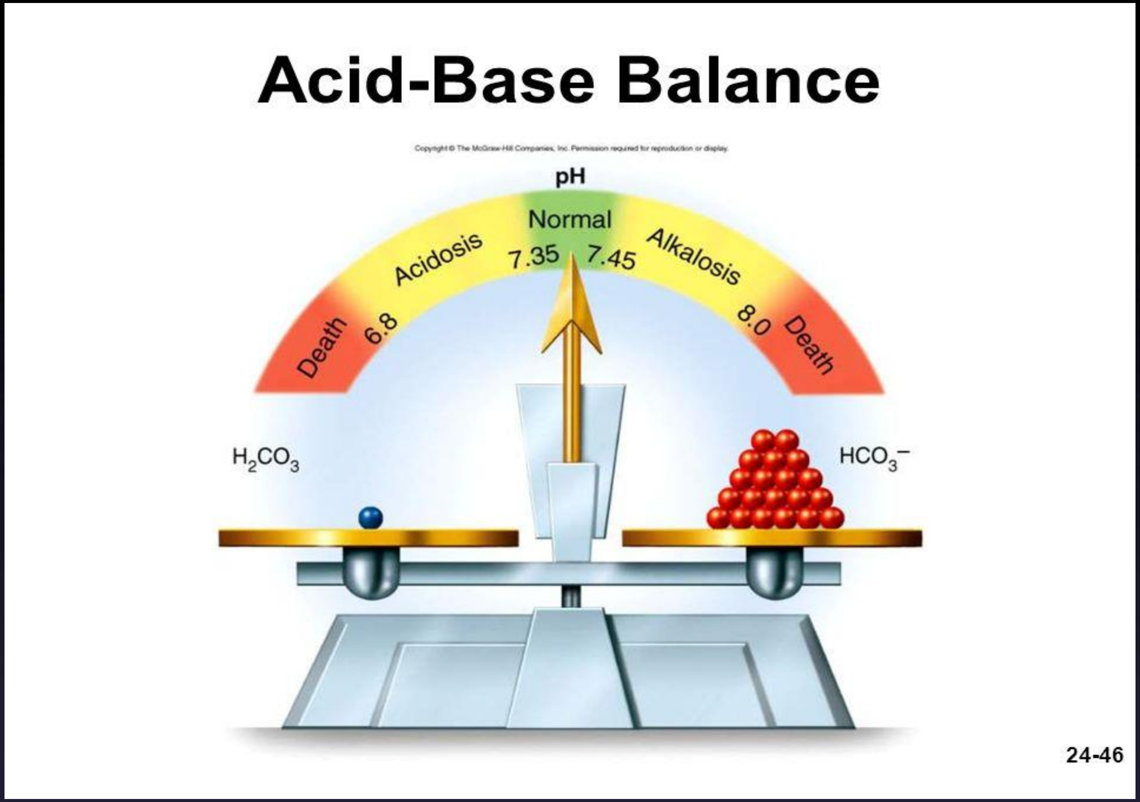
ACID BASE BALANCE



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Lecture 1: Basics of Acid Base

OBJECTIVES

At the end of this lecture you should be able to:

- Define: acid and base.
- Explain what is meant by strong and weak acids and bases
- List and identify the names/formulas for the common strong acids and strong bases.
- To explain the role of Henderson-Hasselbalch equation in acid-base regulation

NEXT

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

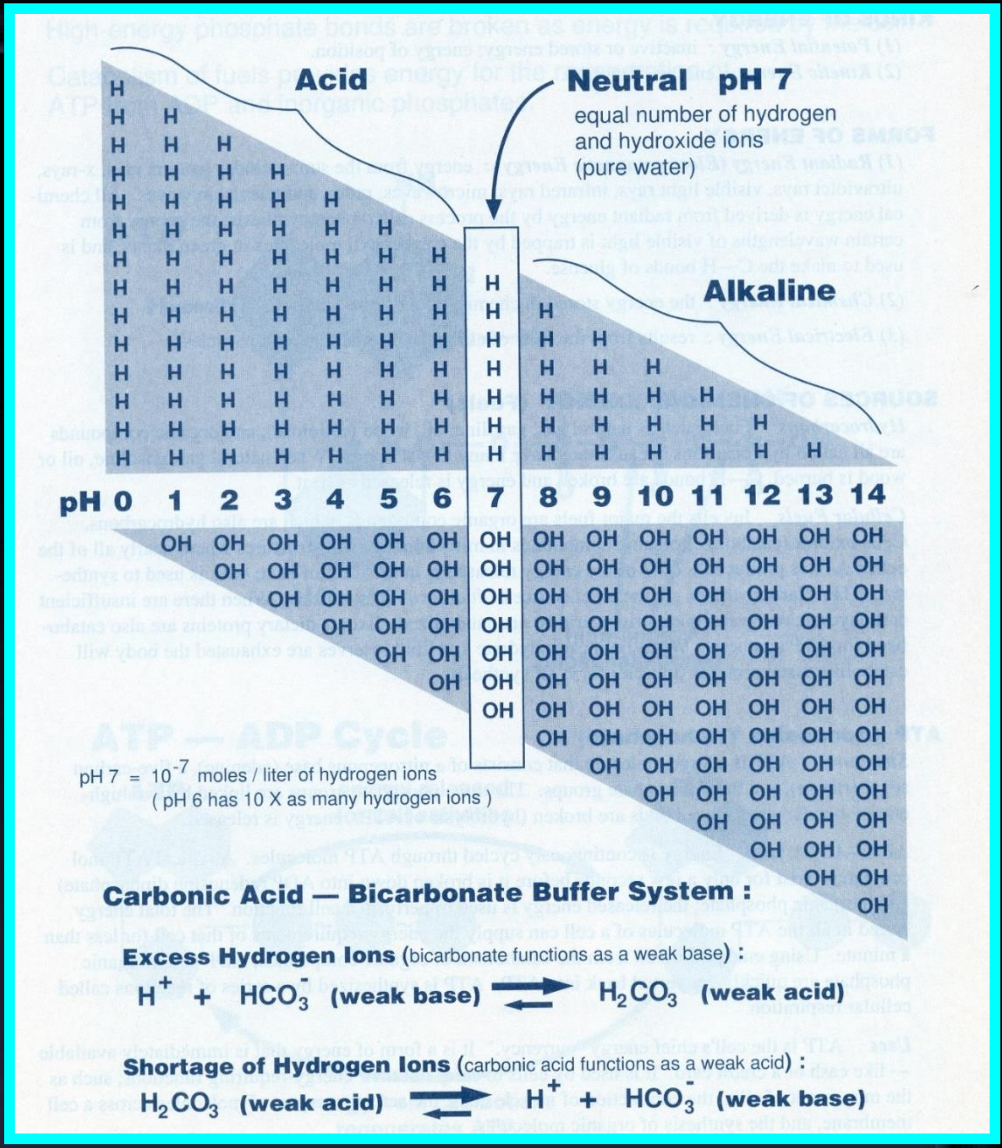
- Bases are ions or molecules that bind free H^+ and remove it from solution

  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

20	7.70
30	7.52
40	7.40
50	7.30
60	7.22

H+= 80 -last two digits of pH



pH

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

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

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 or 0.00000004 Eq/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?

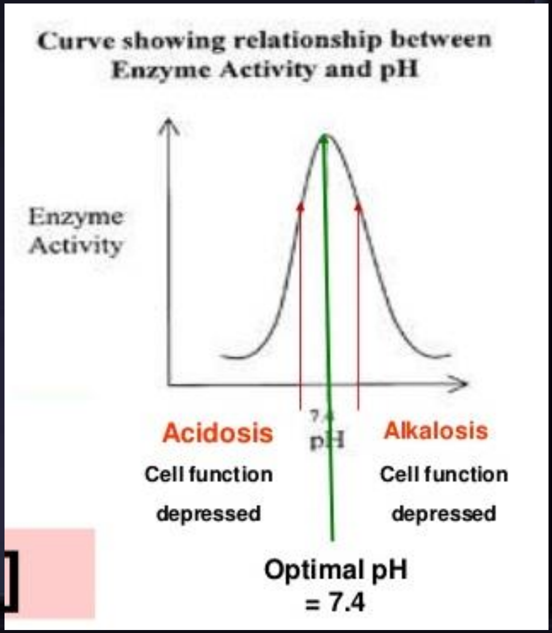
7.35 – 7.45

	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

- H^+ ions are deadly because they can affect cell function by altering the charge of functional proteins including enzymes
- H ions are very reactive cations and bind to protein anions strongly if they are in high amounts and impair their activity

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



ACID PRODUCTION

H+ is continually produced by metabolic activity:

- **Volatile acids: (e.g. carbonic acid, H_2CO_3; formation catalyzed by carbonic anhydrase)**

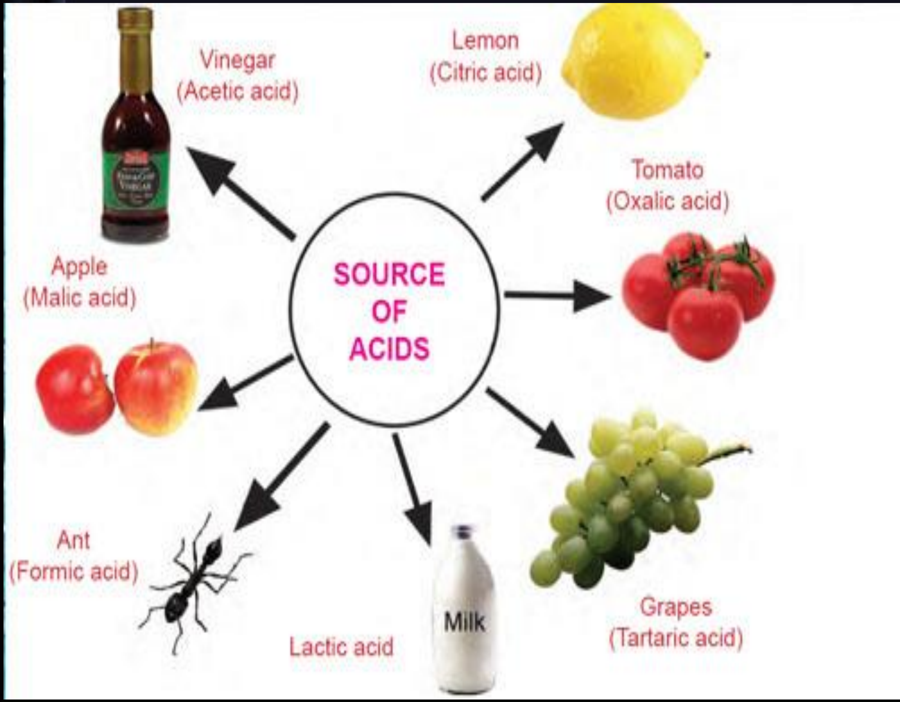
$$H^+ + HCO_3^- \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$$

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/day or mmol/day 300 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

$$pH = pK \times \log \frac{Base}{Acid}$$

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: $K = [H^+][HCO_3^-] / [H_2CO_3]$

$$\text{H2CO3} \rightleftharpoons \text{H+} + \text{HCO3-}$$

$$K' = \frac{H^{+} \times HCO3^{-}}{\text{H2CO3}}$$

$$H^{+} = K' \times \frac{\text{H2CO3}}{\text{HCO3-}}$$

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

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

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

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

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

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

pK

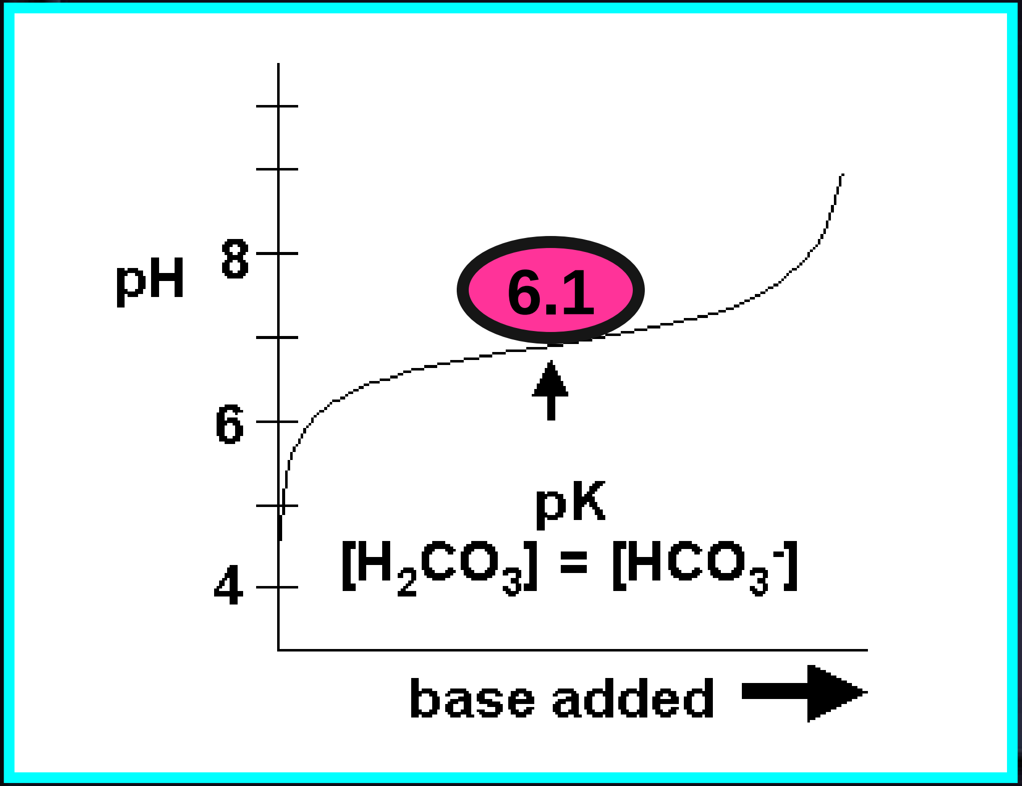
Dissociation Constant

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 HCO_3^- than H_2CO_3)

pK

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



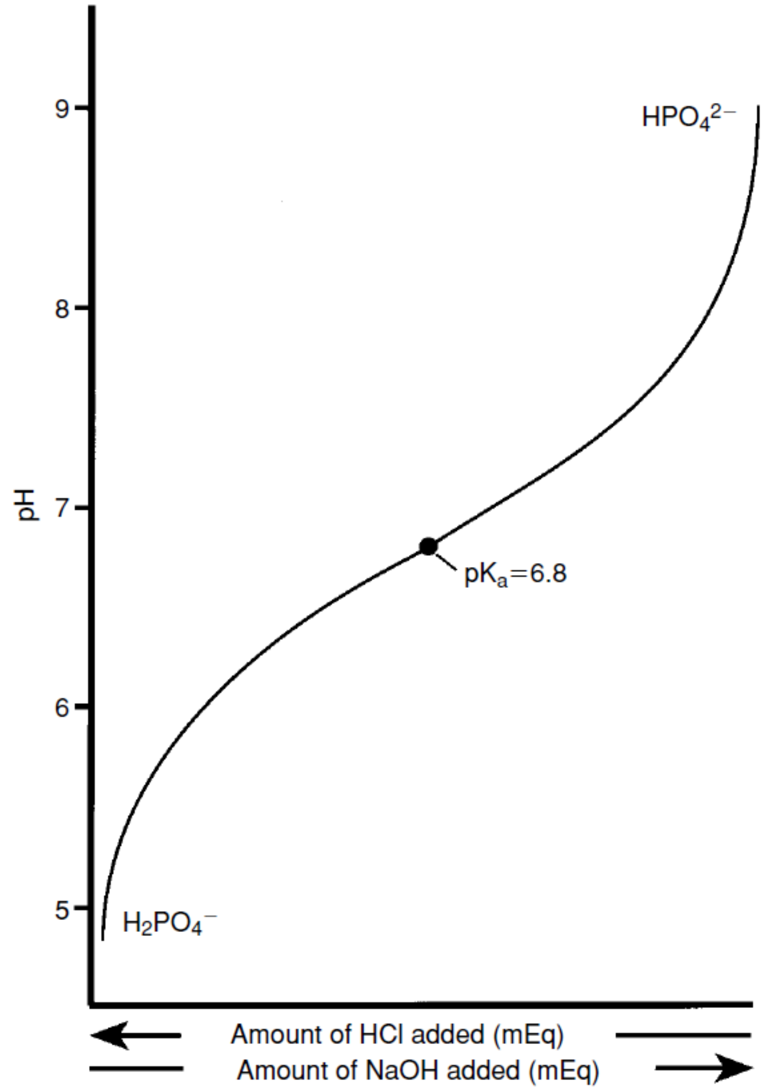
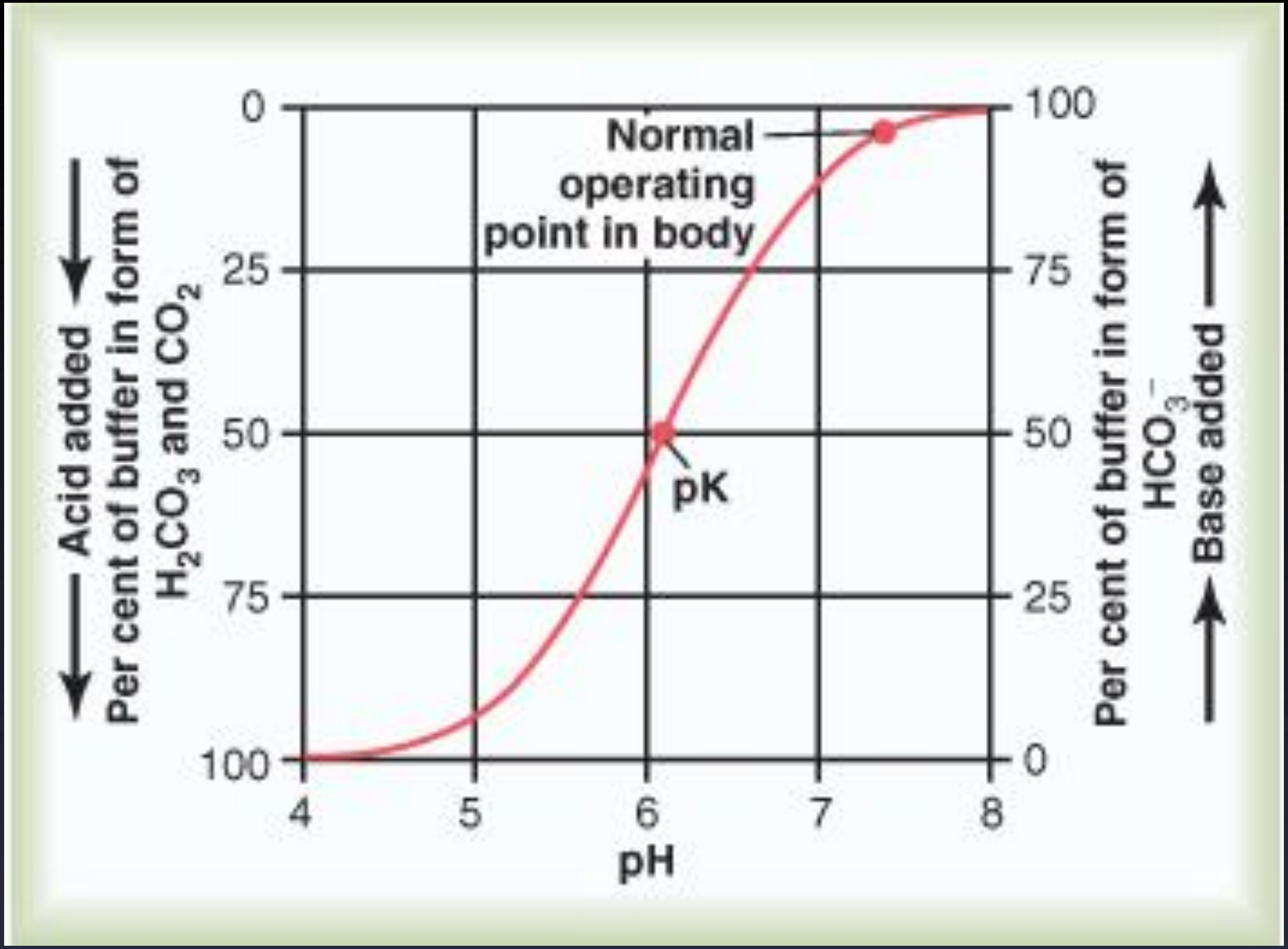
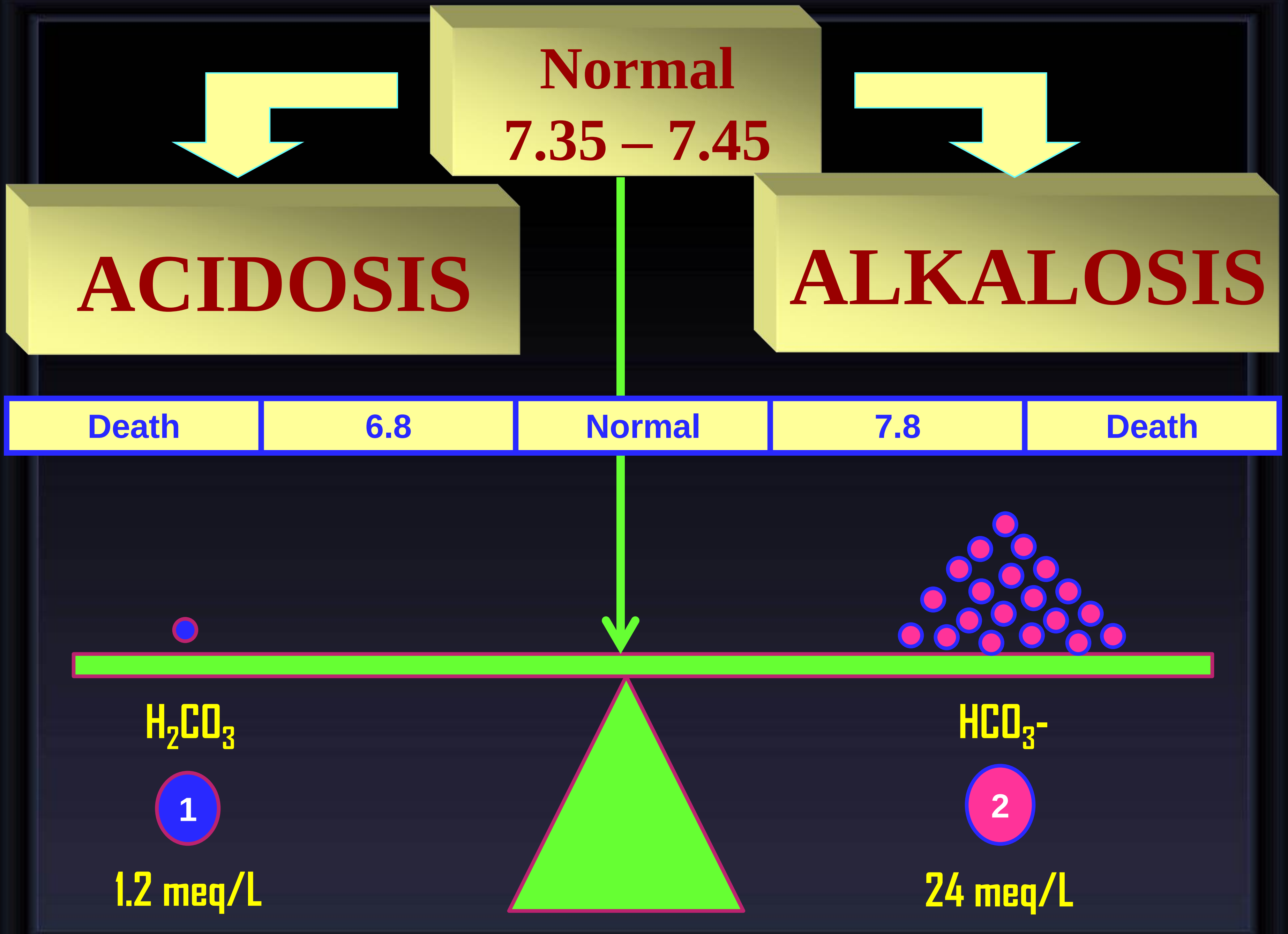


FIGURE 25.1 **A titration curve for a phosphate buffer.** The pK_a for $H_2PO_4^-$ is 6.8. A strong acid (HCl) (right to left) or strong base (NaOH) (left to right) was added and the resulting solution pH recorded (y-axis). Notice that buffering is best (i.e., the change in pH upon the addition of a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





Normal
7.35 – 7.45
ACIDOSIS
ALKALOSIS
Death
6.8
Normal
7.8
Death
H_2CO_3
1
1.2 meq/L
HCO_3-
2
24 meq/L

Lecture 2: Buffer systems

OBJECTIVES

At the end of this lecture you should be able to:

- To define buffer system and discuss the role of blood buffers and to explain their relevant roles in the body
- To describe the role of kidneys in the regulation of acid-base balance
- To describe the role of lungs in the regulation of acid-base balance

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

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

ADD STRONG ACID

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

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]

$$pH = pK + \log HCO_3^- / H_2CO_3$$

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

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

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:

HCO_3^- / H_2CO_3

- pK = 6.1
- major plasma buffer

– PHOSPHATE: HPO_4^- / H_2PO_4

- 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 HCO_3^- which is 24 mmol/L

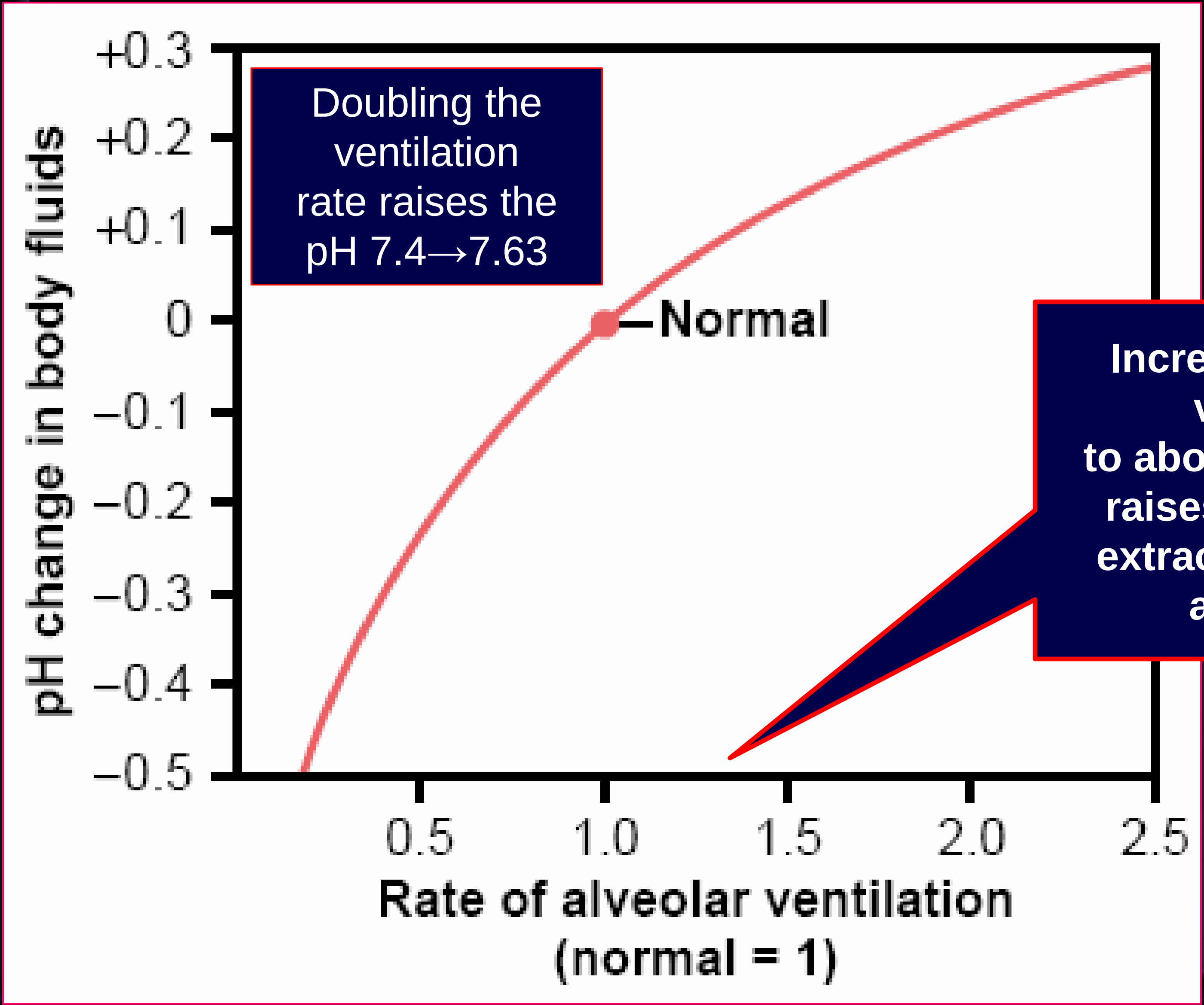
BODY BUFFER SYSTEMS

- AMMONIA: NH_3 / NH_4^+
  - pK = 9.0
  - used to buffer the urine
- PROTEINS (Amphoteric) : Prot / H Prot
  - important in ICF
- HEMOGLOBIN: Hb / HHb
  - important in ICF

Proteins Are
Excellent Buffers
WHY?

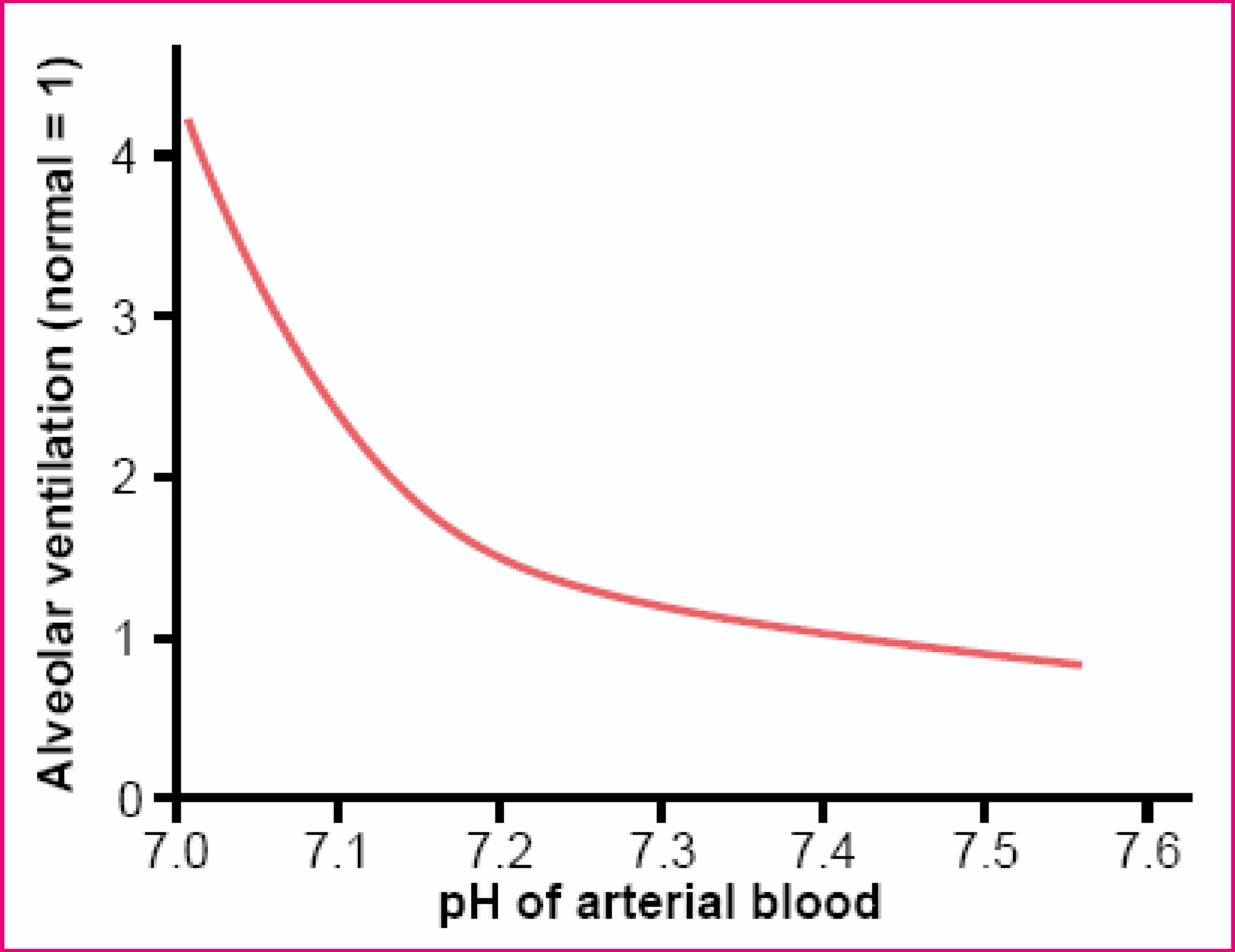
What is zwitterion?

Respiratory Regulation of Acid-Base Balance



Increasing alveolar ventilation to about twice normal raises the pH of the extracellular fluid by about 0.23.

Effect of blood pH on rate of alveolar ventilation.



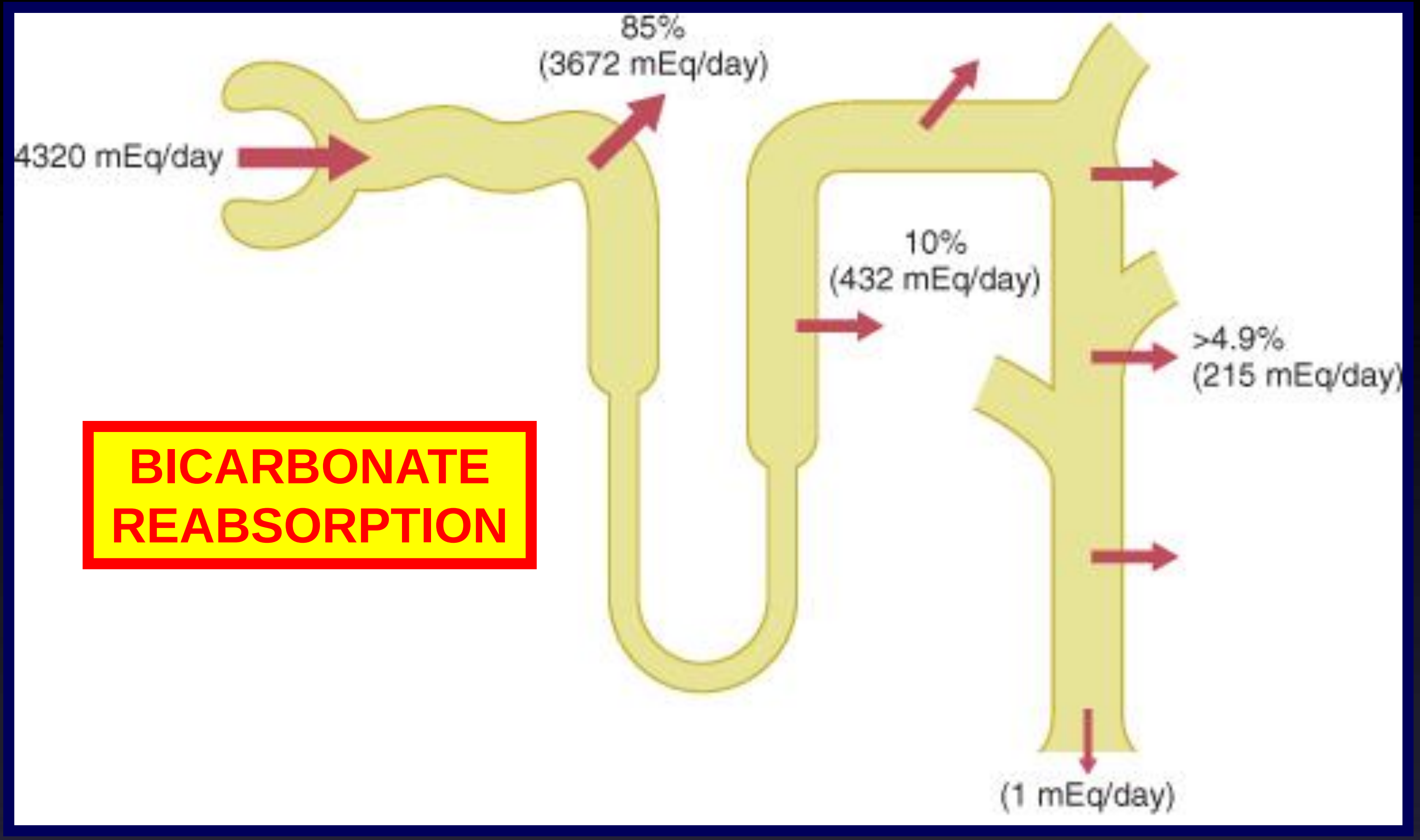
RENAL MECHANISMS TO REGULATE BODY pH

RENAL CONTROL

In PCT, LOH(A) and DCT: Na and H Counter Transport
HCO3- Buffer System

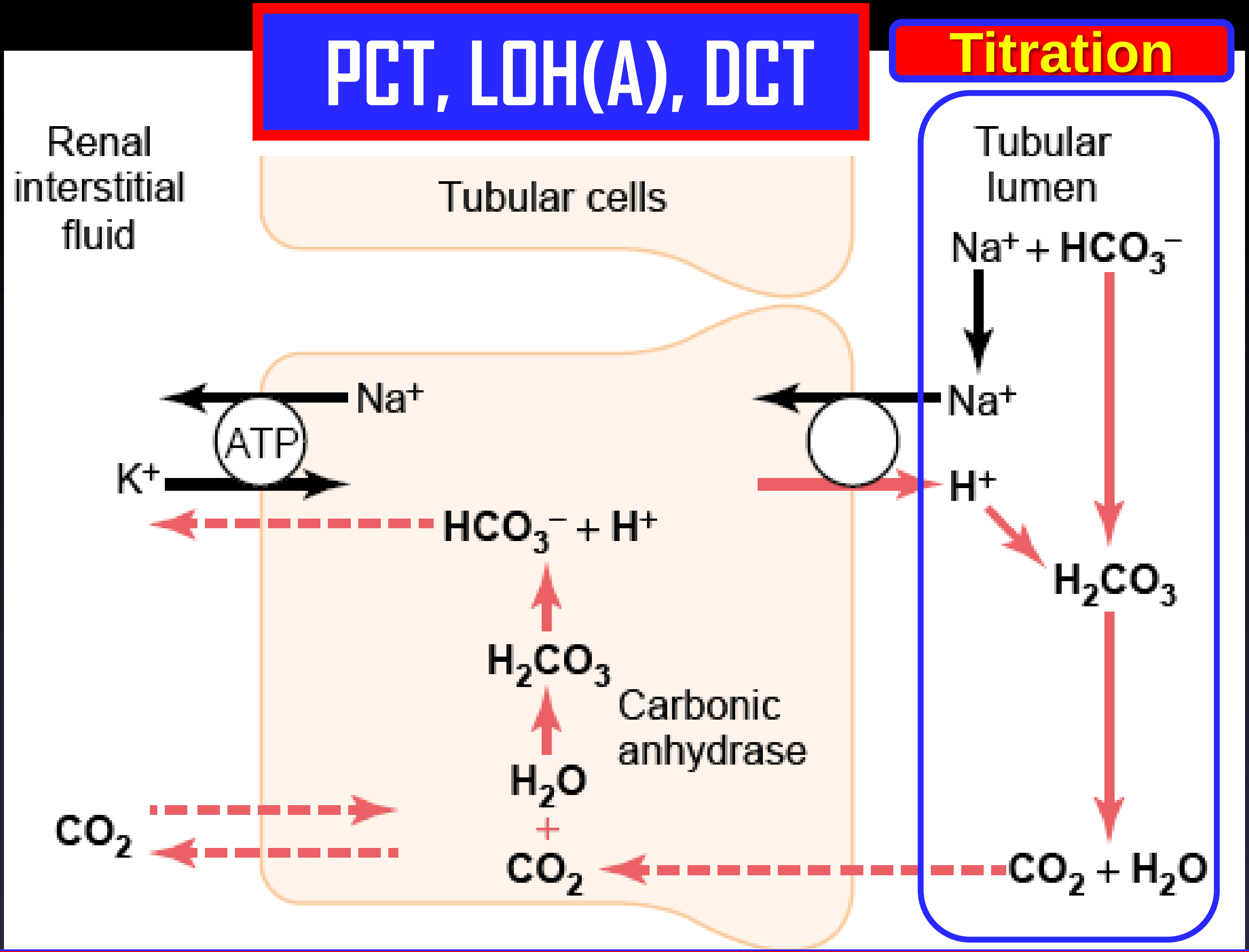
In DCT and CT: Proton Pump (Prim Active Transport)

In PCT, LOH (A) and DCT: PO_4 Buffer system



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

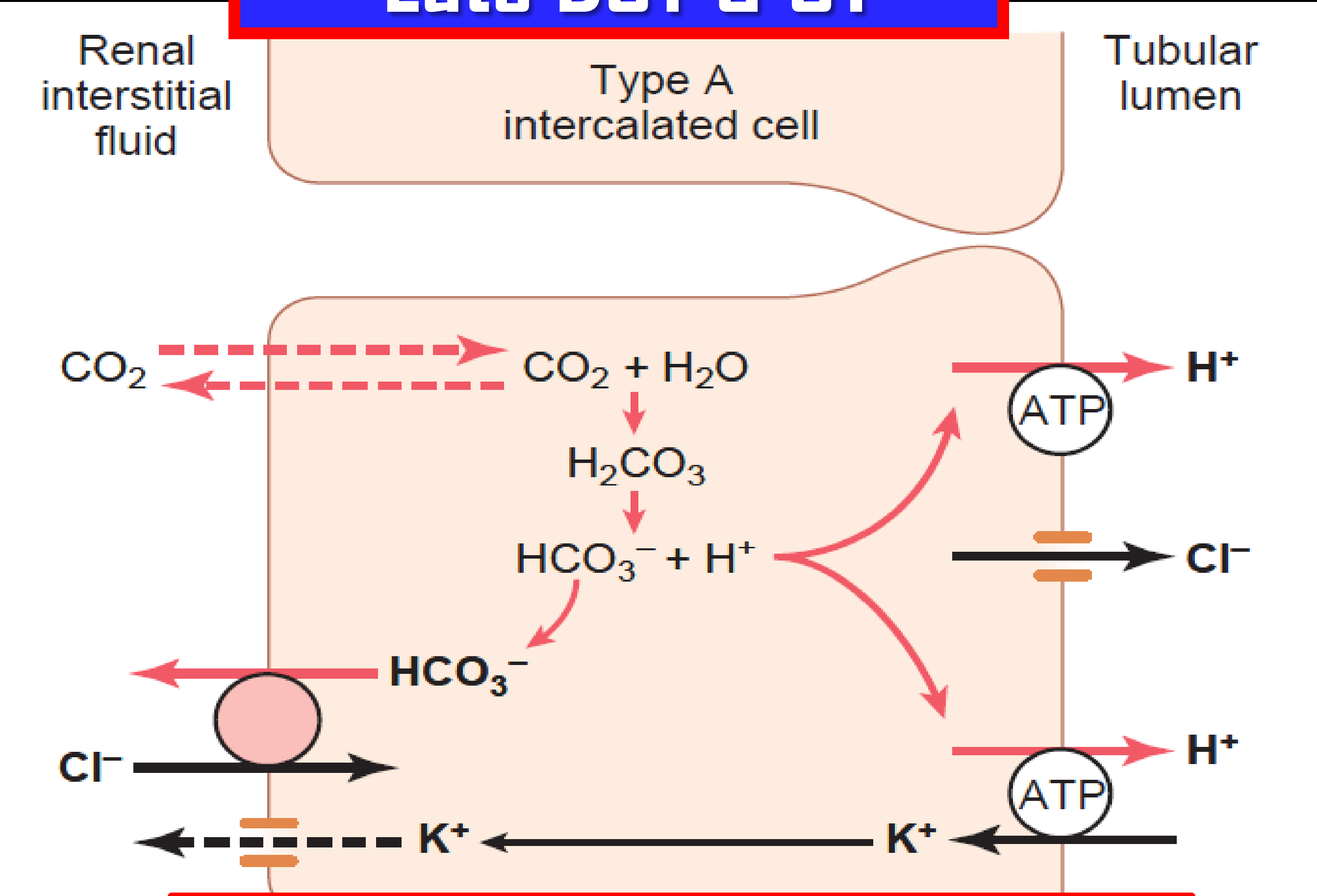
HYDROGEN ION SECRETION



HCO3− Is "Titrated" Against H+ in the Tubules

HYDROGEN ION SECRETION

Late DCT & CT

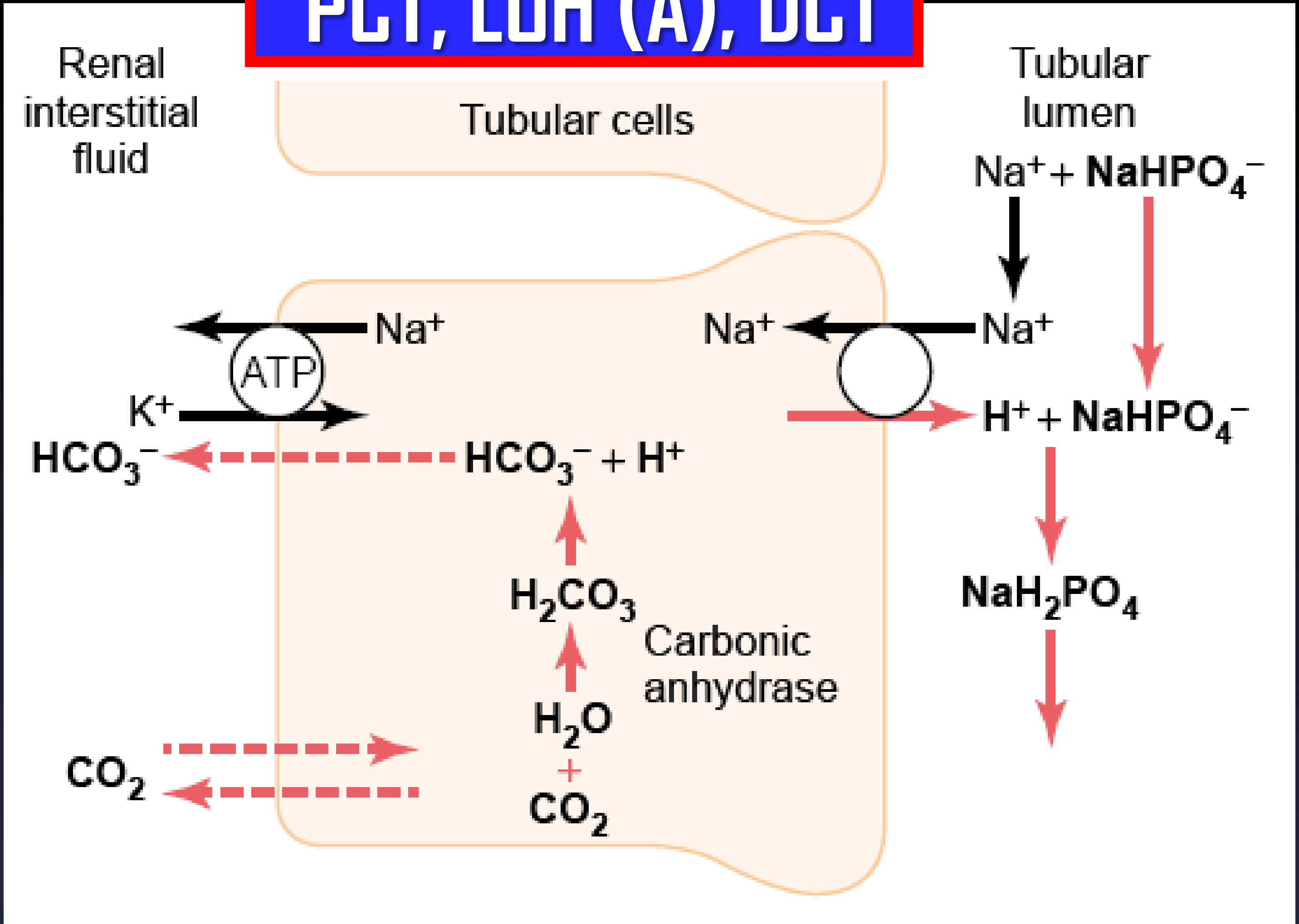


- α intercalated cell ➔ acid-secretion
- β intercalated cell ➔bicarbonate-secretion

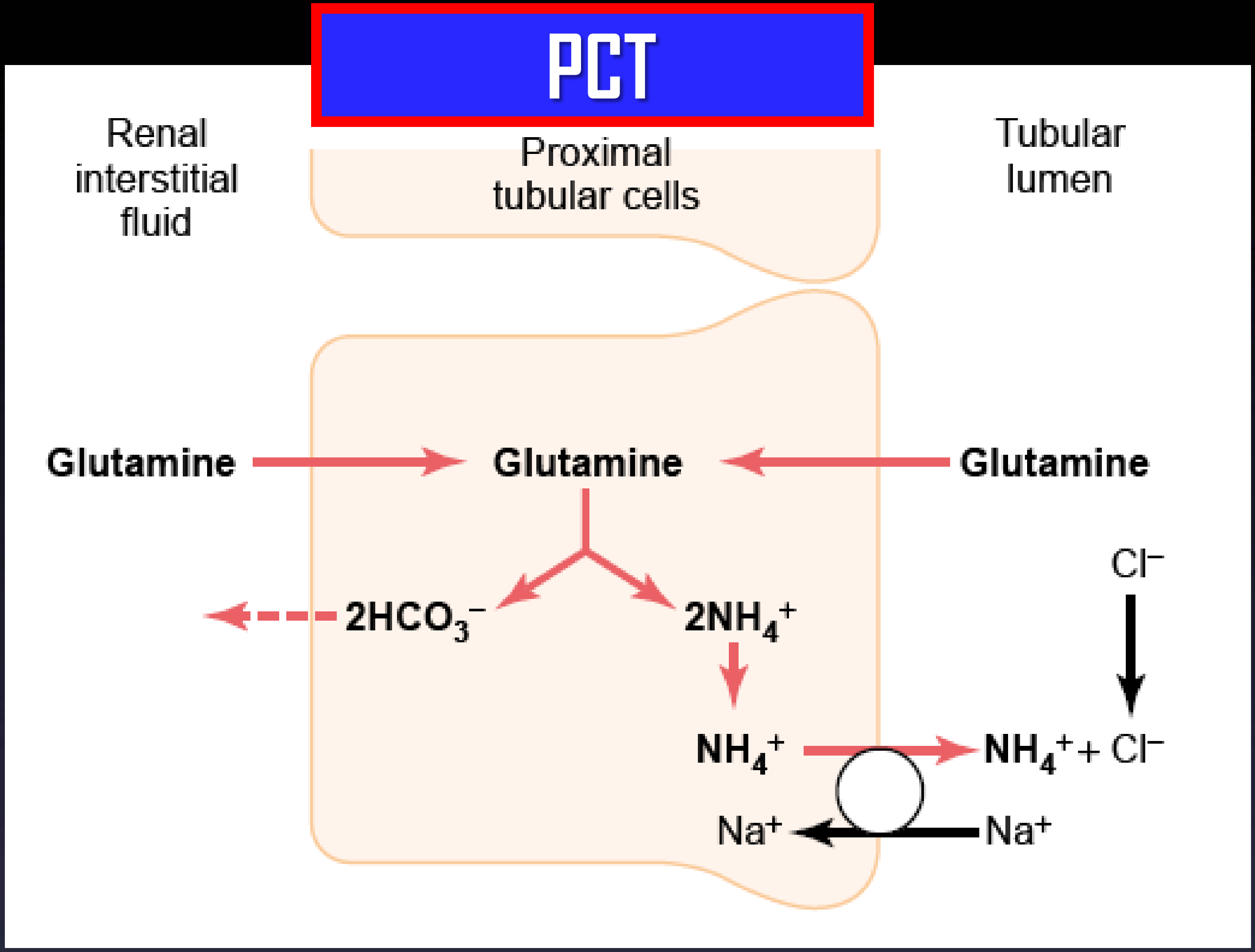
Remember that I Cells have H-ATPase and H/K-ATPase

PHOSPHATE BUFFER SYSTEM

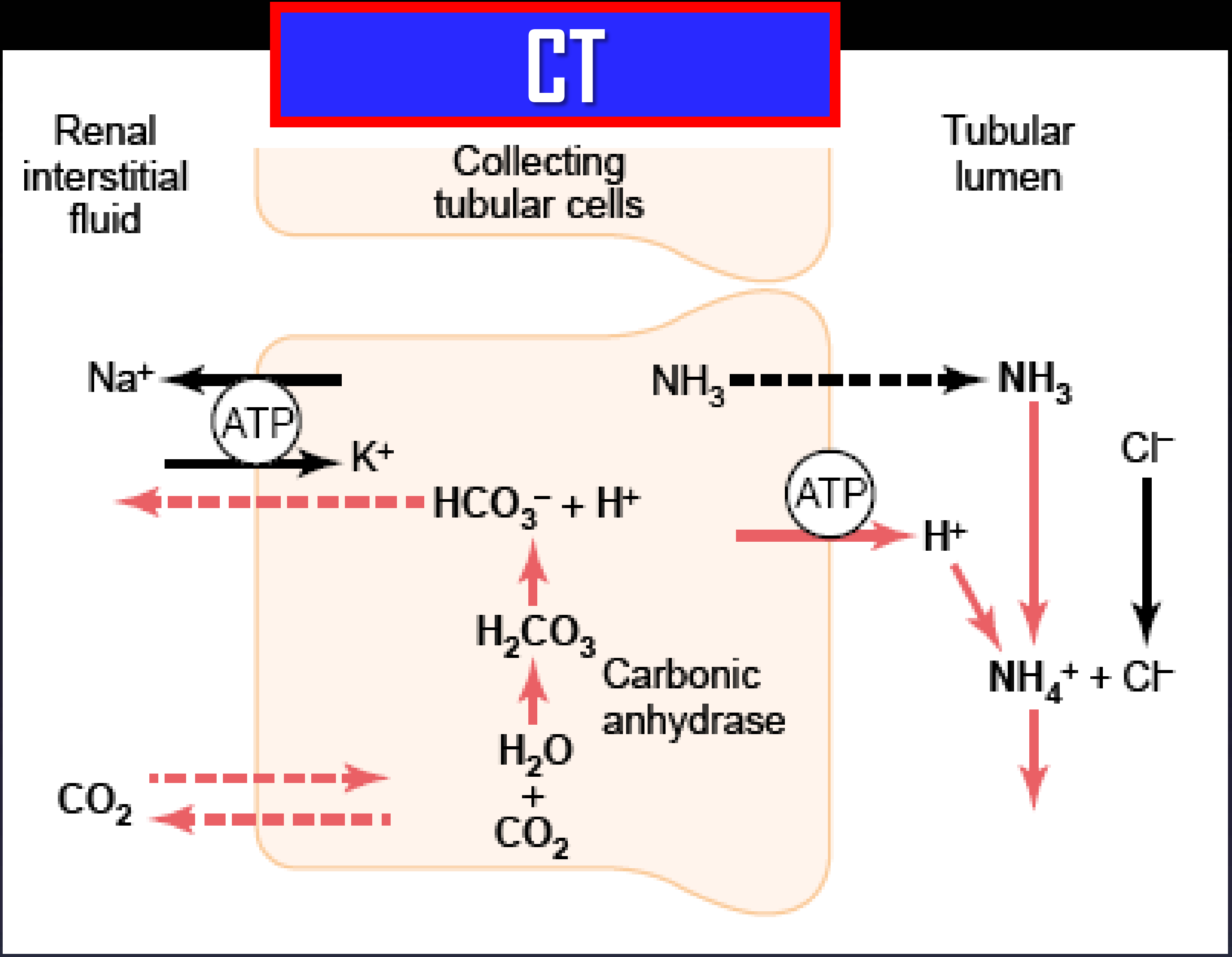
PCT, LOH (A), DCT



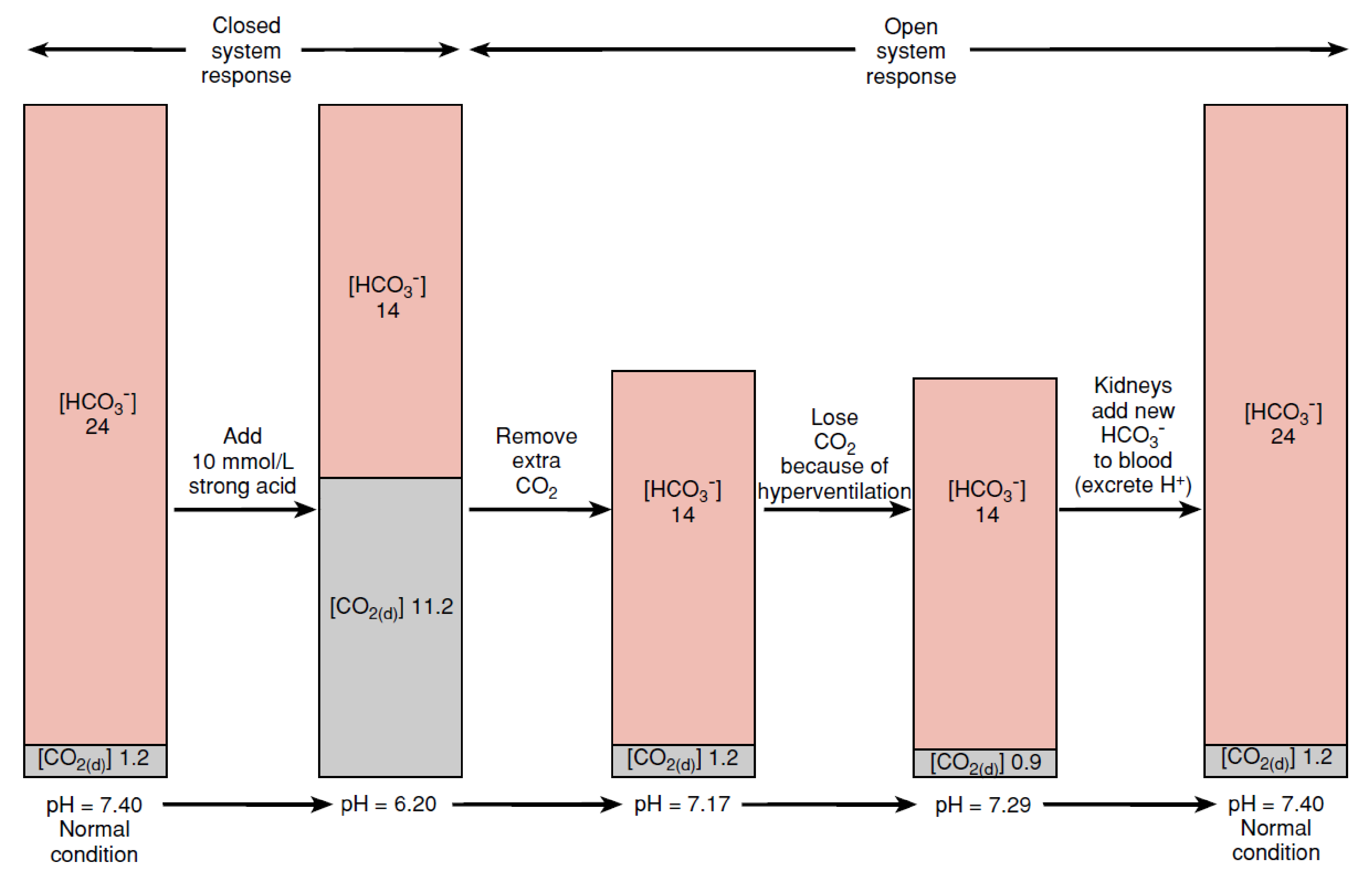
AMMONIA BUFFER SYSTEM



AMMONIA BUFFER SYSTEM



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



Lecture 3: Acid Base Disorders

OBJECTIVES

At the end of this lecture you should be able to:

- To explain the principles of blood gas and acid-base analysis
- To interpret blood gas analysis and diagnose various acid base disorders
- Describe causes of acid base disorders
- Understand use of acid base nomograms

BASE/ACID RATIO

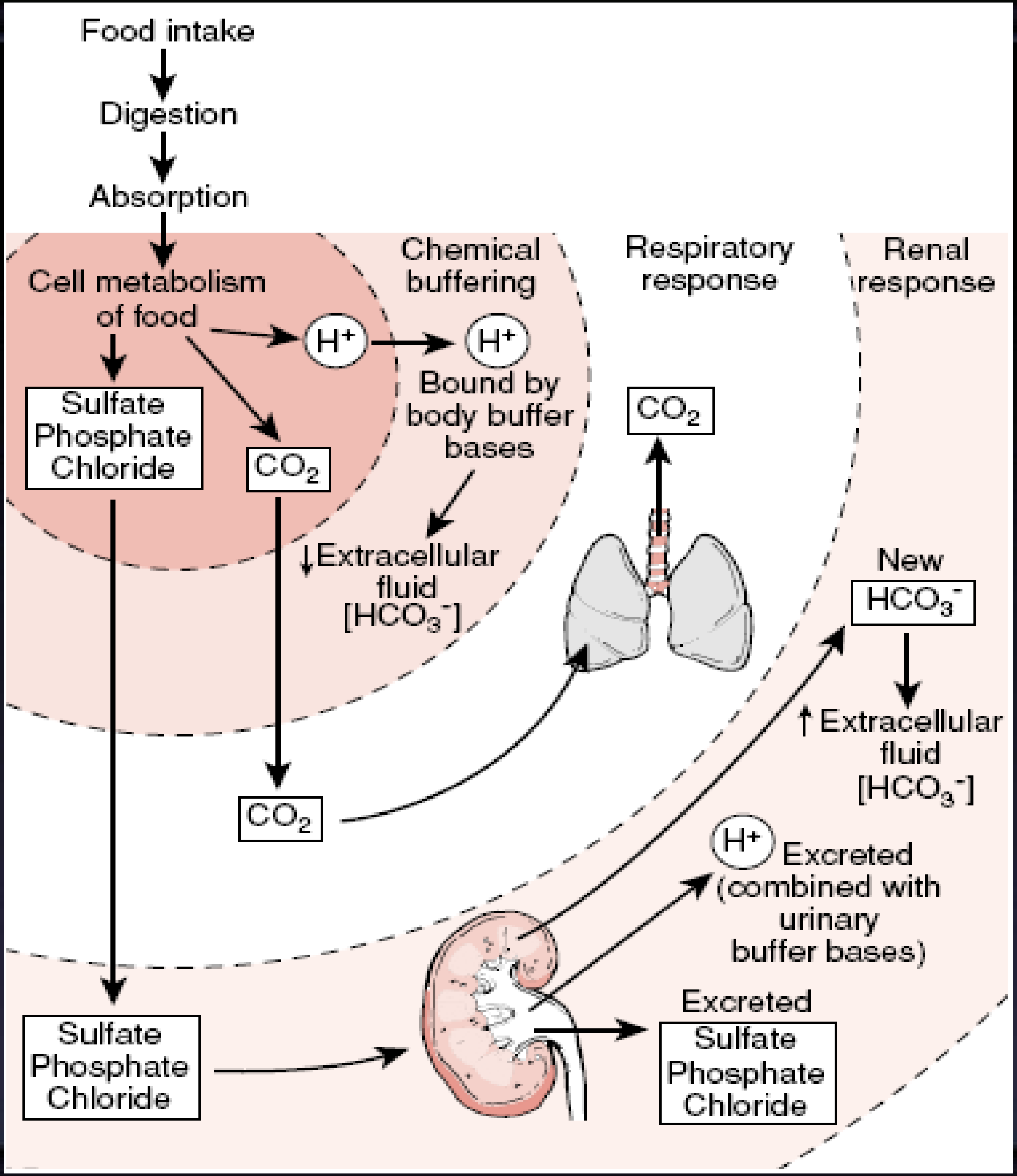
Base / Acid → NaHCO3 / H2CO3 → HCO3- / CO2

→ 20 / 1 → Kidneys / Lungs

→ Metabolic / Respiratory → Compensation by Respiratory / Compensation by Kidney

ARTERIAL BLOOD ANALYSIS

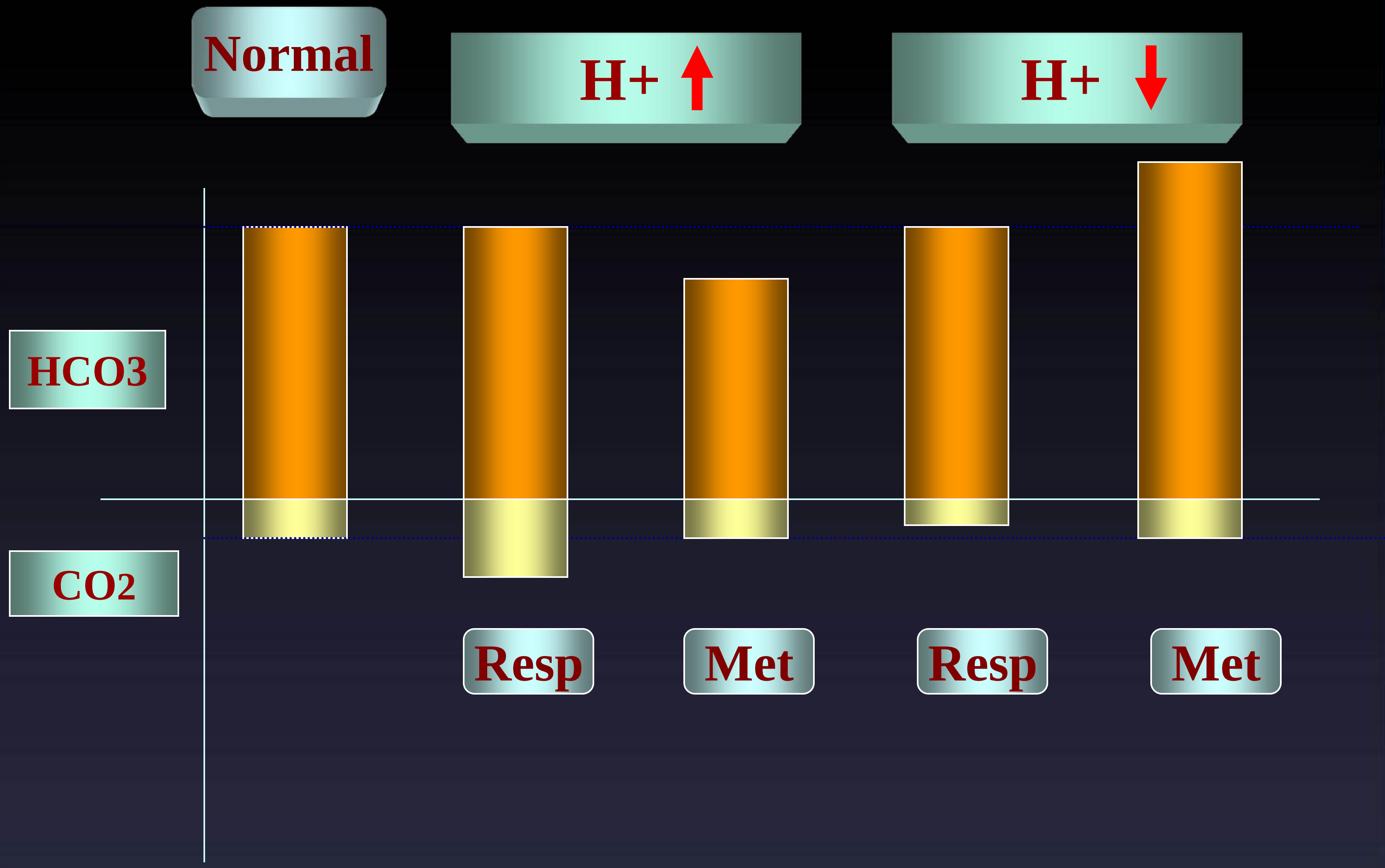
ANALYTE	REF. RANGE
pH	7.4 ± 0.05
PO_2	75-100 mmHg (10.0-13.3 kpa)
PCO_2	36.0-46.0 mmHg (4.8-6.1 kpa)
HCO_3^-	22.0-26.0 mmol/L
O_2 Saturation	95-100 %
Base Excess	± 2.5 (Normal)



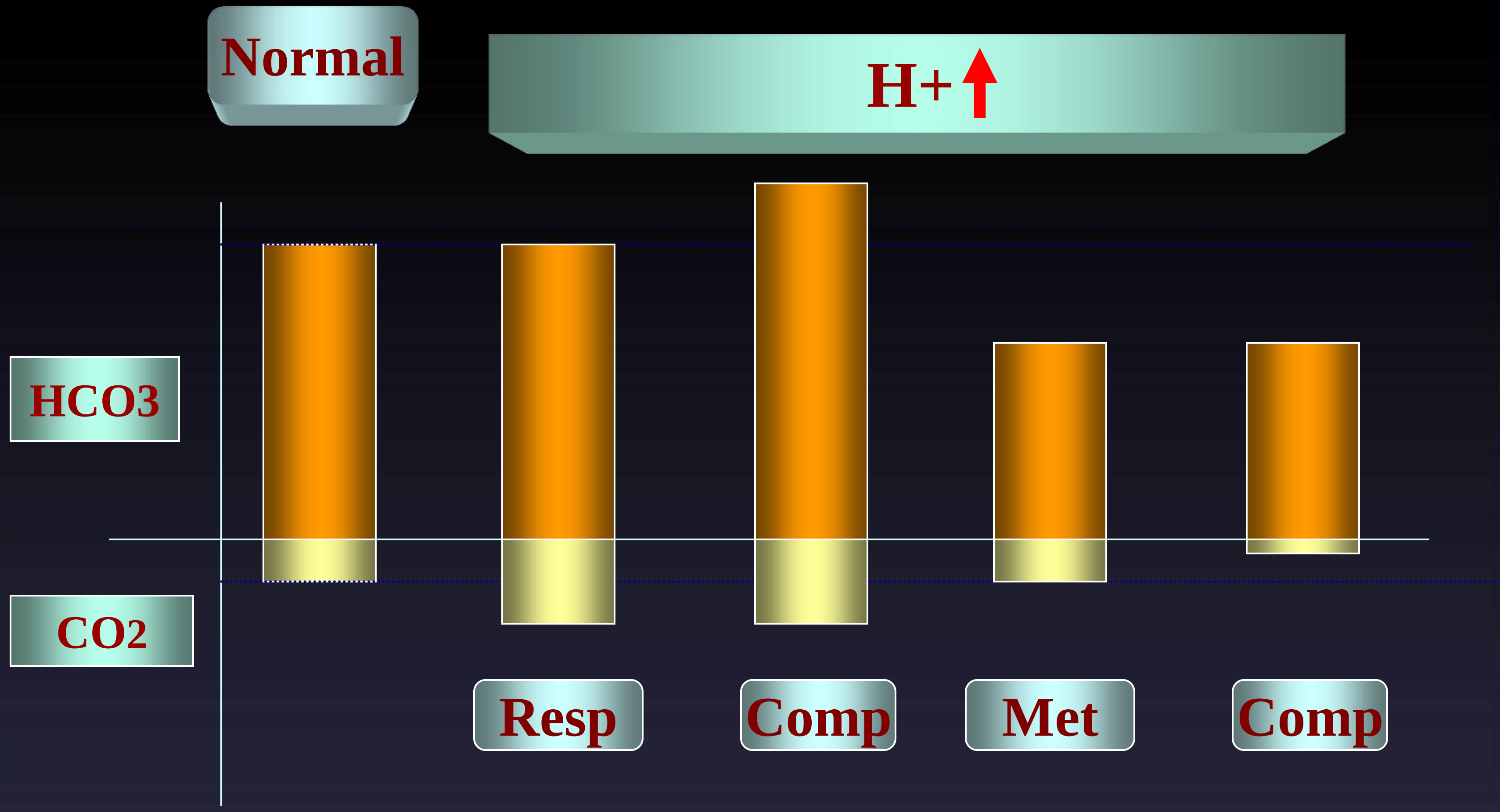
Food intake
Digestion
Absorption
Cell metabolism of food
Chemical buffering
Respiratory response
Renal response
H^+
H^+
Bound by body buffer bases
Sulfate Phosphate Chloride
CO_2
CO_2
↓Extracellular fluid $[HCO_3^-]$
New HCO_3^-
↑Extracellular fluid $[HCO_3^-]$
CO_2
H^+ Excreted (combined with urinary buffer bases)
Sulfate Phosphate Chloride
Excreted
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) • Renal tubular acidosis & CRF • Diarrhea, ileostomy (normal anion gap)
Metabolic Alkalosis	• Excessive alkali ingestion (antacids) • H+ loss (vomiting)

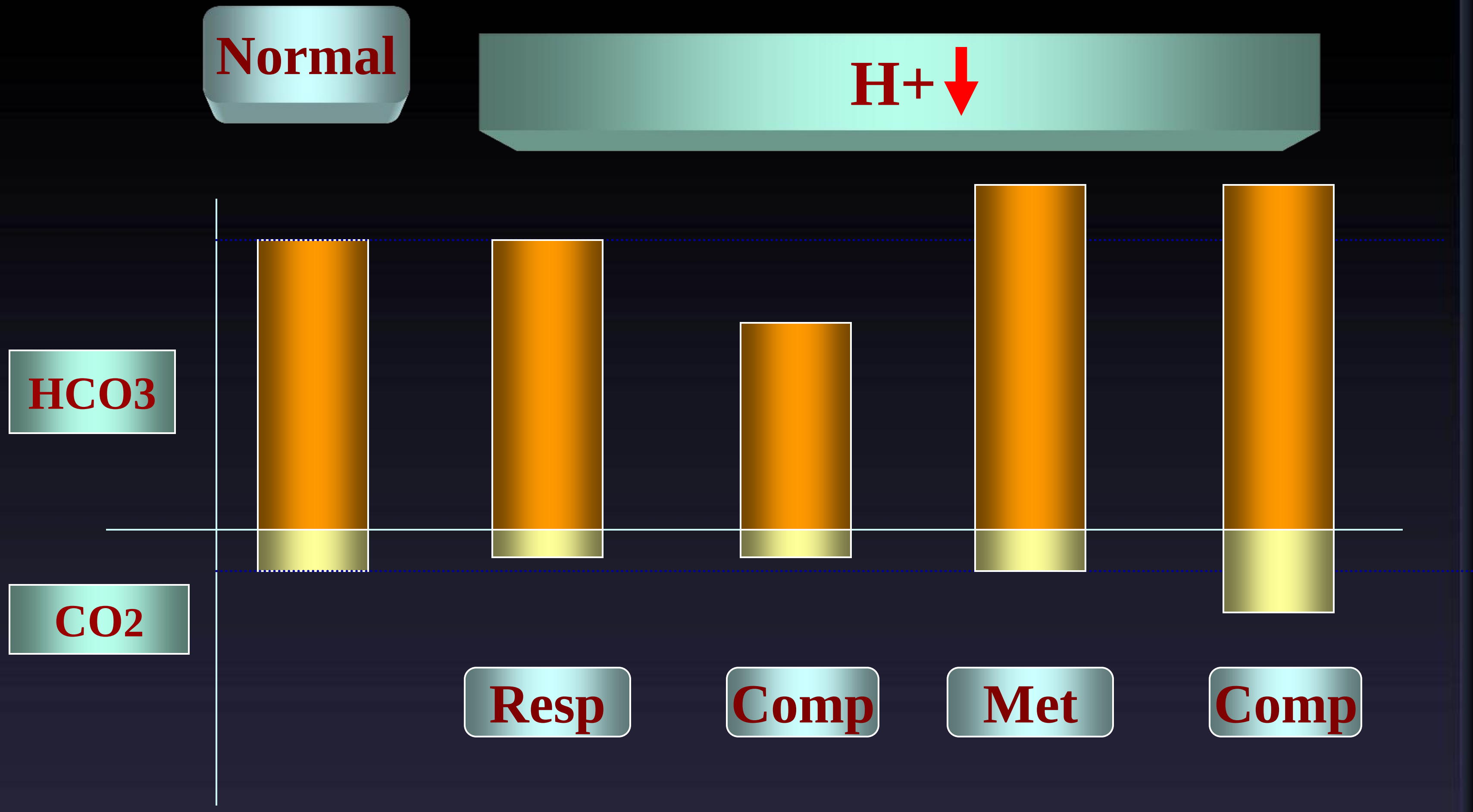
ACIDOSIS AND ALKALOSIS



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 ↓
CO_2 ↑	CO_2 ↓↓↓
HCO_3 ↑↑↑	HCO_3 ↓

ALKALOSIS

RESPIRATORY	METABOLIC
H+ ↓	H+ ↓
pH ↑	pH ↑
CO_2 ↓	CO_2 ↑↑↑
HCO_3 ↓↓↓	HCO_3 ↑

ACIDOSIS AND ALKALOSIS

	pH	H^+	P_{CO_2}	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
Respiratory acidosis	↓	↑	↑↑	↑
Respiratory alkalosis	↑	↓	↓↓	↓
Metabolic acidosis	↓	↑	↓	↓↓
Metabolic alkalosis	↑	↓	↑	↑↑

ANION GAP = Na^{+} - Cl^{-} - $HCO3^{-}$
12 + 2 mMol /L

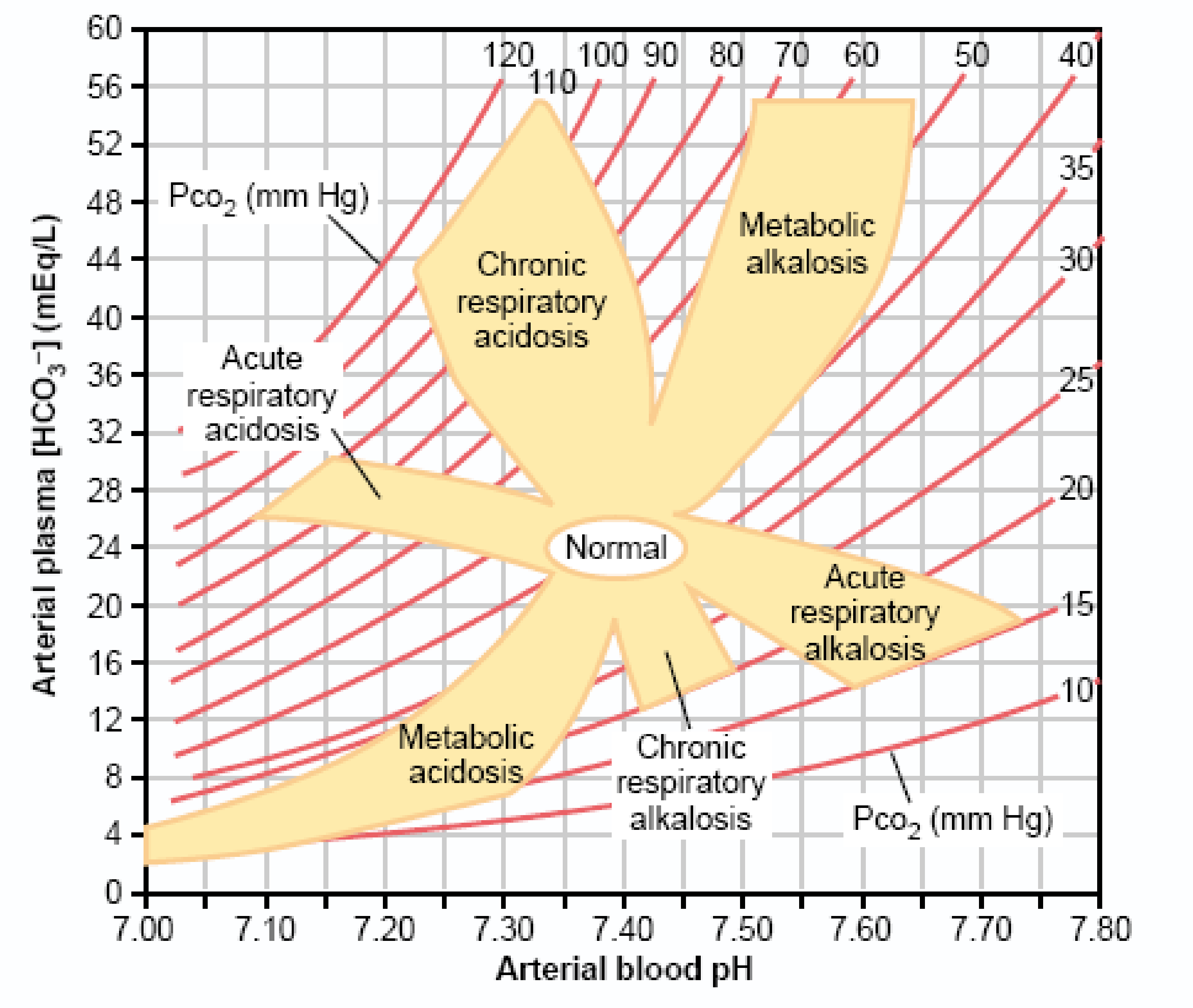
High anion gap metabolicacidosis
Methanol intoxication
Uremia
Lactic acid
Ethylene glycol intoxication
p-Aldehyde intoxication
Ketoacidosis
Salicylate intoxication
Normal anion gap metabolic acid
Diarrhea
Renal tubular acidosis
Ammonium chloride ingestion

Increased Anion Gap Acidosis:
[MUD PILES]
- **M**ethanol
- **U**remia
- **D**iabetic ketoacidosis
- **P**araldehyde
- **I**ron, isoniazid (INH)
- **L**actic acid
- **E**thanol, ethylene glycol
- **S**alicylates

Non-Anion Gap Acidosis:
[USEDCARP]
- **U**retorostomy
- **S**mall bowel fistula
- **E**xtra Chloride
- **D**iarrhea
- **C**arbonic anhydrase inhibitors (acetazolamide)
- **A**drenal insufficiency
- **R**TA
- **P**ancreatic fistula

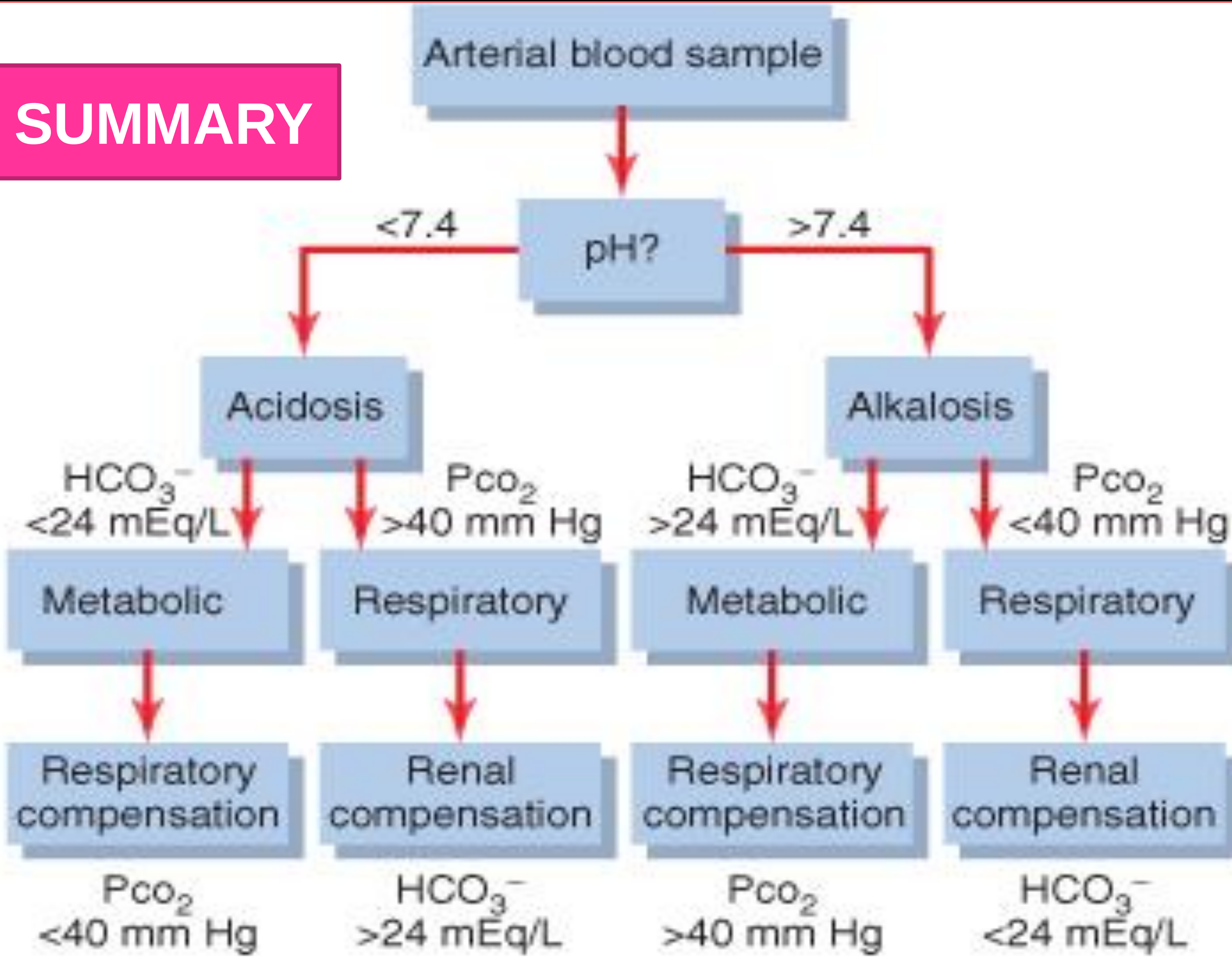
Table 31-2 Plasma or Extracellular Fluid Factors That Increase or Decrease H+ Secretion and HCO3⁻ Reabsorption by the Renal Tubules

Increase H^+ Secretion and HCO_3^- Reabsorption	Decrease H^+ Secretion and HCO_3^- Reabsorption
↑ P_{CO_2}	↓ P_{CO_2}
↑ H^+, ↓ HCO_3^-	↓ H^+, ↑ HCO_3^-
↓ Extracellular fluid volume	↑ Extracellular fluid volume
↑ Angiotensin II	↓ Angiotensin II
↑ Aldosterone	↓ Aldosterone
Hypokalemia	Hyperkalemia



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)
0
4
8
12
16
20
24
28
32
36
40
44
48
52
56
60
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
Pco_2 >40 mm Hg
HCO_3^- >24 mEq/L
Pco_2 <40 mm Hg
Metabolic
Respiratory
Metabolic
Respiratory
Respiratory compensation
Renal compensation
Respiratory compensation
Renal compensation
Pco_2 <40 mm Hg
HCO_3^- >24 mEq/L
Pco_2 >40 mm Hg
HCO_3^- <24 mEq/L