H^+])$$

WHY WE EXPRESS IT AS pH?

pH

- The normal H ion concentration in blood is 40 nmol/l or 0.00004 mmol/l
- For example for Na it is 140 mmol/l
- Because H ion concentration in blood is so low that it is expressed in negative log to the base 10 of H ion concentration

40 nmol/l or 0.00004 mmol/l is equal to pH 7.4

pH and H^+ ion concentration

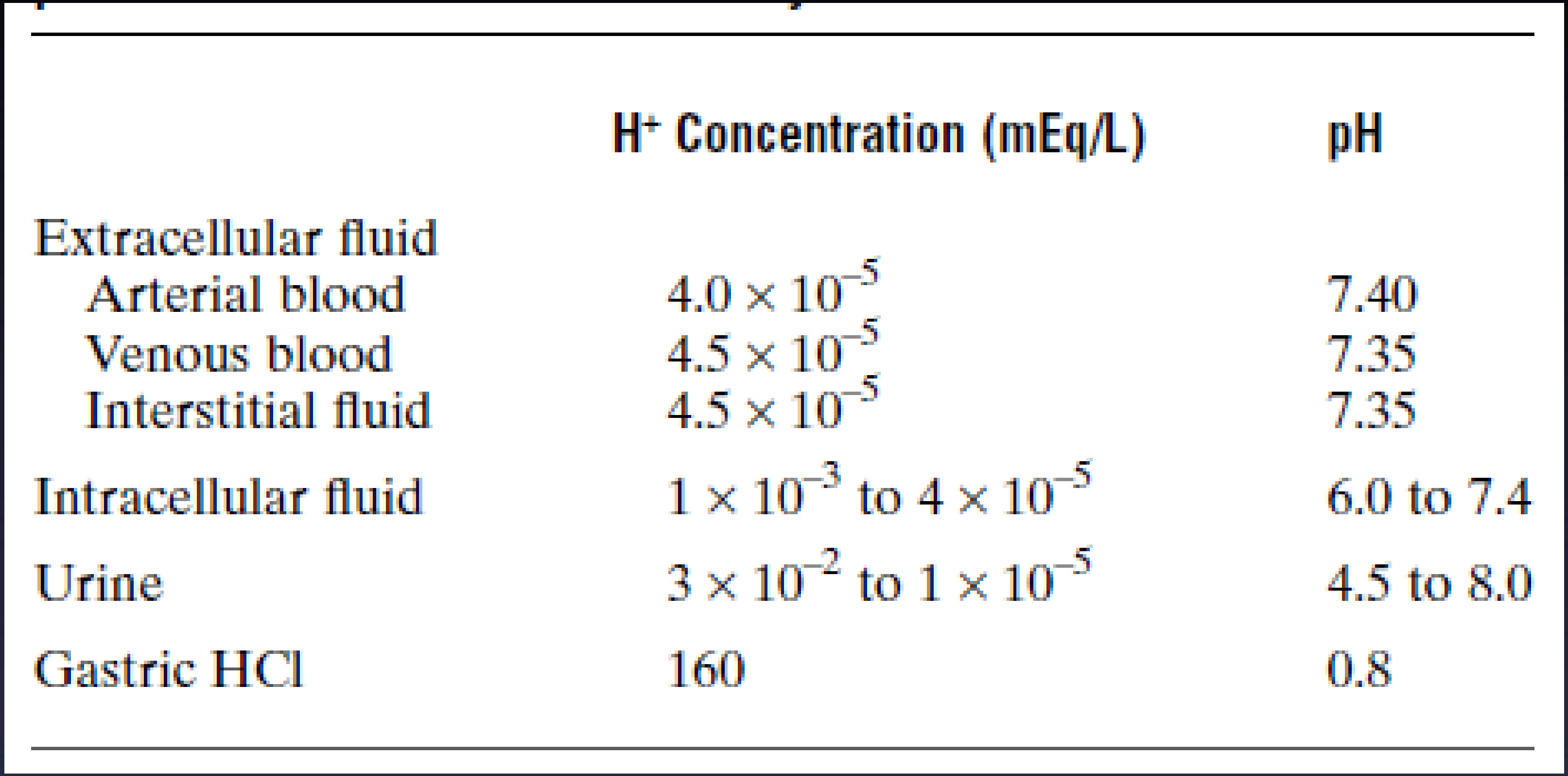
pH	H^+ ion in nmol/lit
6.0	1000
7.0	100
8.0	10
9.0	1.0

One point change in pH results in a ten fold change in H^+ ion conc.

	$[OH^-]$ concentration (mol/L)	pH	$[H^+]$ concentration (mol/L)		
1×10^{-14}	0.00000000000001	0	1	1×10^{0}	
1×10^{-13}	0.0000000000001	1	0.1	1×10^{-1}	
1×10^{-12}	0.000000000001	2	0.01	1×10^{-2}	
1×10^{-11}	0.00000000001	3	0.001	1×10^{-3}	Increasing
1×10^{-10}	0.0000000001	4	0.0001	1×10^{-4}	acidity
1×10^{-9}	0.000000001	5	0.00001	1×10^{-5}	
1×10^{-8}	0.00000001	6	0.000001	1×10^{-6}	
1×10^{-7}	0.0000001	7	0.0000001	1×10^{-7}	Neutral
1×10^{-6}	0.000001	8	0.00000001	1×10^{-8}	
1×10^{-5}	0.00001	9	0.000000001	1×10^{-9}	
1×10^{-4}	0.0001	10	0.0000000001	1×10^{-10}	Increasing
1×10^{-3}	0.001	11	0.00000000001	1×10^{-11}	basicity
1×10^{-2}	0.01	12	0.000000000001	1×10^{-12}	
1×10^{-1}	0.1	13	0.0000000000001	1×10^{-13}	
1×10^{0}	1	14	0.00000000000001	1×10^{-14}	

WHAT IS THE NORMAL BODY pH?

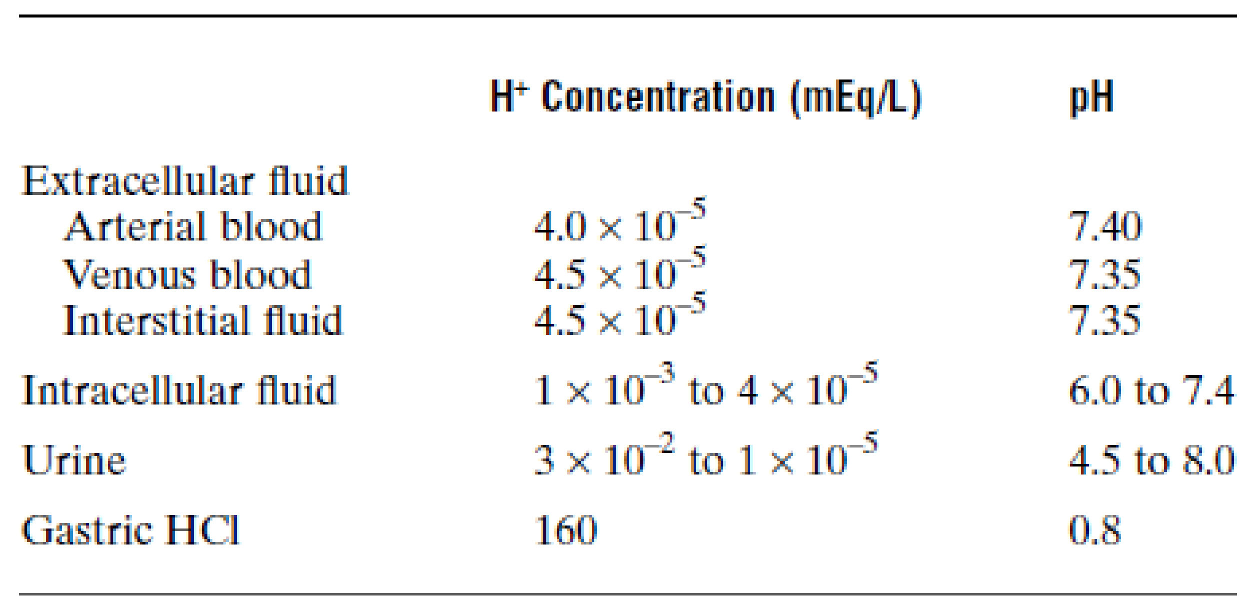
7.35 – 7.45



	H^+ Concentration (mEq/L)	pH
Extracellular fluid		
Arterial blood	4.0×10^{-5}	7.40
Venous blood	4.5×10^{-5}	7.35
Interstitial fluid	4.5×10^{-5}	7.35
Intracellular fluid	1×10^{-3} to 4×10^{-5}	6.0 to 7.4
Urine	3×10^{-2} to 1×10^{-5}	4.5 to 8.0
Gastric HCl	160	0.8

IMPORTANCE

ACTIVITIES OF ALL ENZYME SYSTEMS IN THE BODY IS INFLUENCED BY HYDROGEN IONS



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Gastric HCl	160	0.8

ACID PRODUCTION

H+ is continually produced by metabolic activity:

- ❖ Volatile acids: (e.g. carbonic acid, H2CO3; formation catalyzed by carbonic anhydrase)

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

ACID PRODUCTION (Cont.)

- **Non-volatile acids:** ingested acids and products of fat, amino acid, and sugar metabolism:
  - e.g. phosphoric acid, lactic acid, butyric acid
- Incomplete Carbohydrate and Fat Metabolism Produces Nonvolatile Acids (strenuous exercise, hemorrhagic or cardiogenic shock, uncontrolled diabetes mellitus, starvation, and alcoholism)

ACID LOAD

- Amino Acid Metabolism yields about 50 meq/day for example H_2SO_4, HCl, and H_3PO_4
- CO_2 production yields 12,500 meq/day300 L of CO_2
- Normal daily diet yields 80 meq/day

HENDERSON-HASSELBACH EQUATION

Relates pH to the Ratio of the Conc. of Conjugate Base and Acid

$$\mathrm{pH} = \mathrm{pK\ x\ \log} \ \frac{\mathrm{Base}}{\mathrm{Acid}}$$

The ratio of dissociated to undissociated forms of an acid is CONSTANT (K) and shows the Strength of an Acid

$$K = [H+][A-] / [HA]$$

eg: $K = [H+][HCO_3-] / [H2CO_3]$

$$\text{H2CO3} \quad \overset{\xleftarrow{\hspace{4em}}}{\longrightarrow} \quad \text{H+} \; + \; \text{HCO3-}$$

$$K' = \frac{H^{+} \;\; x \;\; HCO3^{-}}{H2CO3}$$

$$H^{+} = \; K' \, x \; \frac{H2CO3}{HCO3-}$$

$$H^{+} = \; K \, x \; \frac{0.03 \; x \; CO^{2}}{HCO3-}$$

$$H^{+} = \; K \, x \; \frac{0.03 \; x \; CO^{2}}{HCO3-}$$

$$H^+ = K \times \frac{0.03 \times CO^2}{HCO3-}$$

$$-\log H^+ = -\log K \times -\log \frac{0.03 \times CO^2}{HCO3-}$$

$$pH = pK \times \log \frac{HCO3-}{CO^2}$$

The Henderson-Hasselbalch Equation Relates pH to the Ratio of the Concentrations of Conjugate Base and Acid

pK

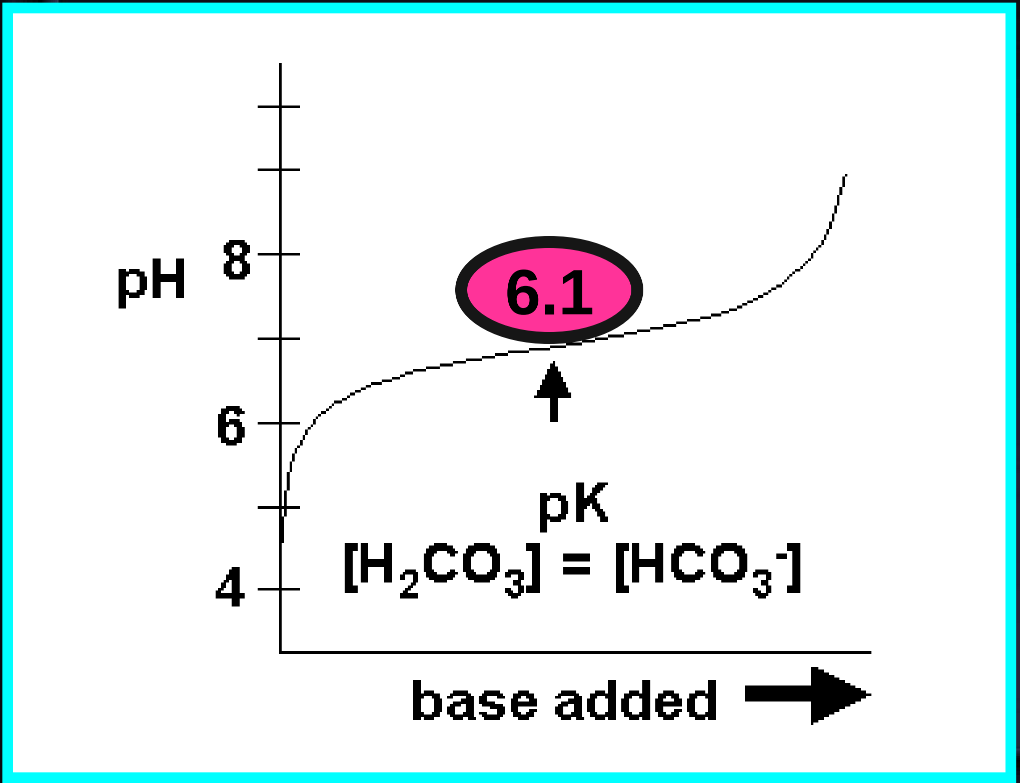
Dissociation Constant

pK (also a log) is where concentration of both components of the buffer are equal.

(**REMEMBER** to maintain plasma pH at 7.4, there needs to be much more HCO3- than H2CO3)

pK

- pH = pK x Base/Acid
- pH = pK x 50/50
- pH = pK



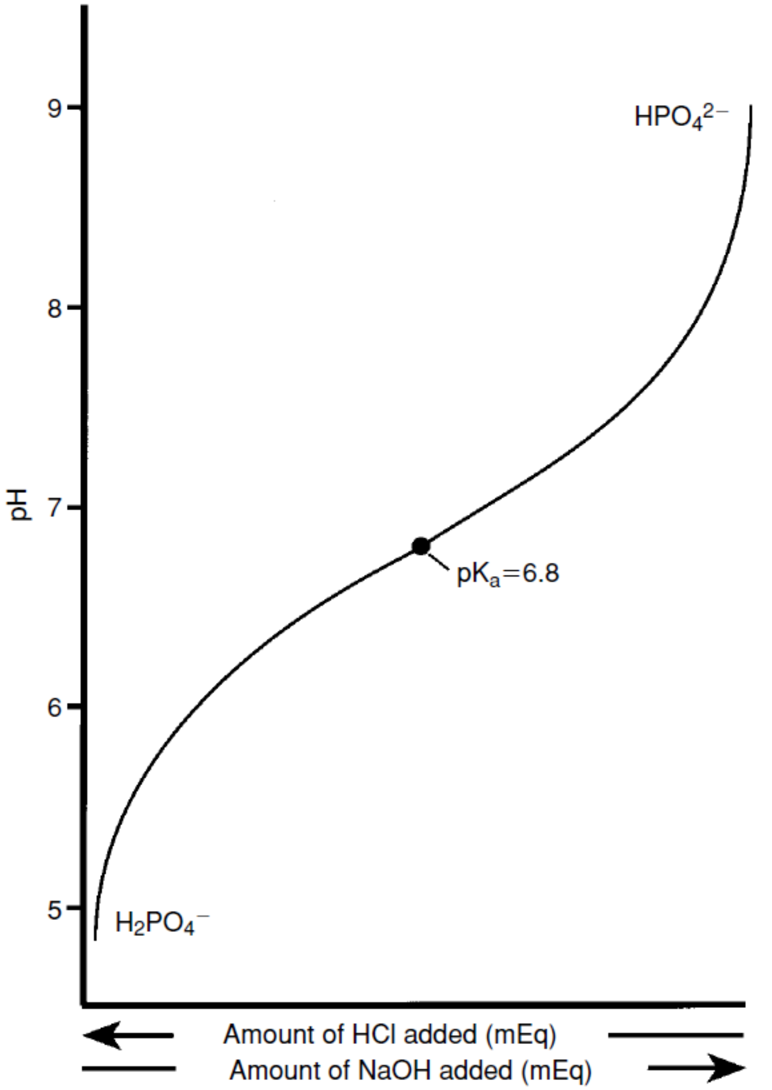
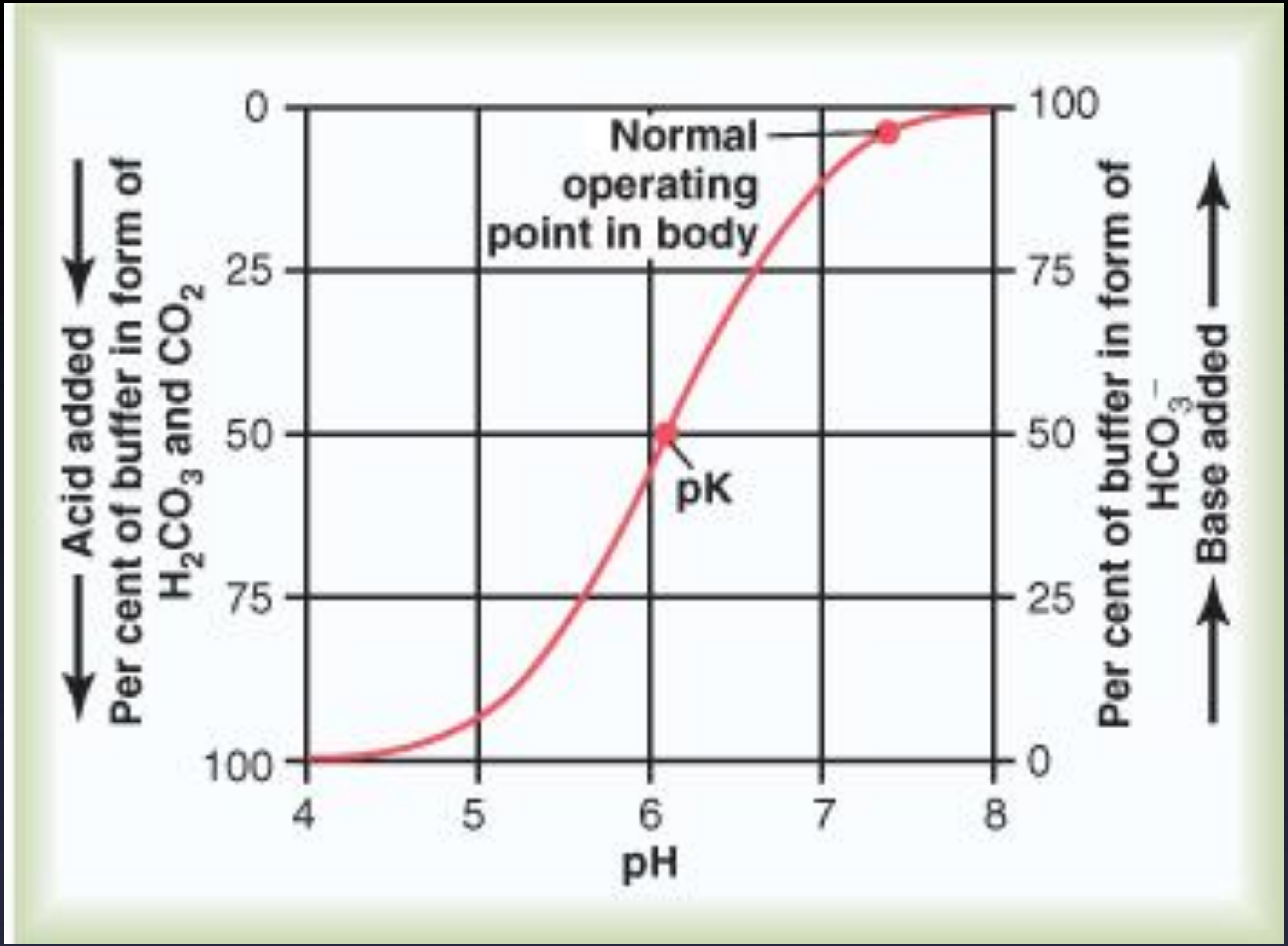


FIGURE 25.1 **A titration curve for a phosphate buffer.** The pK_a for $H_2PO_4^-$ is 6.8. A strong acid (HCl) (right to left) or strong base (NaOH) (left to right) was added and the resulting solution pH recorded (y-axis). Notice that buffering is best (i.e., the change in pH upon the addition of a given amount of acid or base is least) when the solution pH is equal to the pK_a of the buffer.

NORMAL OPERATING POINT FOR BICARBONATE/CARBONIC ACID BUFFER SYSTEM



7.35 – 7.45

ACIDOSIS

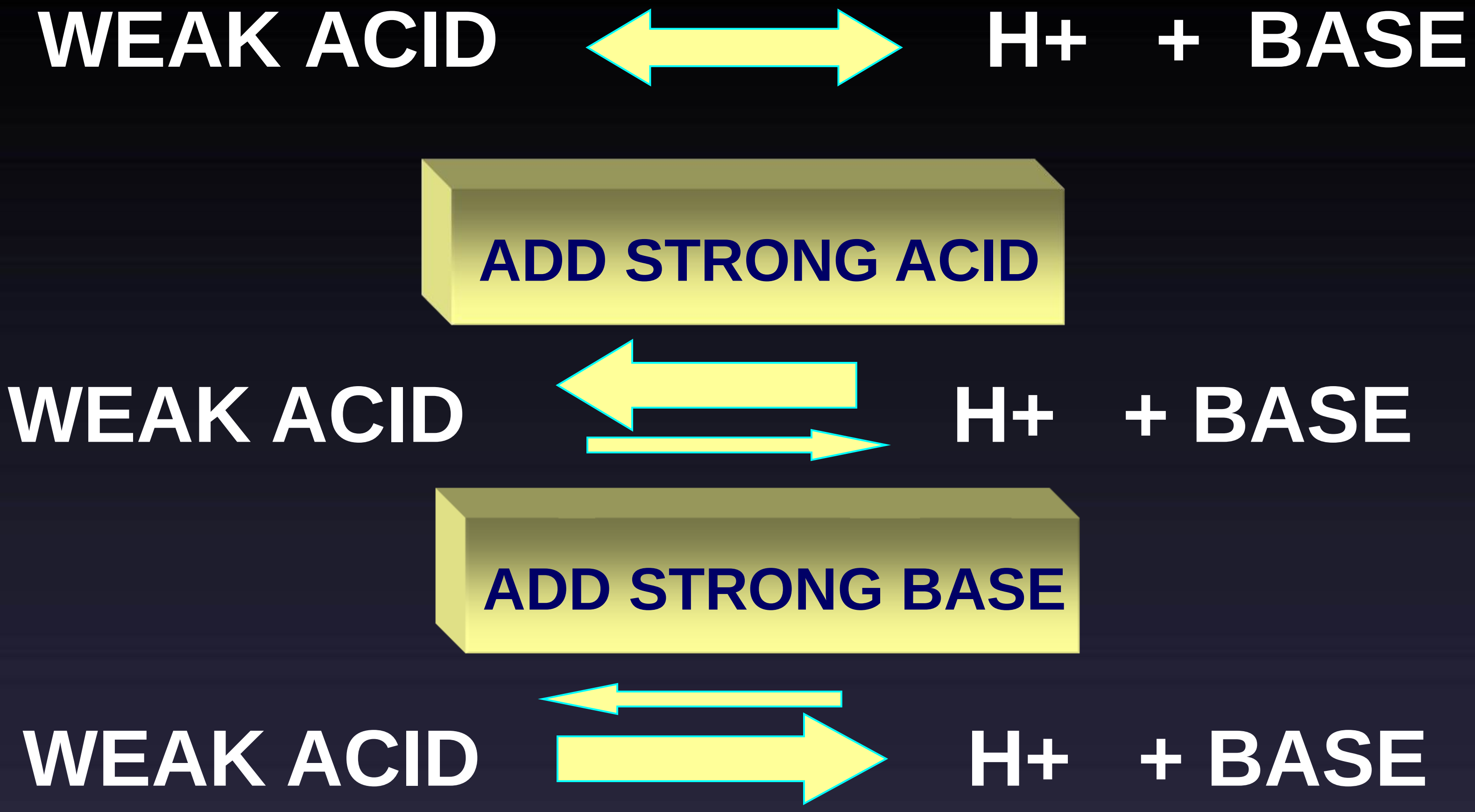
ALKALOSIS

BUFFER SYSTEMS

- Buffer is a solution which minimizes pH changes when acid or base is added to a solution (any substance that can reversibly bind H+)
- It consists of a WEAK ACID and its conjugate base (or a weak base and its conjugate acid)
- For example in Bicarbonate buffer system H_2CO_3 is the weak acid and $NaHCO_3$ is its conjugate base.

Buffers Promote the Stability of pH

BUFFER SYSTEMS



WEAK ACID ⟷ H+ + BASE

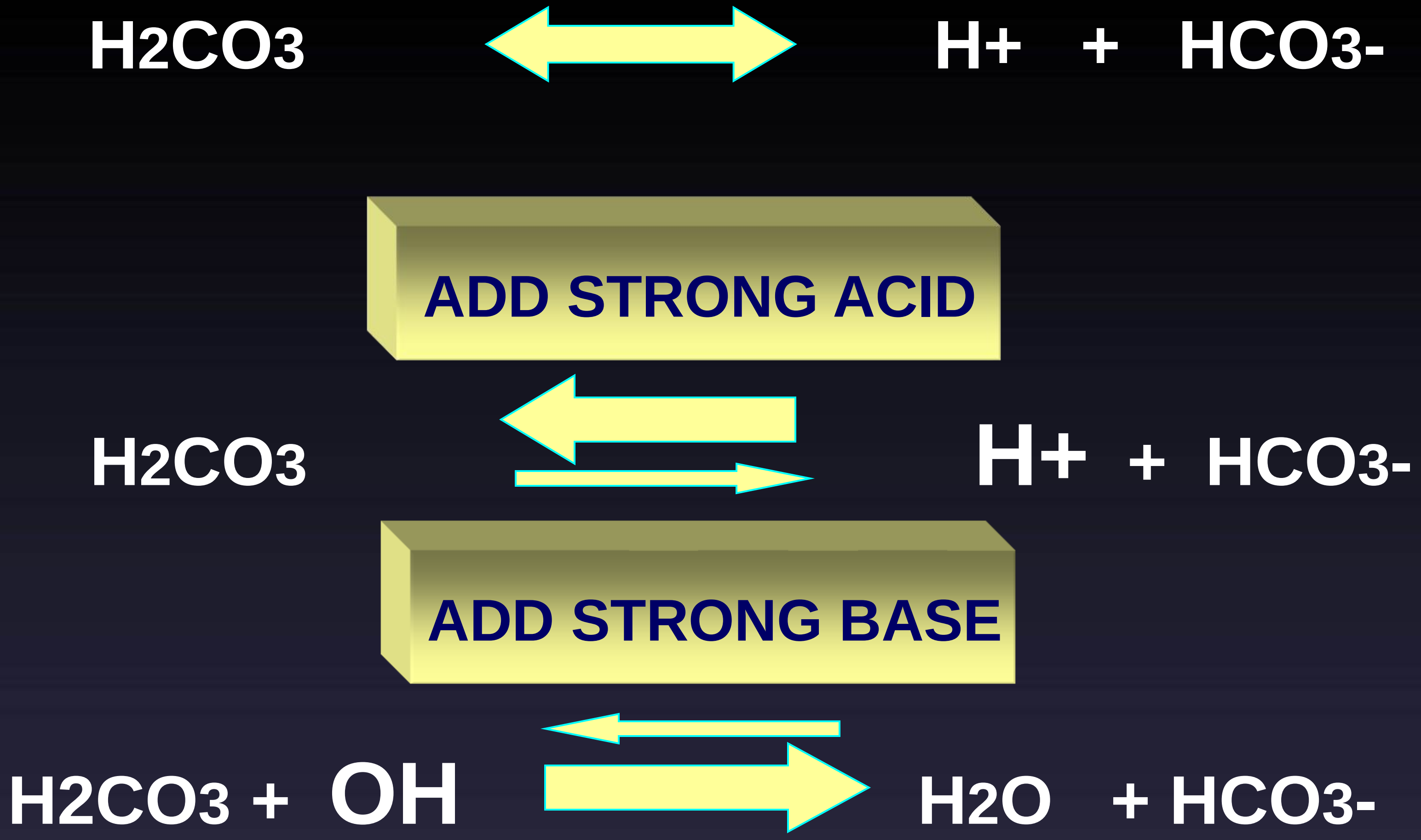
ADD STRONG ACID

WEAK ACID ⇇ H+ + BASE

ADD STRONG BASE

WEAK ACID ⇉ H+ + BASE

BUFFER SYSTEMS



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

ADD STRONG ACID

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

ADD STRONG BASE

$H_2CO_3 + OH \rightleftharpoons H_2O + HCO_3^-$

BUFFER POWER

- Depends on relative amount of Acid and Base in a Buffer solution
- It is maximum when both are in equal amounts
- Absolute concentration of Buffers in body fluids is also important
- If the pH of medium is near pK of buffer system it becomes more effective

pH = pK + log [Base] / [Acid]

$$pH = pK + \log HCO3- / H2CO3$$

$$pH = 6.1 + \log 20 / 1$$

It is not only the amount of base and acid that is important but the ratio between them must remain constant

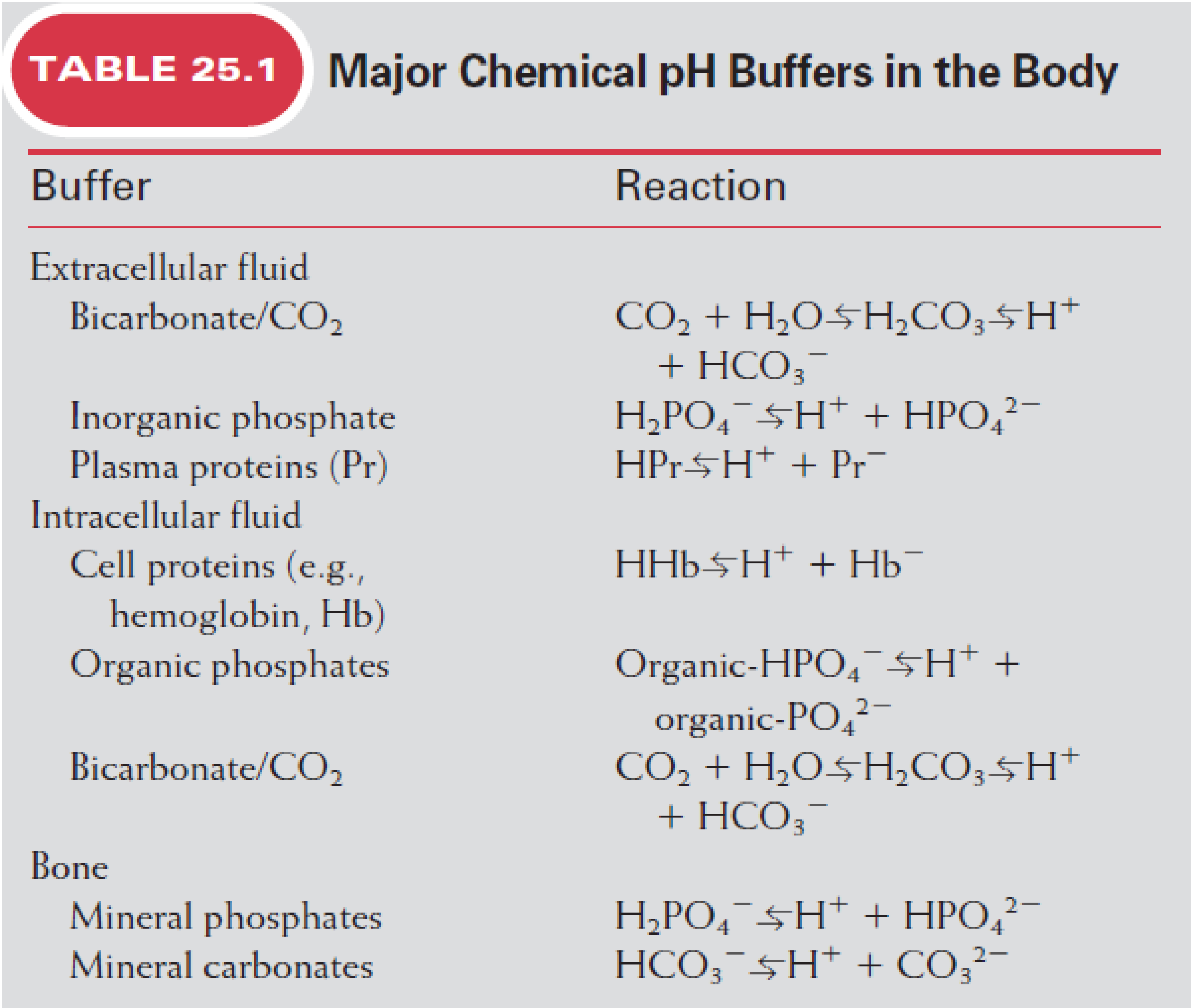


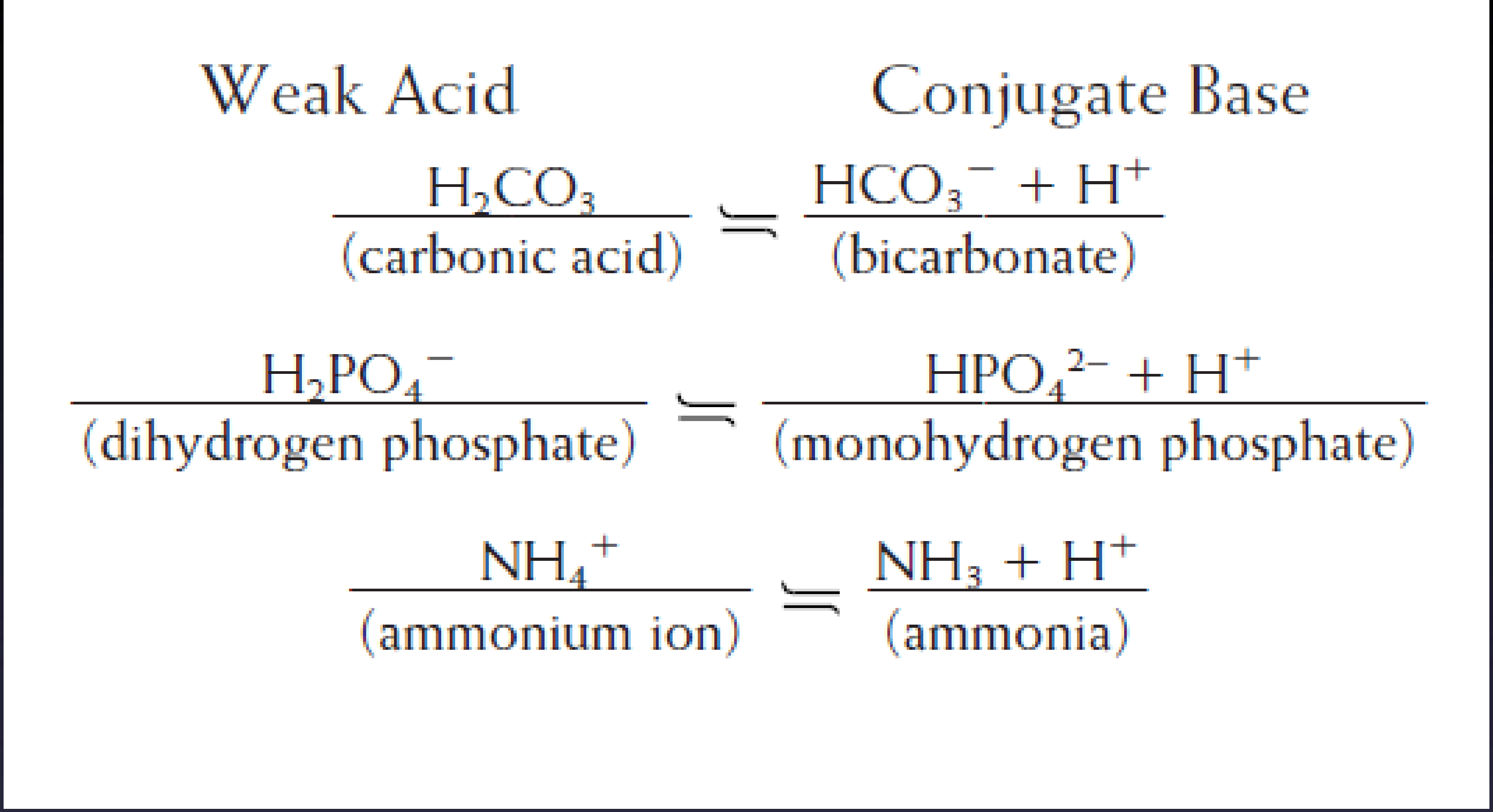
TABLE 25.1 Major Chemical pH Buffers in the Body

Buffer	Reaction
Extracellular fluid	
Bicarbonate/CO_2	$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$
Inorganic phosphate	$H_2PO_4^- \rightleftharpoons H^+ + HPO_4^{2-}$
Plasma proteins (Pr)	$HPr \rightleftharpoons H^+ + Pr^-$
Intracellular fluid	
Cell proteins (e.g., hemoglobin, Hb)	$HHb \rightleftharpoons H^+ + Hb^-$
Organic phosphates	Organic-$HPO_4^- \rightleftharpoons H^+ +$ organic-PO_4^{2-}
Bicarbonate/CO_2	$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$
Bone	
Mineral phosphates	$H_2PO_4^- \rightleftharpoons H^+ + HPO_4^{2-}$
Mineral carbonates	$HCO_3^- \rightleftharpoons H^+ + CO_3^{2-}$

pH DEFENCE MECHANISMS IN THE BODY

- Chemical buffering (First Line) Acid-Base buffer systems of the body fluids
- Respiratory response (Second Line) respiratory center
- Renal response (Third Line) Kidneys [slow to respond & powerful]

BUFFER SYSTEMS



Weak Acid		Conjugate Base
H_2CO_3 (carbonic acid)	$\rightleftharpoons$	$HCO_3^- + H^+$ (bicarbonate)
$H_2PO_4^-$ (dihydrogen phosphate)	$\rightleftharpoons$	$HPO_4^{2-} + H^+$ (monohydrogen phosphate)
NH_4^+ (ammonium ion)	$\rightleftharpoons$	$NH_3 + H^+$ (ammonia)

BODY BUFFER SYSTEMS

- BICARBONATE/CARBONIC ACID:

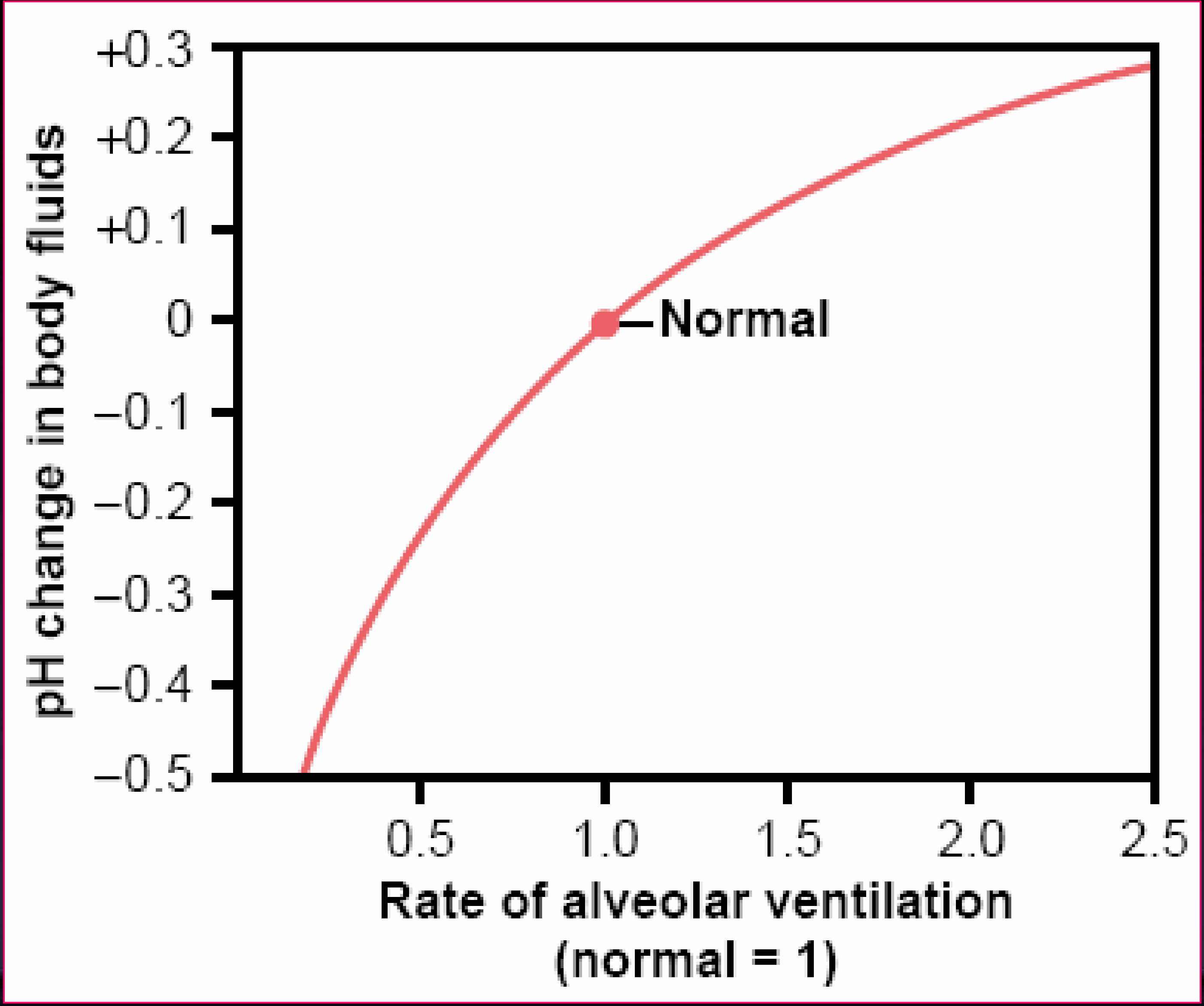
  HCO3- /H2CO3
  - pK = 6.1
  - major plasma buffer
- PHOSPHATE: H2PO4 / HPO4-
  - pK = 6.8
  - major intracellular and urine buffer
  - conc. in ECF is only 8 % of bicarbonate buffer

IMPORTANT NOTE: A pKa of 6.8 Makes Phosphate a Good Buffer in ECF however, its plasma conc. is low (about 1 mmol/L) unlike HCO3- which is 24 mmol/L

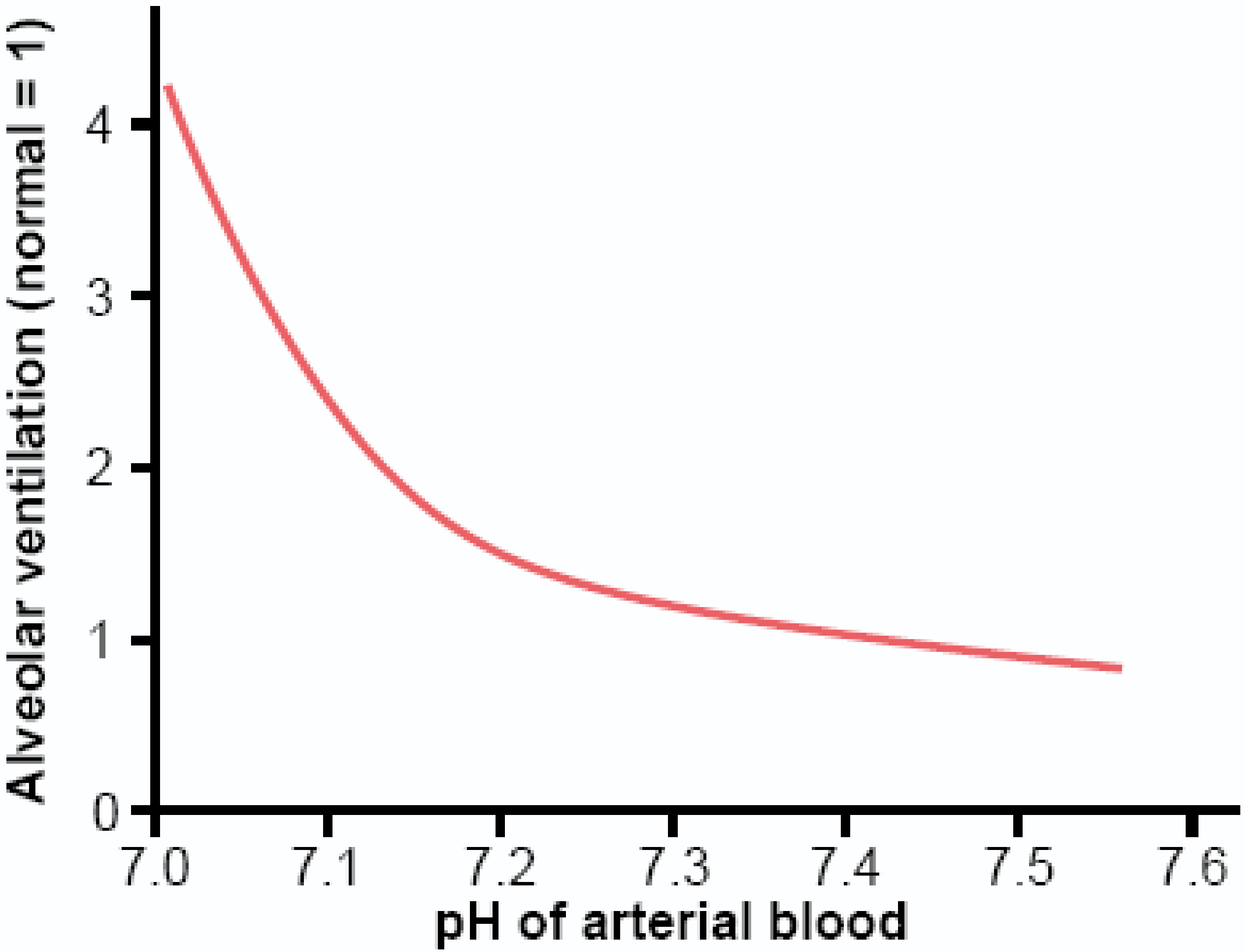
BODY BUFFER SYSTEMS

- AMMONIA: $NH3$ / $NH4+$
  - pK = 9.0
  - used to buffer the urine
- PROTEINS (Amphoteric) : Prot / H Prot
  - important in ICF
- HEMOGLOBIN: Hb / HHb
  - important in ICF

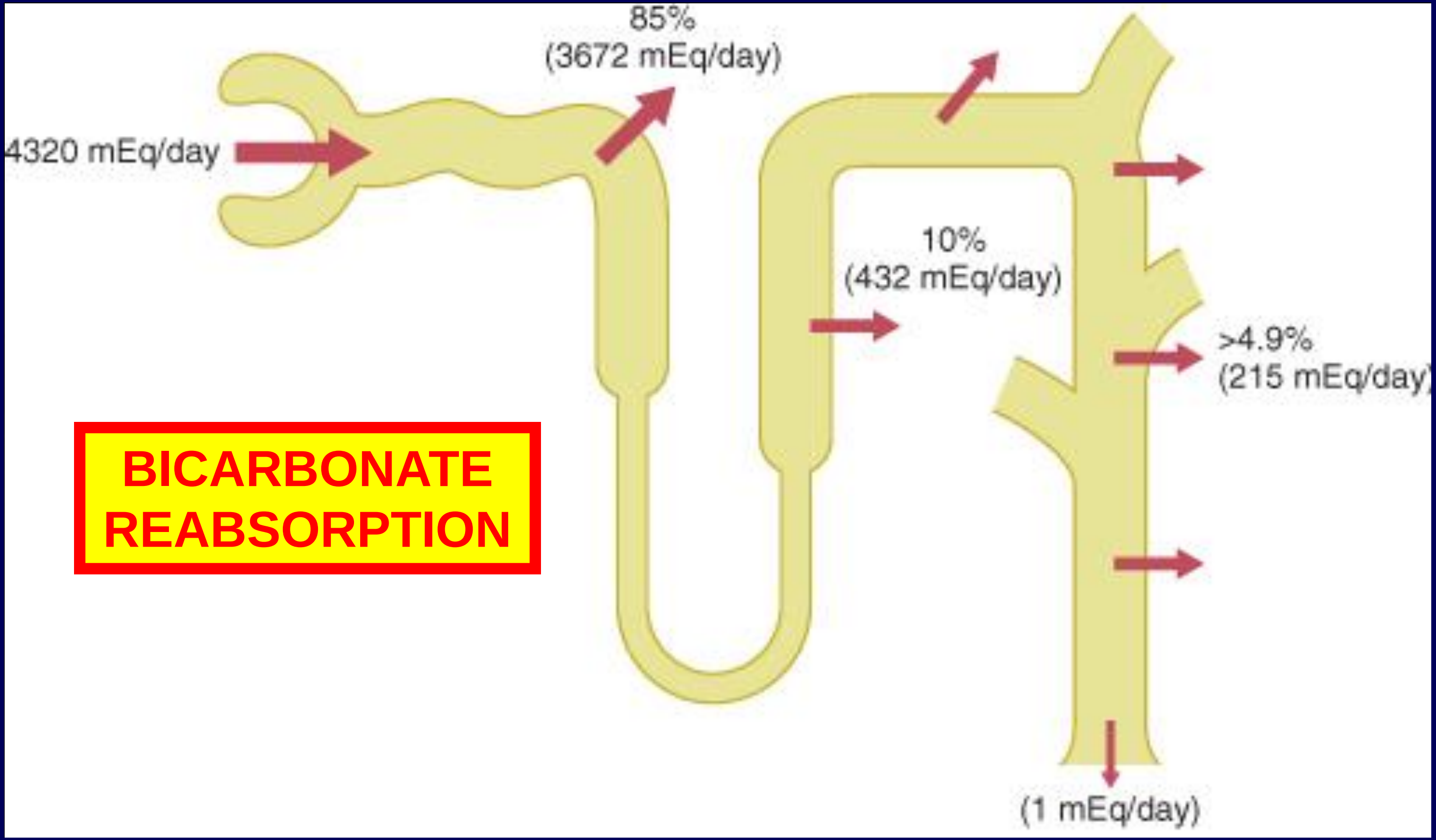
Respiratory Regulation of Acid-Base Balance



Effect of blood pH on rate of alveolar ventilation.



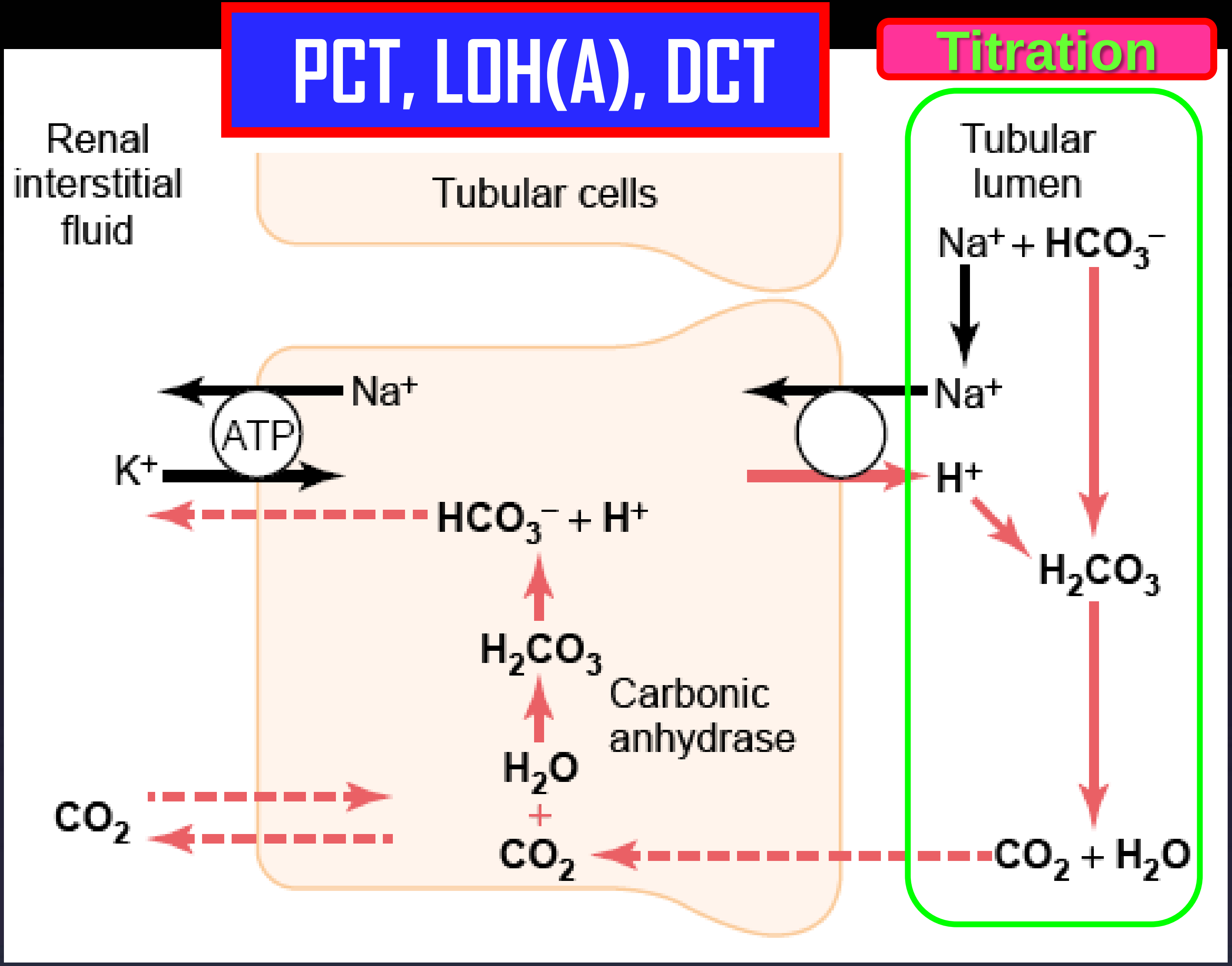
RENAL CONTROL



BICARBONATE REABSORPTION

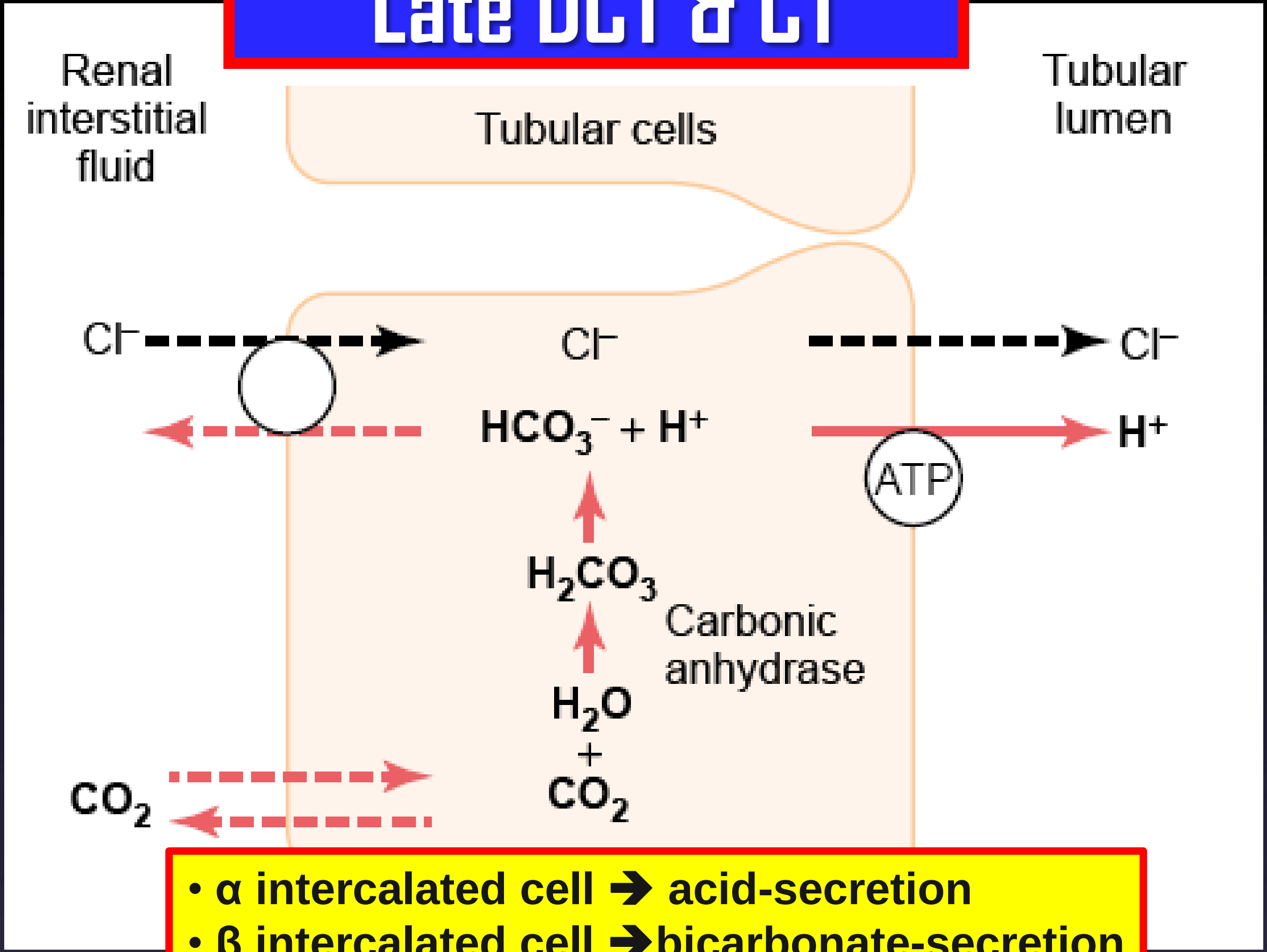
About 80 to 90 per cent of the bicarbonate reabsorption (and H+ secretion) occurs in the proximal tubule

HYDROGEN ION SECRETION



HYDROGEN ION SECRETION

Late DCT & CT

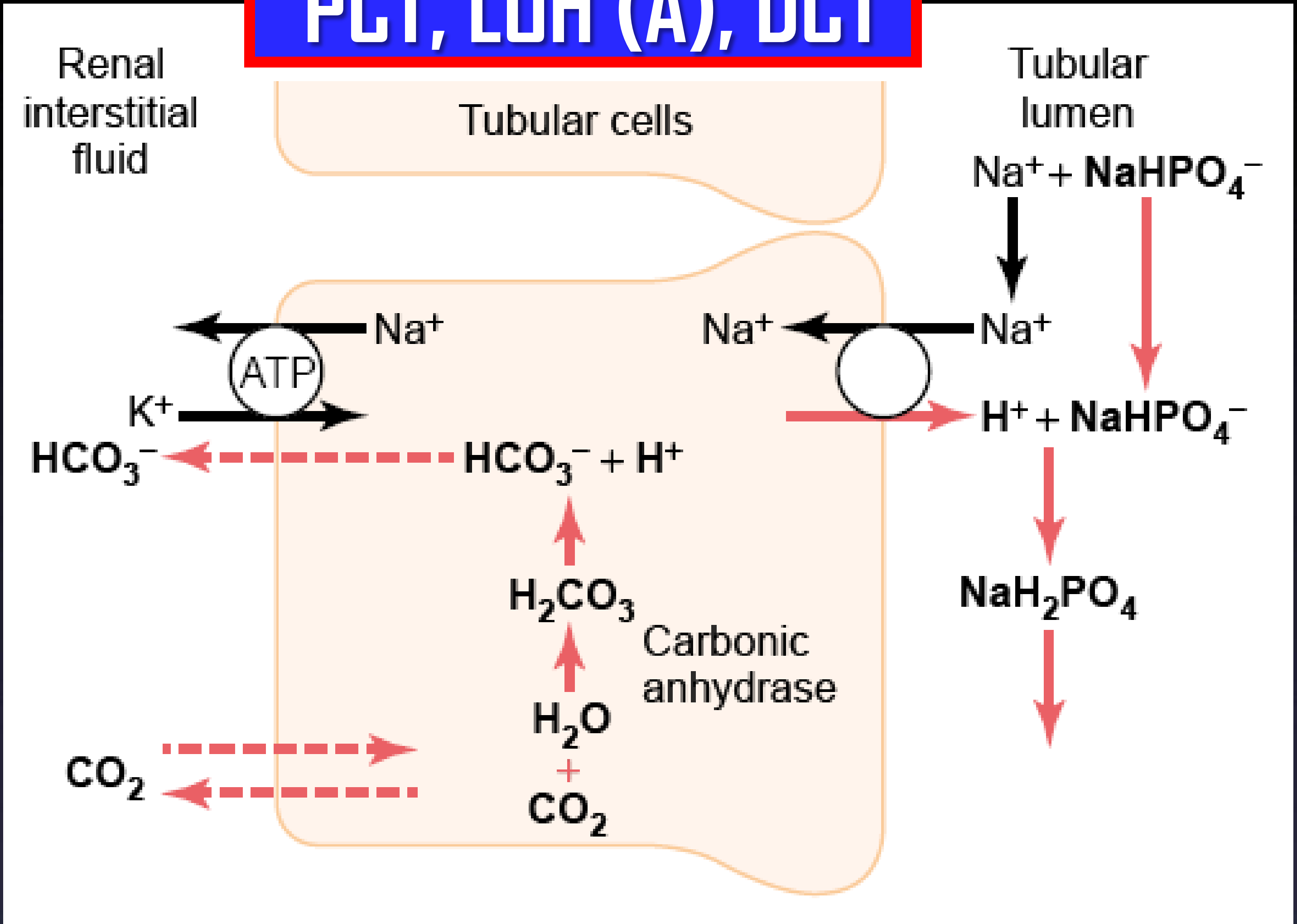


- α intercalated cell ➔ acid-secretion
- β intercalated cell ➔bicarbonate-secretion

Remember that I Cells have H-ATPase and H/K-ATPase

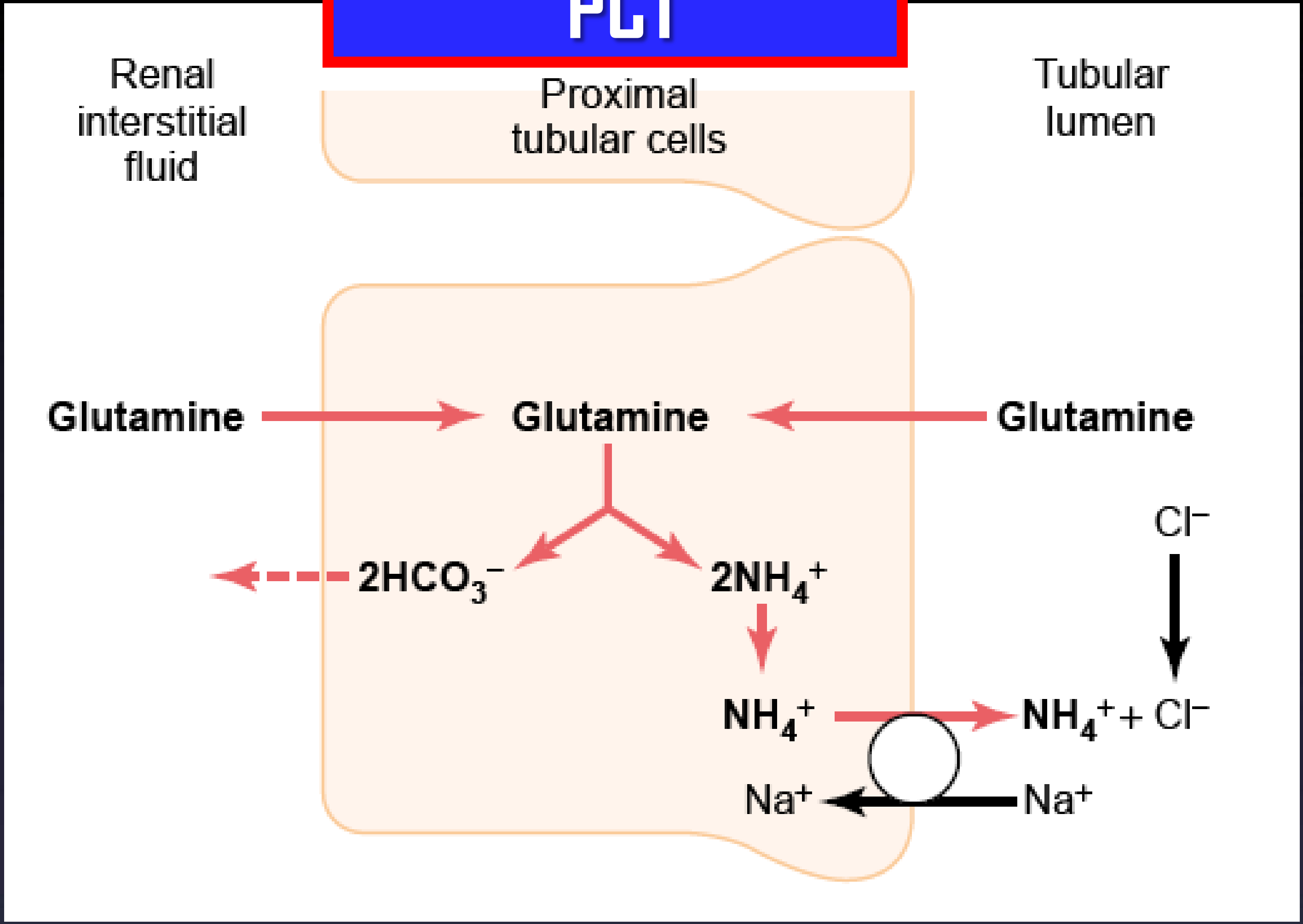
PHOSPHATE BUFFER SYSTEM

PCT, LOH (A), DCT

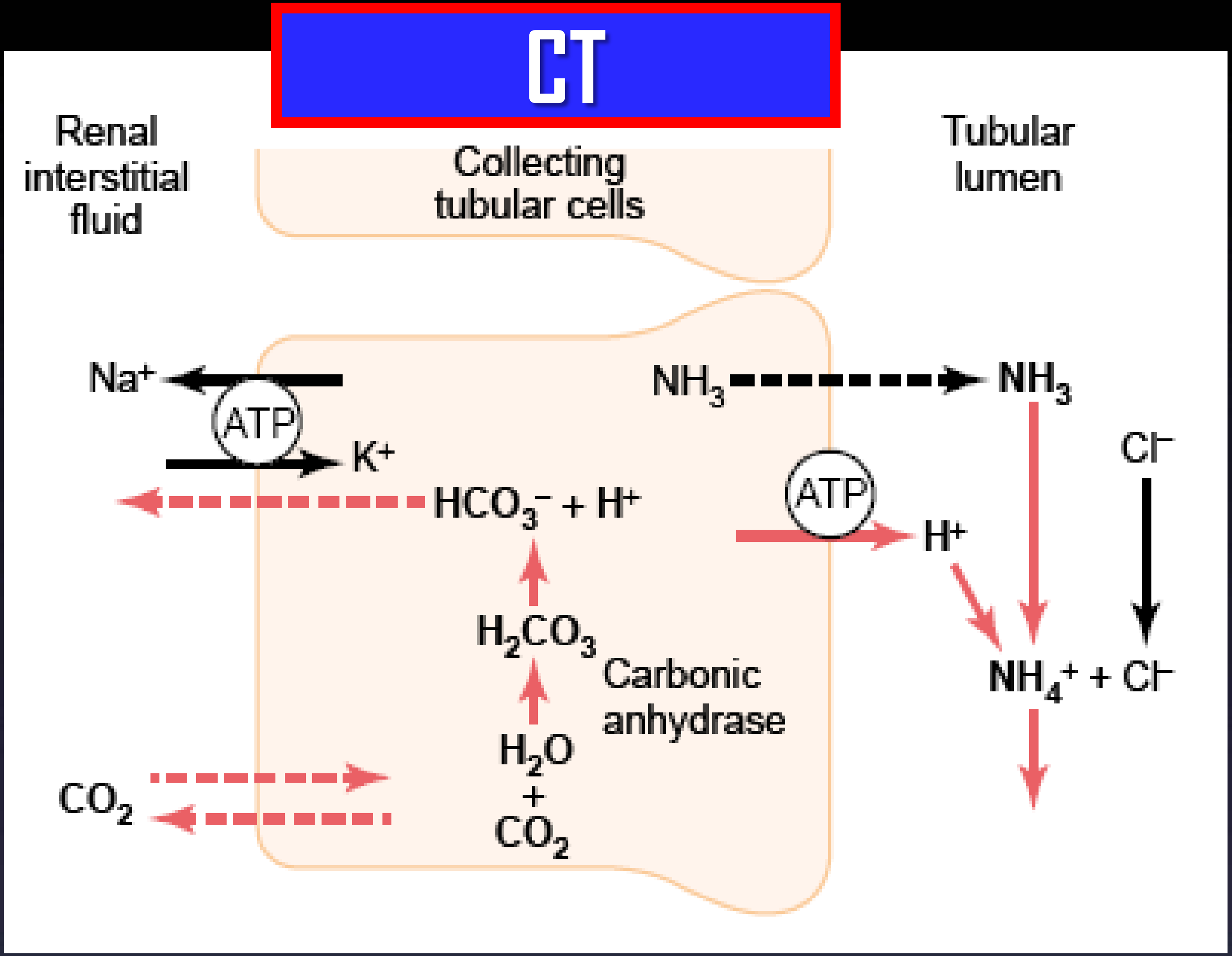


AMMONIA BUFFER SYSTEM

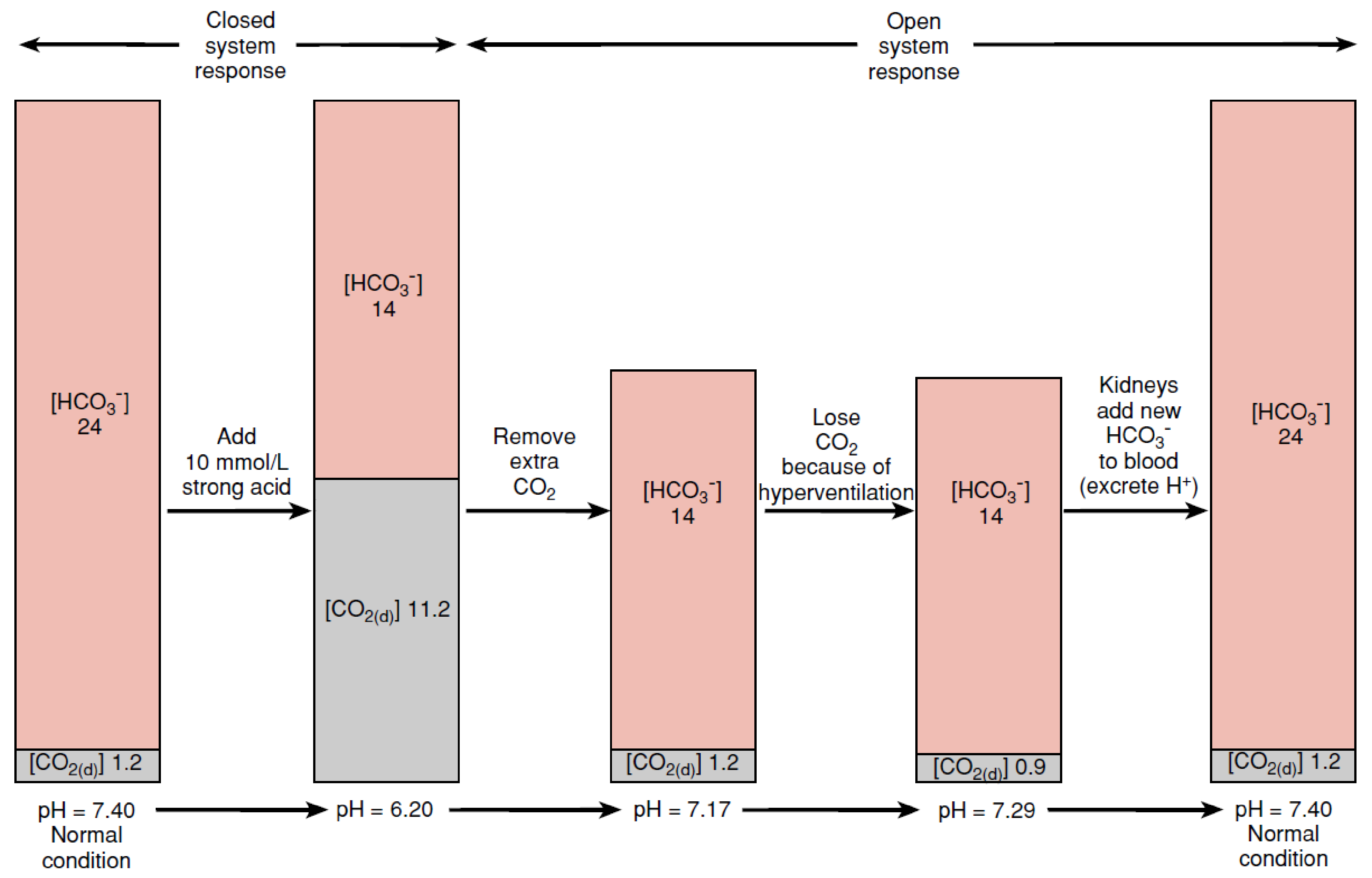
PCT



AMMONIA BUFFER SYSTEM



The HCO3/CO2 system. This system is remarkably effective in buffering added strong acid in the body because it is open



Closed system response

Open system response

$[HCO_3^-]$ 24

$[CO_{2(d)}]$ 1.2

pH = 7.40
Normal condition

Add 10 mmol/L strong acid →

$[HCO_3^-]$ 14

$[CO_{2(d)}]$ 11.2

pH = 6.20

Remove extra CO_2 →

$[HCO_3^-]$ 14

$[CO_{2(d)}]$ 1.2

pH = 7.17

Lose CO_2 because of hyperventilation →

$[HCO_3^-]$ 14

$[CO_{2(d)}]$ 0.9

pH = 7.29

Kidneys add new HCO_3^- to blood (excrete H^+) →

$[HCO_3^-]$ 24

$[CO_{2(d)}]$ 1.2

pH = 7.40
Normal condition

BASE/ACID RATIO

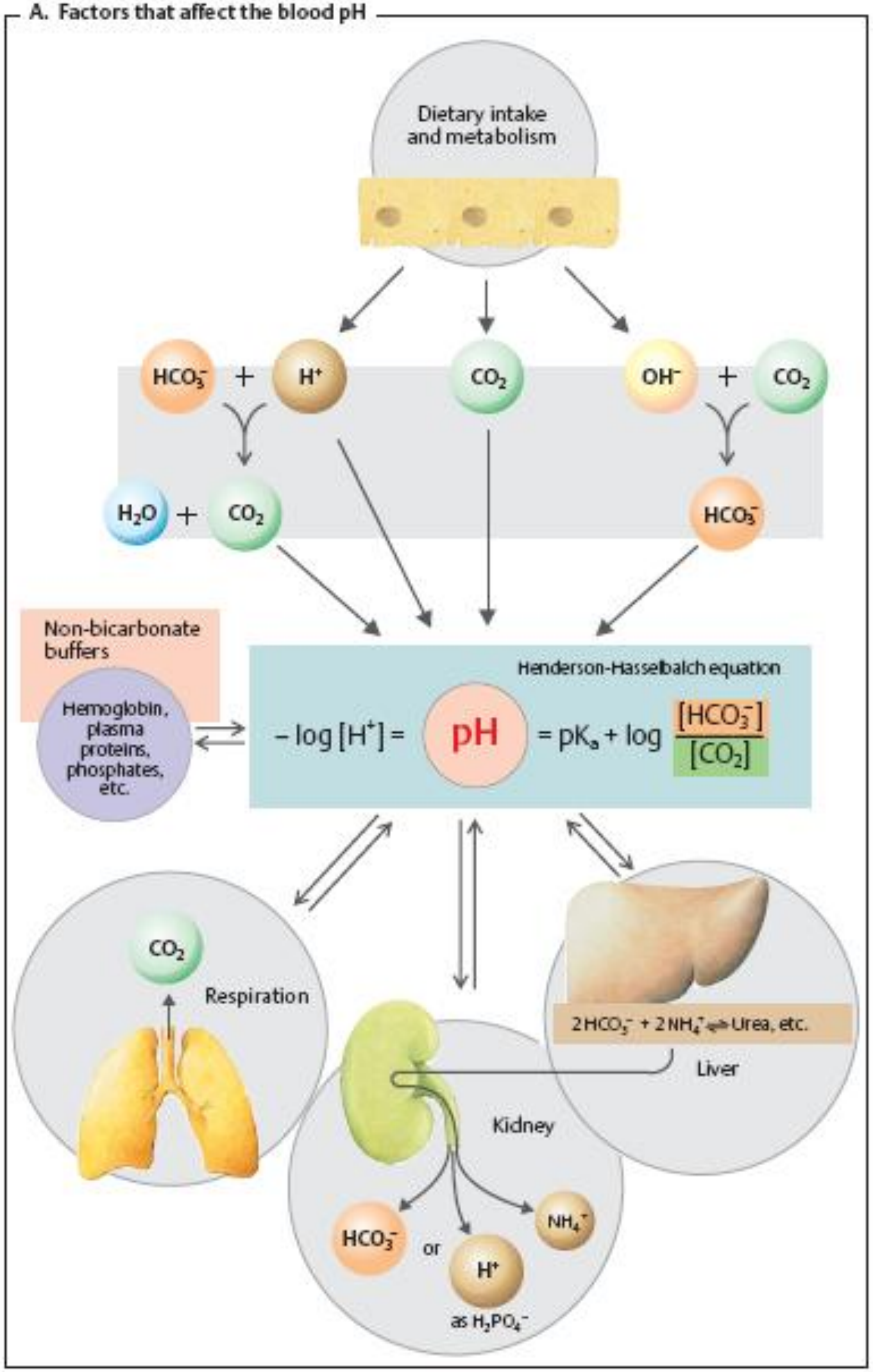
$\frac{\text{Base}}{\text{Acid}}$ → $\frac{NaHCO_3}{H_2CO_3}$ → $\frac{HCO_3^-}{CO_2}$

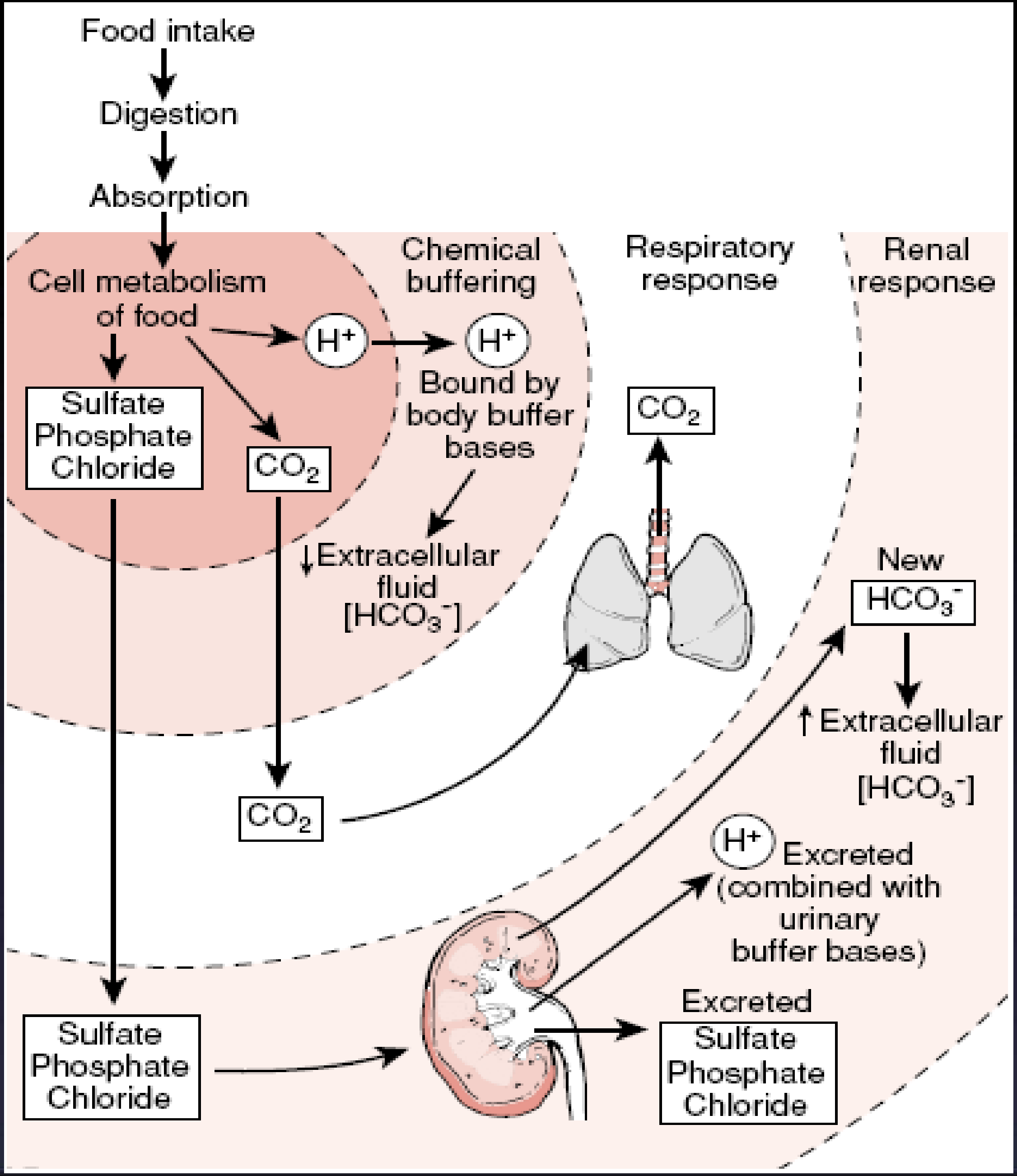
→ $\frac{20}{1}$ → $\frac{\text{Kidneys}}{\text{Lungs}}$

→ $\frac{\text{Metabolic}}{\text{Respiratory}}$ → $\frac{\text{Compensation by Respiratory}}{\text{Compensation by Kidney}}$

ARTERIAL BLOOD ANALYSIS

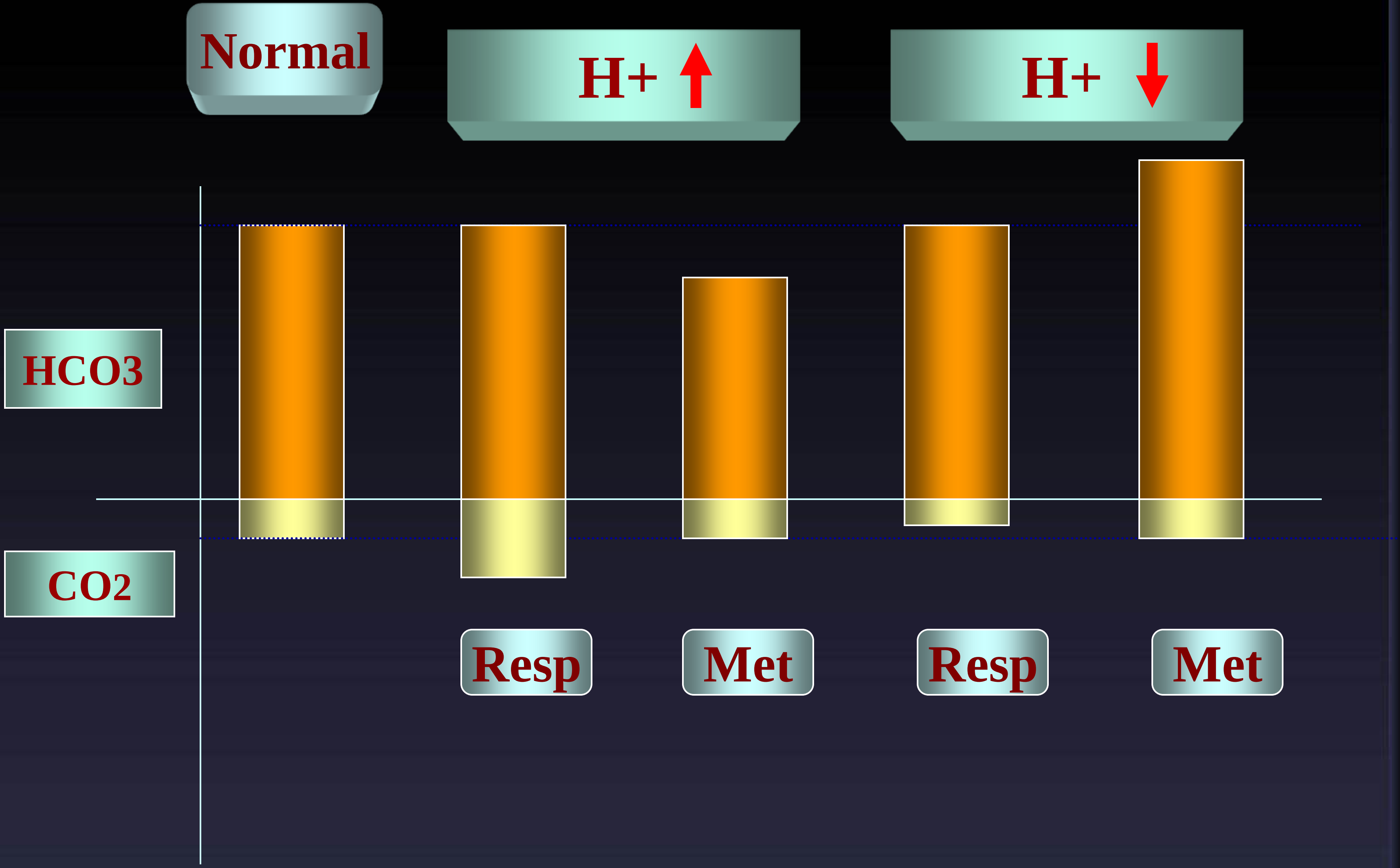
ANALYTE	REF. RANGE
pH	7.4 ± 0.05
PO_2	75-100 mmHg (10.0-13.3 kpa)
PCO_2	36.0-46.0 mmHg (4.8-6.1 kpa)
HCO_3-	22.0-26.0 mmol/L
O_2 Saturation	95-100 %
Base Excess	± 2.5 (Normal)


A. Factors that affect the blood pH
Dietary intake and metabolism
HCO_3^- + H^+
CO_2
OH^- + CO_2
H_2O + CO_2
HCO_3^-
Non-bicarbonate buffers
Hemoglobin, plasma proteins, phosphates, etc.
Henderson-Hasselbalch equation
$-\log[H^+] =$ pH $= pK_a + \log \frac{[HCO_3^-]}{[CO_2]}$
CO_2
Respiration
$2\,HCO_3^- + 2\,NH_4^+ \rightleftharpoons$ Urea, etc.
Liver
Kidney
HCO_3^-
or
H^+
as $H_2PO_4^-$
NH_4^+


Food intake
Digestion
Absorption
Cell metabolism of food
Chemical buffering
Respiratory response
Renal response
H+
H+
Bound by body buffer bases
Sulfate
Phosphate
Chloride
CO2
CO2
↓Extracellular fluid [HCO3-]
New
HCO3-
↑Extracellular fluid [HCO3-]
CO2
H+
Excreted (combined with urinary buffer bases)
Excreted
Sulfate
Phosphate
Chloride
Sulfate
Phosphate
Chloride

DISORDER	IMORTANT CAUSES
Respiratory Acidosis	• inadequate ventilation
Respiratory Alkalosis	• hyperventilation
Metabolic Acidosis	• diabetic ketoacidosis, • lactic acidosis • ethylene glycol or salicylate poisoning (elevated anion gap) • diarrhea, ileostomy (normal anion gap)
Metabolic Alkalosis	• excessive alkali ingestion (antacids) • H+ loss (vomiting)

ACIDOSIS AND ALKALOSIS



Normal

H+ ↑

H+ ↓

HCO3

CO2

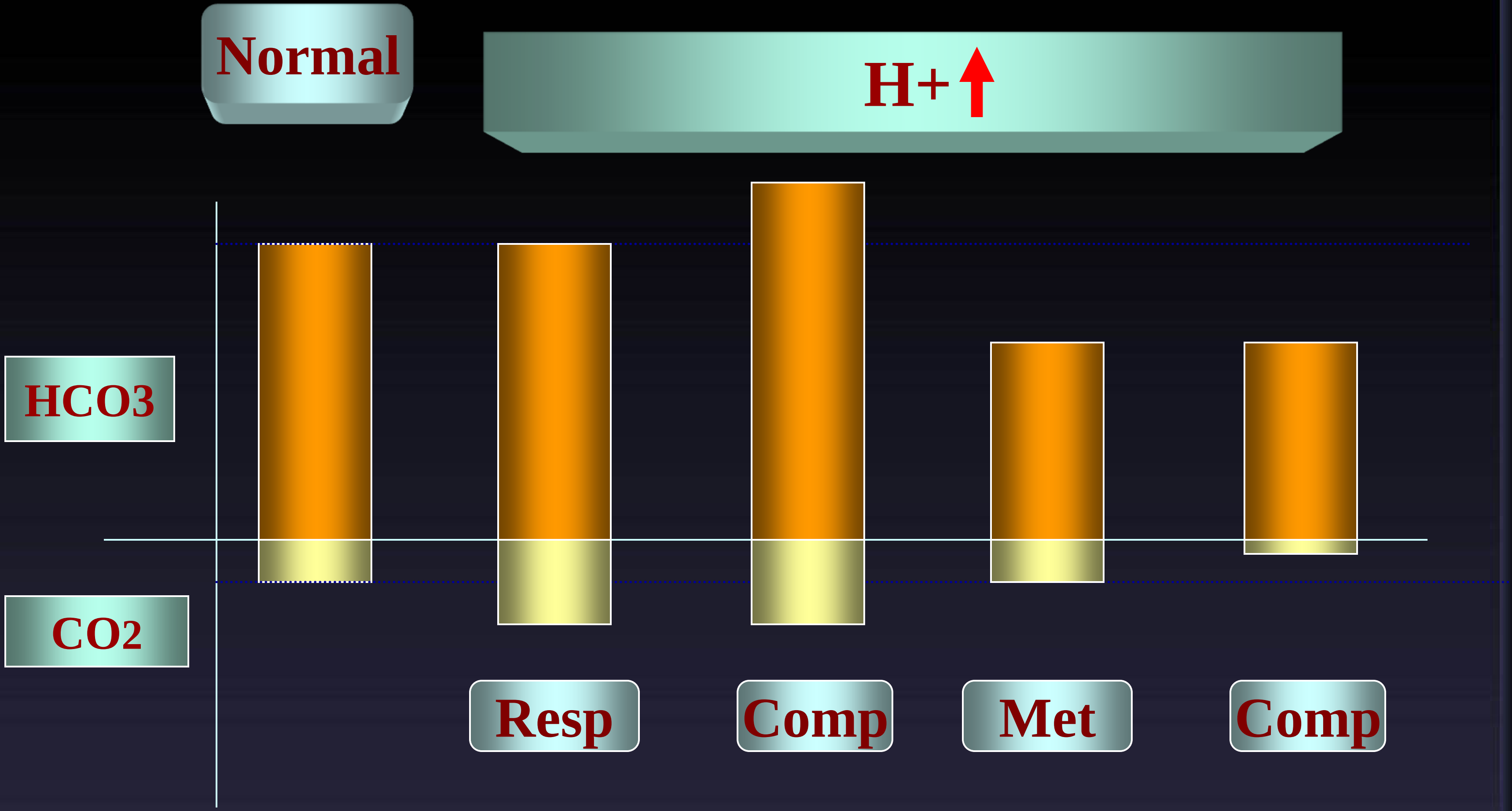
Resp

Met

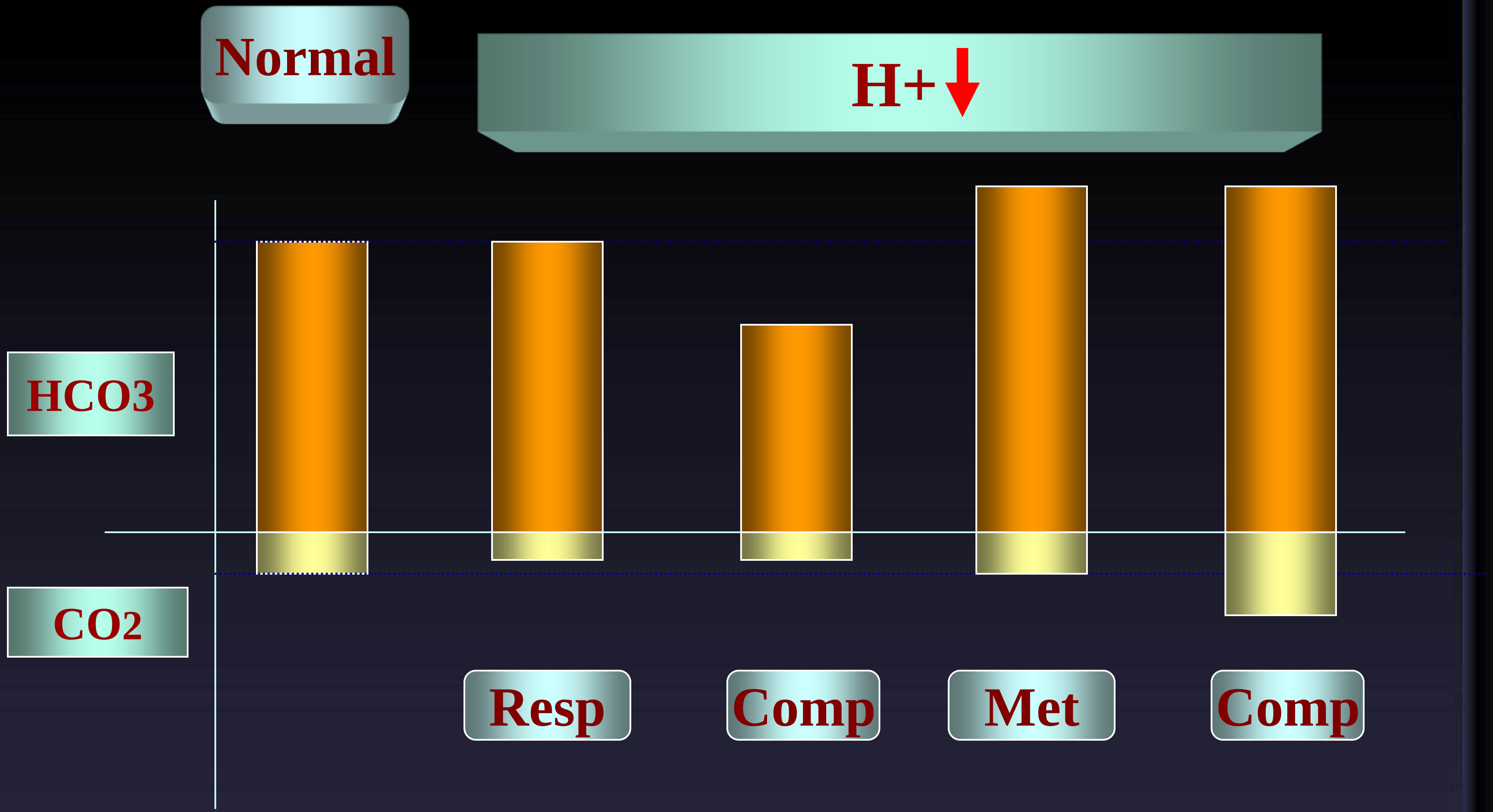
Resp

Met

COMPENSATION OF ACIDOSIS



COMPENSATION OF ALKALOSIS



UNCOMPENSATED

ACIDOSIS

RESPIRATORY	METABOLIC
H+ ↑	H+ ↑
pH ↓	pH ↓
CO2 ↑	CO2 *N*
HCO3 *N*	HCO3 ↓

ALKALOSIS

RESPIRATORY	METABOLIC
H+ ↓	H+ ↓
pH ↑	pH ↑
CO2 ↓	CO2 *N*
HCO3 *N*	HCO3 ↑

COMPENSATED

ACIDOSIS

RESPIRATORY	METABOLIC
H+ ↑	H+ ↑
pH ↓	pH ↓
CO2 ↑	**CO2 ↓↓↓**
HCO3 ↑↑↑	HCO3 ↓

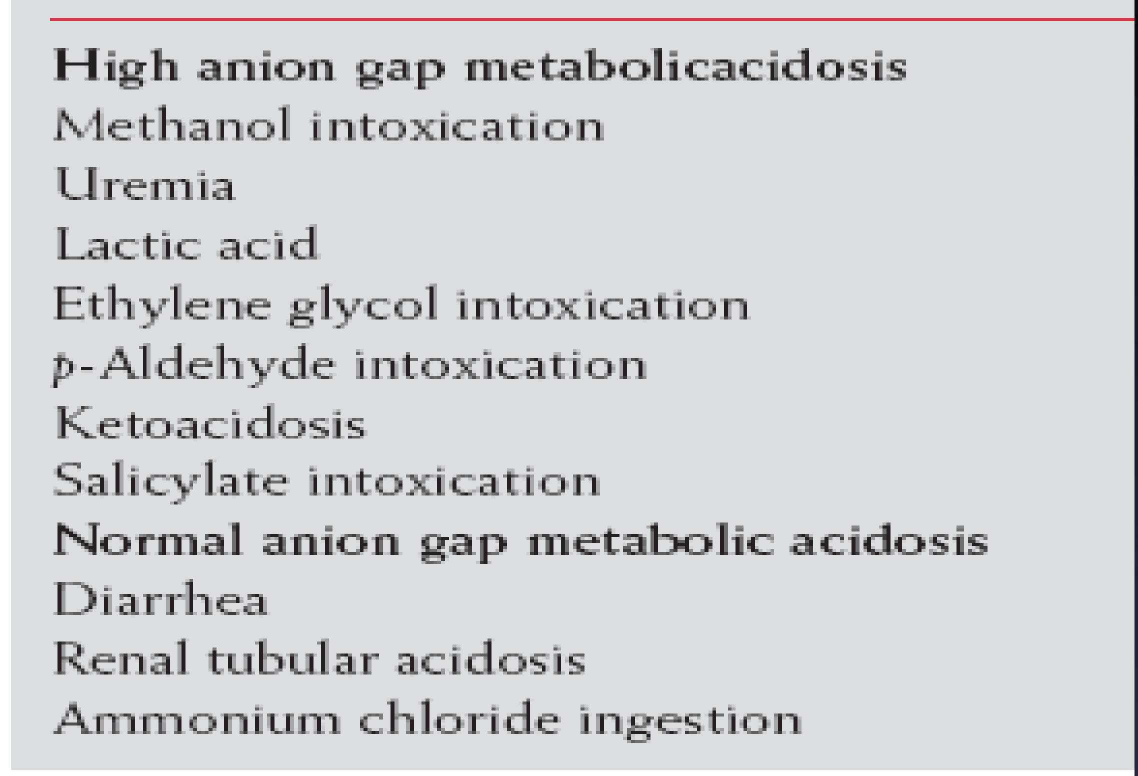
ALKALOSIS

RESPIRATORY	METABOLIC
H+ ↓	H+ ↓
pH ↑	pH ↑
CO2 ↓	**CO2 ↑↑↑**
HCO3 ↓↓↓	HCO3 ↑

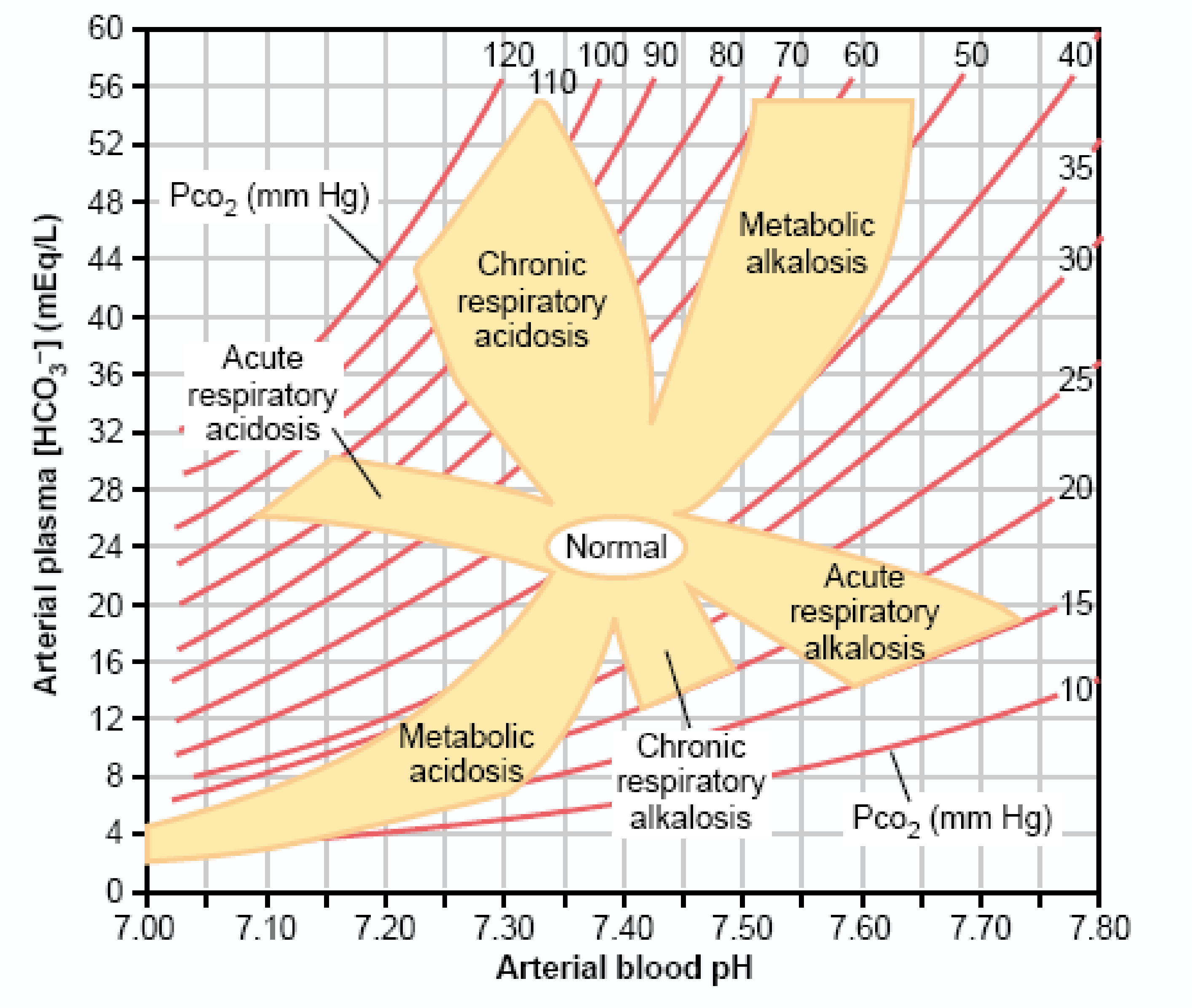
ACIDOSIS AND ALKALOSIS

	pH	H+	PCO_2	HCO_3^-
Normal	7.4	40 nEq/L	40 mmHg	24 meq/L
Respiratory Acidosis	↓	↑	↑	↑
Respiratory Alkalosis	↑	↓	↓	↓
Metabolic Acidosis	↓	↑	↓	↓
Metabolic Alkalosis	↑	↓	↑	↑

ANION GAP =
{[Na+] + [K]} – {[HCO3-] + [Cl-]}
10-18 mmol/L

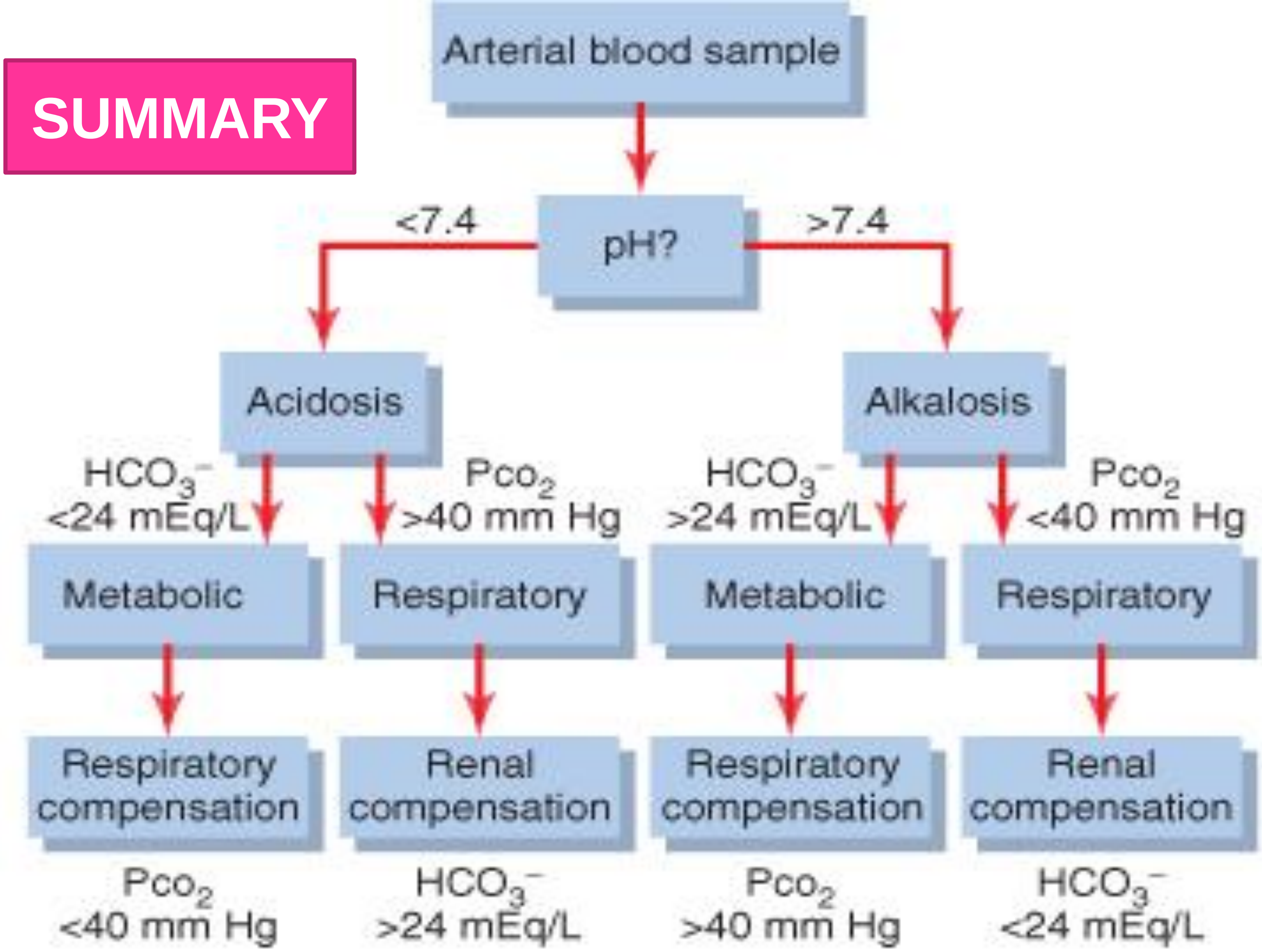


High anion gap metabolicacidosis
Methanol intoxication
Uremia
Lactic acid
Ethylene glycol intoxication
p-Aldehyde intoxication
Ketoacidosis
Salicylate intoxication
Normal anion gap metabolic acidosis
Diarrhea
Renal tubular acidosis
Ammonium chloride ingestion



Pco2 (mm Hg)
120
110
100
90
80
70
60
50
40
35
30
25
20
15
10
Chronic respiratory acidosis
Metabolic alkalosis
Acute respiratory acidosis
Normal
Acute respiratory alkalosis
Metabolic acidosis
Chronic respiratory alkalosis
Pco2 (mm Hg)
Arterial plasma [HCO3−] (mEq/L)
60
56
52
48
44
40
36
32
28
24
20
16
12
8
4
0
7.00
7.10
7.20
7.30
7.40
7.50
7.60
7.70
7.80
Arterial blood pH

SUMMARY



Arterial blood sample

pH?

<7.4

>7.4

Acidosis

Alkalosis

HCO_3^- <24 mEq/L

Metabolic

Respiratory compensation

Pco_2 <40 mm Hg

Pco_2 >40 mm Hg

Respiratory

Renal compensation

HCO_3^- >24 mEq/L

HCO_3^- >24 mEq/L

Metabolic

Respiratory compensation

Pco_2 >40 mm Hg

Pco_2 <40 mm Hg

Respiratory

Renal compensation

HCO_3^- <24 mEq/L