RENAL PHYSIOLOGY

ACID BASE PHYSIOLOGY

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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**

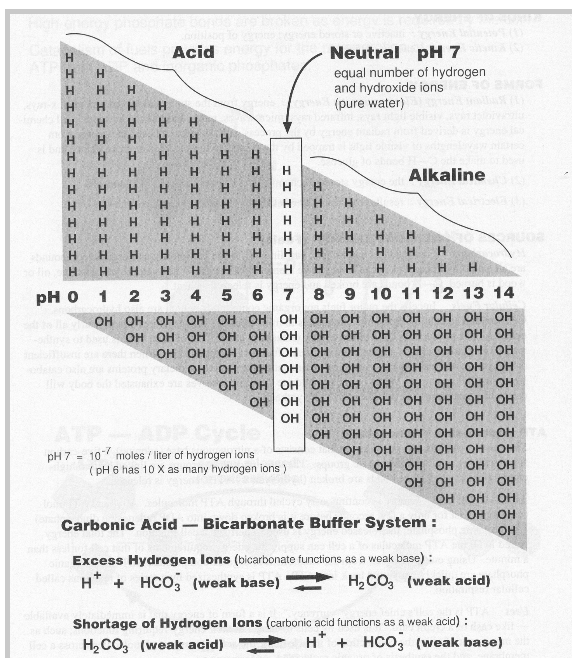
BASES

- 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)

pH SCALE



pH

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

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

OR

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

WHY ?

pH

- The normal H ion concentration in blood is 40 nmol/l or 0.00004 mmol/l
- 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

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.

WHAT IS THE NORMAL BODY pH ?

7.35 – 7.45

	Women	Men
$[H^+]$ (nmol/L)	39.8 ± 1.4	40.7 ± 1.4
pH	7.40 ± 0.015	7.39 ± 0.015
P_{CO_2} (kPa)	5.07 ± 0.3	5.47 ± 0.3
(mmHg)	38.9 ± 2.3	41.0 ± 2.3
$[HCO_3^-]$ (mmol/L)	24 ± 2.5	24 ± 2.5

pH of Body Fluids

Extracellular fluid	pH
Arterial blood	7.40
Venous blood	7.35
Interstitial fluid	7.35
Intracellular fluid	6.0 to 7.4
Urine	4.5 to 8.0
Gastric HCl	0.8

IMPORTANCE

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)**

$CO_2 + H_2O \text{ -----> } H_2CO_3 \text{ -------> } H^+ + HCO_3^-$

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**

ACID LOAD

- Amino Acid Metabolism yields about 50 meq/day
- CO_2 production yields 12,500 meq/day
- Normal daily diet yields 80 meq/day

HENDERSON-HASSELBACH EQUATION

- The ratio of dissociated to undissociated forms of an acid is CONSTANT (K) i.e. if you add more H+, it is balanced by more Weak Acid being formed

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

eg.

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

$$H2CO3 \rightleftharpoons H+ \ + \ HCO3-$$

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

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

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

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

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

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

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

pK

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

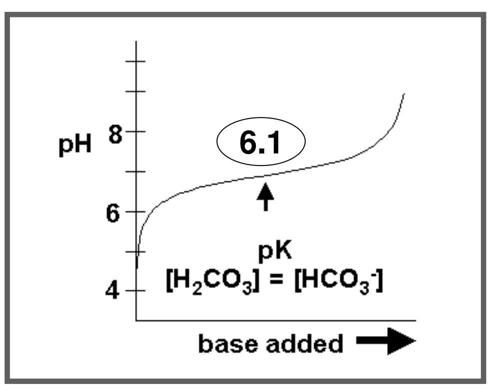
(REMEMBER to maintain plasma pH at 7.4, there needs to be much more HCO3- than H2CO3)

pK

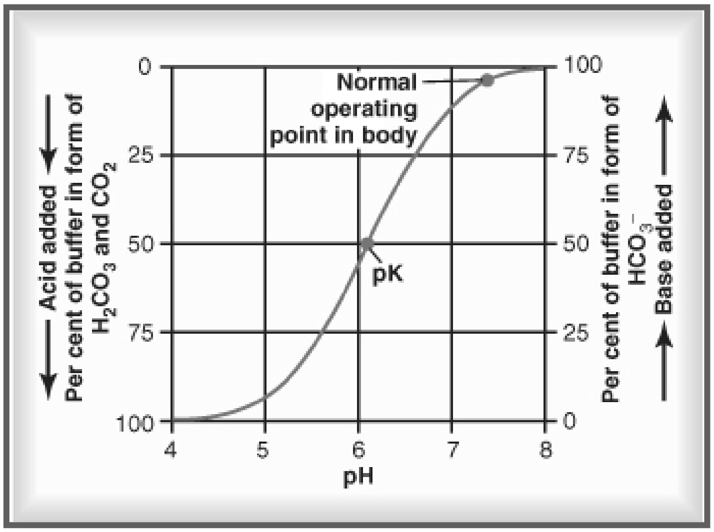
pH = pK x Base/Acid

pH = pK x 50/50

pH = pK



Bicarbonate Buffer System Titration Curve.



7.35 – 7.45

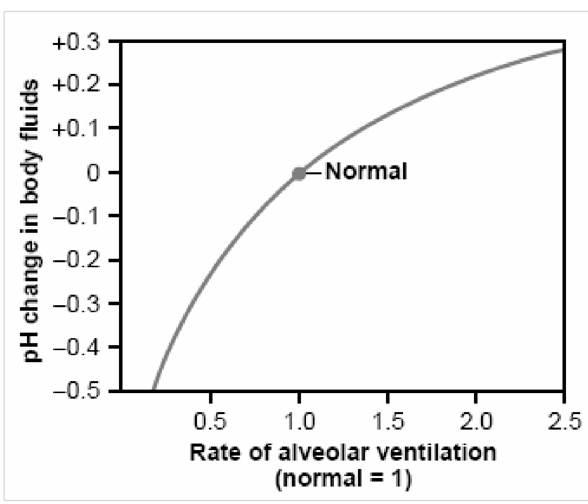
ACIDOSIS

ALKALOSIS

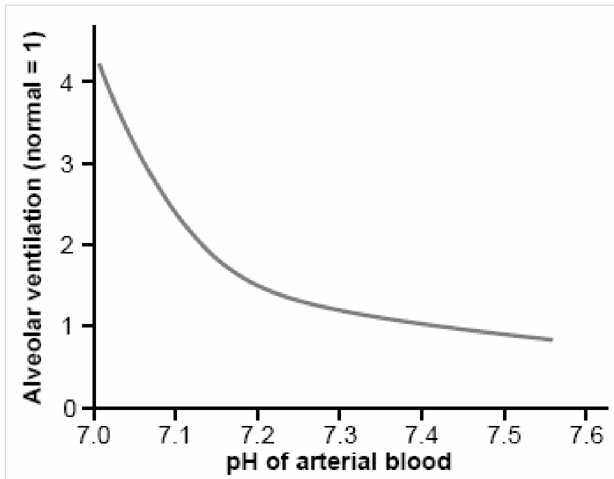
DEFENCE MECHANISMS IN THE BODY

- **Acid-Base buffer systems of the body fluids**
- **respiratory center**
- **Kidneys** **[slow to respond & most powerful]**

RESPIRATORY REGULATION OF ACID-BASE BALANCE



INCREASED HYDROGEN ION CONCENTRATION STIMULATES ALVEOLAR VENTILATION



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 SALT**
- **For example in Bicarbonate buffer system H_2CO_3 is the weak acid and $NaHCO_3$ is its salt.**

BUFFER SYSTEMS

WEAK ACID ⇌ H+ + BASE

ADD STRONG ACID

WEAK ACID ⇌ H+ + BASE

ADD STRONG BASE

WEAK ACID ⇌ H+ + BASE

BUFFER SYSTEMS

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

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

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

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

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

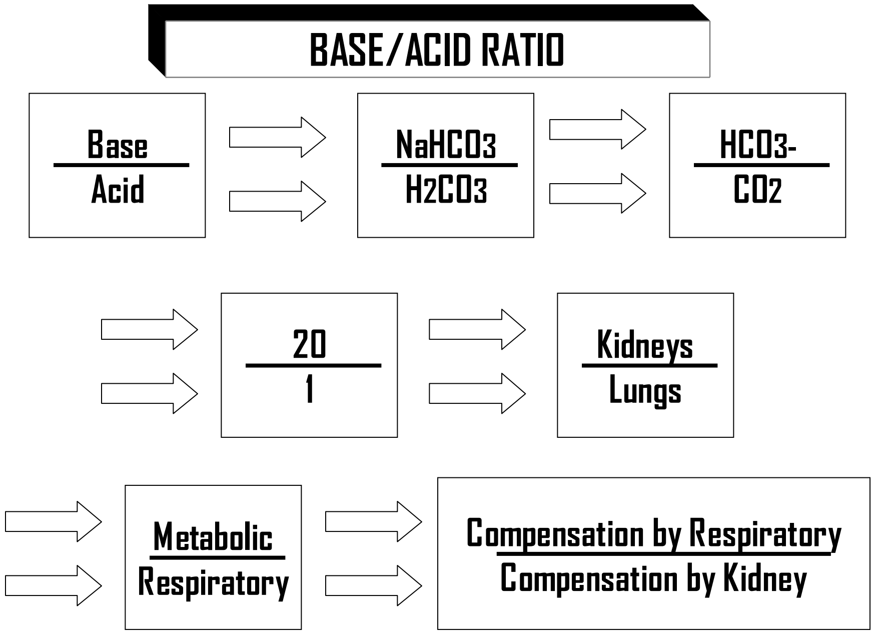
It is not only the amount of base and acid that is important but the ratio between them must remain constant

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 urine buffer
  - conc. in ECF is only 8 % of bicarbonate buffer

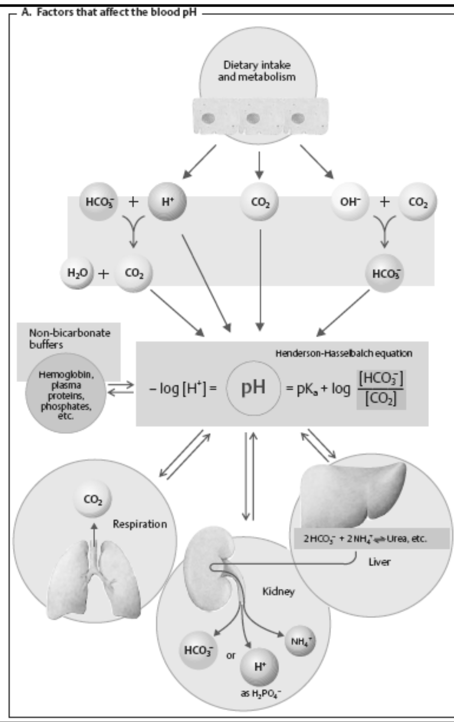
BODY BUFFER SYSTEMS

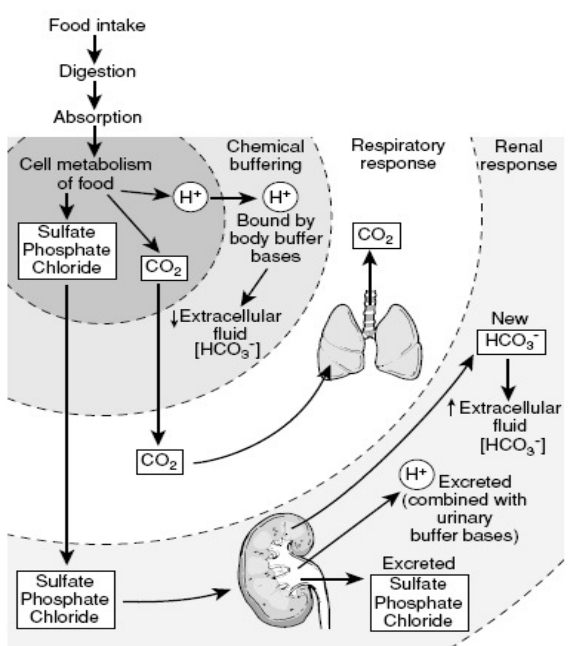
- AMMONIUM: NH_4^+ / NH_3
  - pK = 9.0
  - used to buffer the urine
- PROTEINS: Prot / H Prot
  - important in ICF
- HEMOGLOBIN: Hb / HHb
  - important in ICF



ARTERIAL BLOOD ANALYSIS

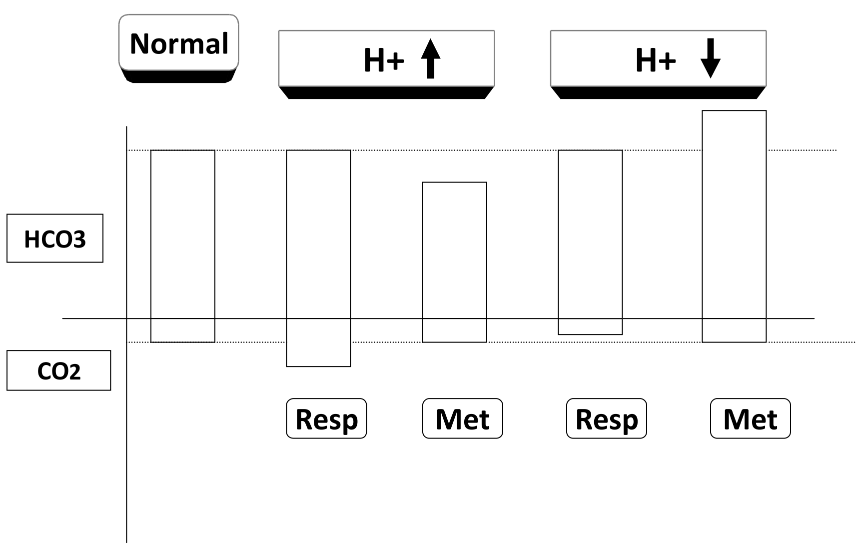
ANALYTE	REF. RANGE
pH	7.4 ± 0.05
PO_2	75-100 mmHg (10.0-13.3 kpa)
PCO_2	36.0-46.0 mmHg (4.8-6.1 kpa)
HCO_3^-	22.0-26.0 mmol/L
O_2 Saturation	95-100 %
Base Excess	± 2.5 (Normal)


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
Kidney
HCO_3^- or H^+ as $H_2PO_4^-$
NH_4^+
$2HCO_3^- + 2NH_4^+ \rightleftharpoons$ Urea, etc.
Liver

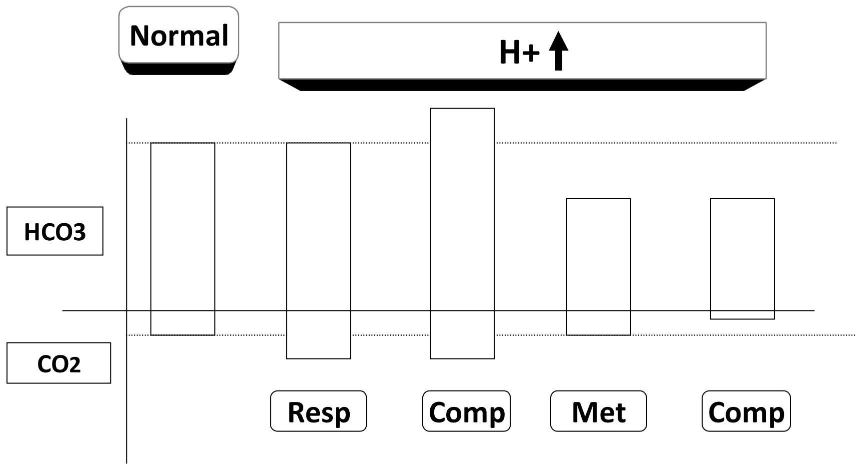

Food intake
Digestion
Absorption
Cell metabolism of food
Chemical buffering
Respiratory response
Renal response
H^+
H^+
Bound by body buffer bases
Sulfate Phosphate Chloride
CO_2
CO_2
↓Extracellular fluid $[HCO_3^-]$
New HCO_3^-
↑Extracellular fluid $[HCO_3^-]$
CO_2
H^+ Excreted (combined with urinary buffer bases)
Sulfate Phosphate Chloride
Excreted Sulfate Phosphate Chloride

DISORDER	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)

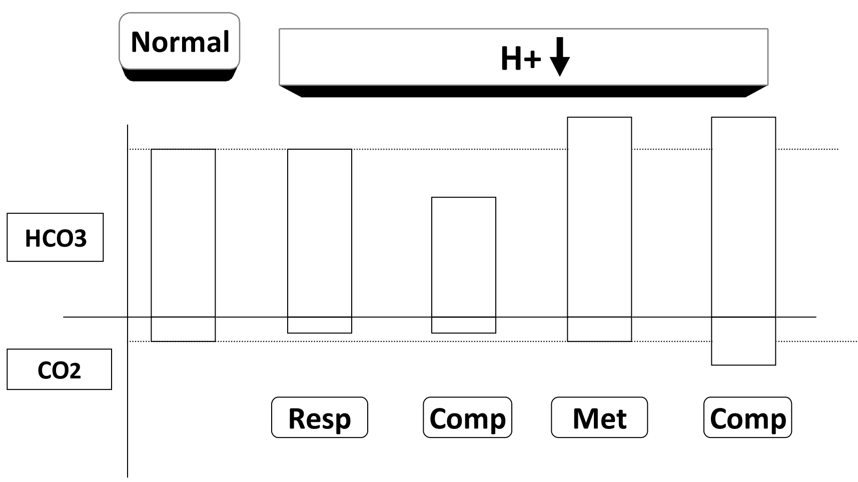
ACIDOSIS AND ALKALOSIS



COMPENSATION OF ACIDOSIS



COMPENSATION OF ALKALOSIS



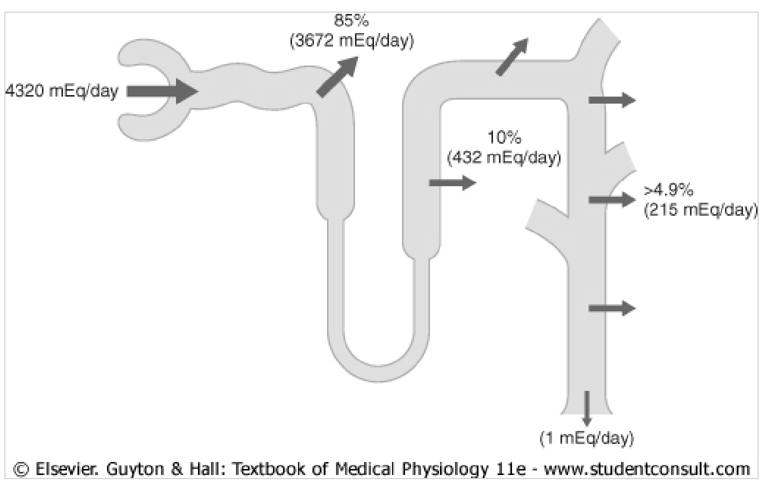
UNCOMPENSATED

ACIDOSIS	
RESPIRATORY	METABOLIC
H+ ↑ pH ↓ CO_2 ↑ HCO_3 *N*	H+ ↑ pH ↓ CO_2 *N* HCO_3 ↓
ALKALOSIS	
RESPIRATORY	METABOLIC
H+ ↓ pH ↑ CO_2 ↓ HCO_3 *N*	H+ ↓ pH ↑ CO_2 *N* HCO_3 ↑

COMPENSATED

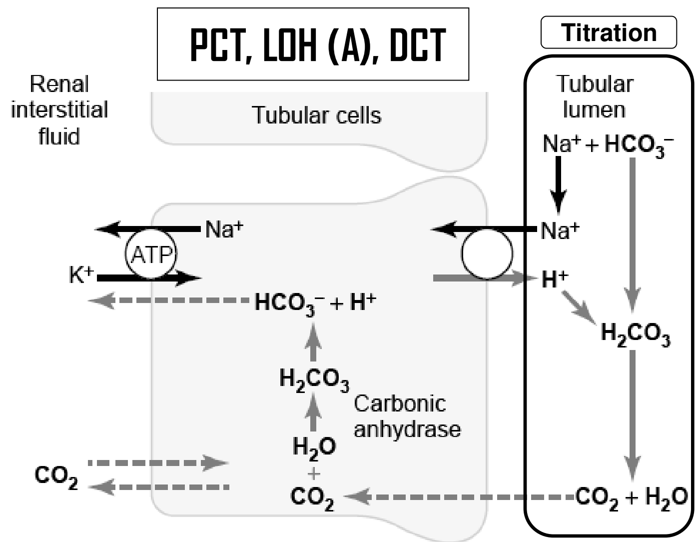
ACIDOSIS	
RESPIRATORY	METABOLIC
H+ ↑ pH ↓ CO_2 ↑ HCO_3 ↑↑↑	H+ ↑ pH ↓ CO_2 ↓↓↓ HCO_3 ↓
ALKALOSIS	
RESPIRATORY	METABOLIC
H+ ↓ pH ↑ CO_2 ↓ HCO_3 ↓↓↓	H+ ↓ pH ↑ CO_2 ↑↑↑ HCO_3 ↑

RENAL CONTROL

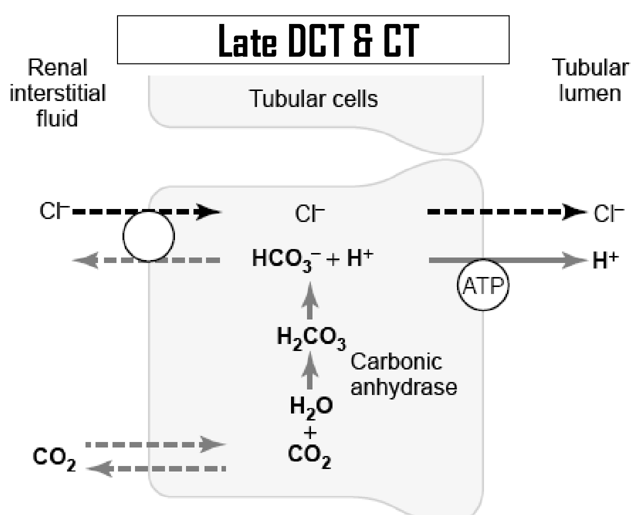


About 80 to 90 per cent of the bicarbonate reabsorption (and H+ secretion) occurs in the proximal tubule

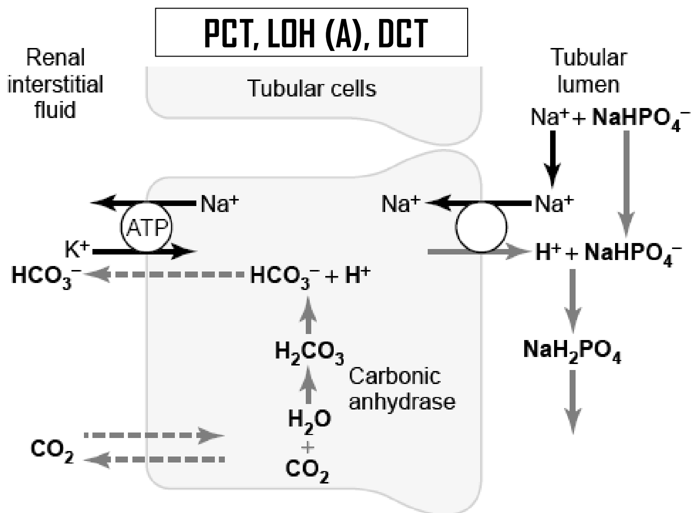
HYDROGEN ION SECRETION



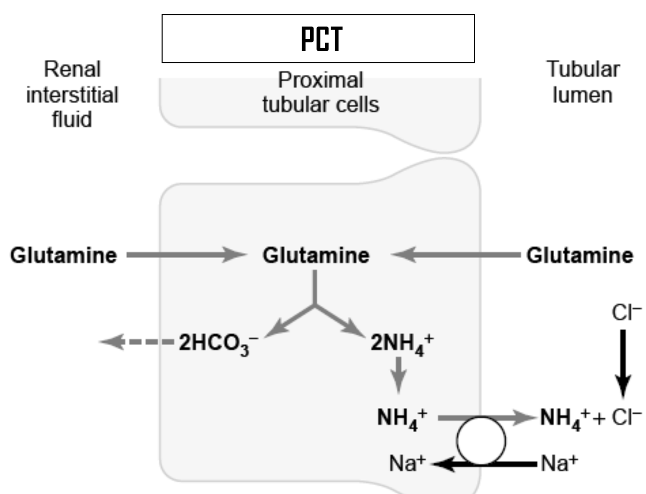
HYDROGEN ION SECRETION



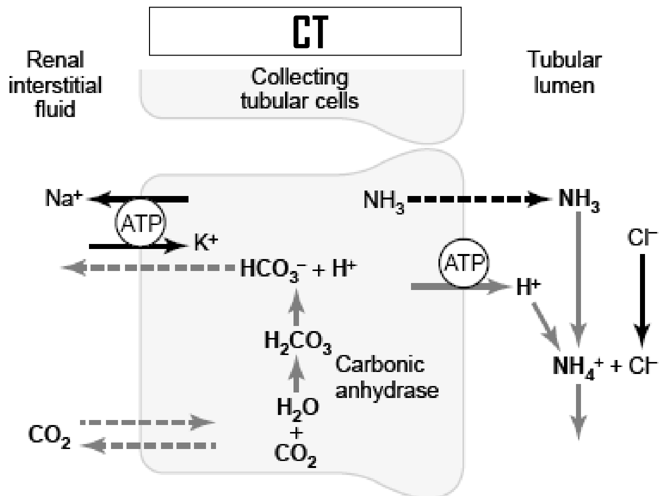
PHOSPHATE BUFFER SYSTEM



AMMONIA BUFFER SYSTEM



AMMONIA BUFFER SYSTEM



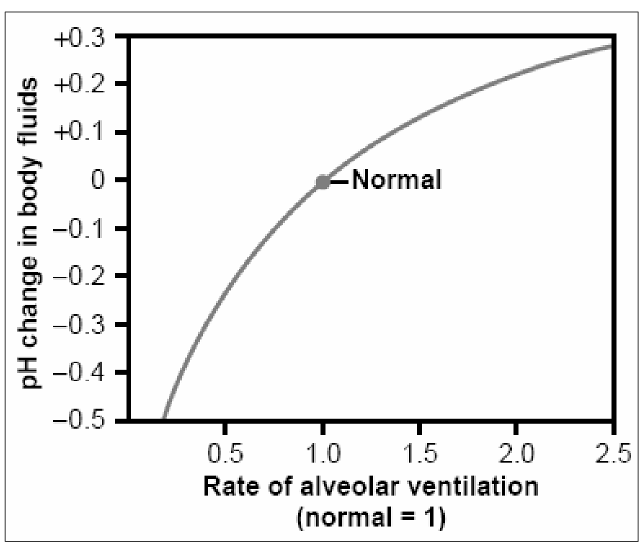
ACIDOSIS AND ALKALOSIS

	pH	H+	PCO2	HCO3-
Normal	7.4	40 nEq/L	40 mmHg	24 meq/L
Respiratory Acidosis	↓	↑	↑	↑
Respiratory Alkalosis	↑	↓	↓	↓
Metabolic Acidosis	↓	↑	↓	↓
Metabolic Alkalosis	↑	↓	↑	↑

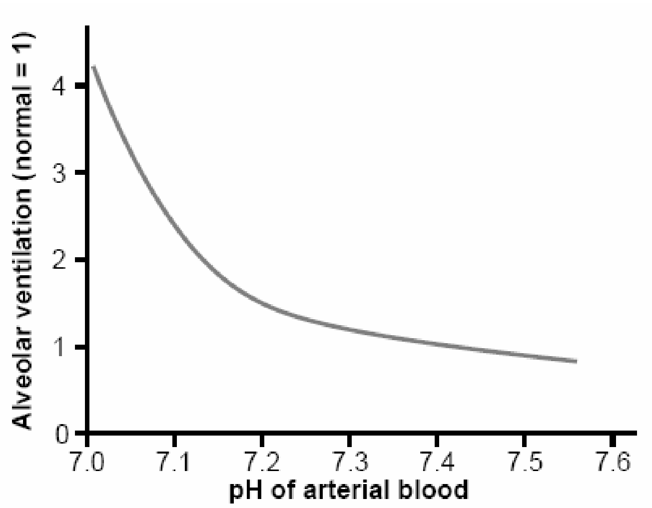
ANION GAP = {[Na+] + [K]} – {[HCO3-] + [Cl-]} 10-18 mmol/L

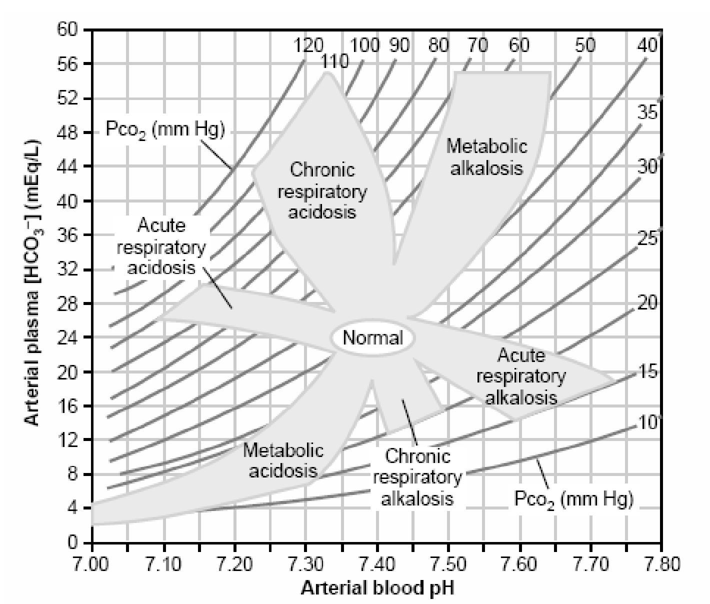
High anion gap metabolicacidosis
Methanol intoxication
Uremia
Lactic acid
Ethylene glycol intoxication
p-Aldehyde intoxication
Ketoacidosis
Salicylate intoxication
Normal anion gap metabolic acidosis
Diarrhea
Renal tubular acidosis
Ammonium chloride ingestion

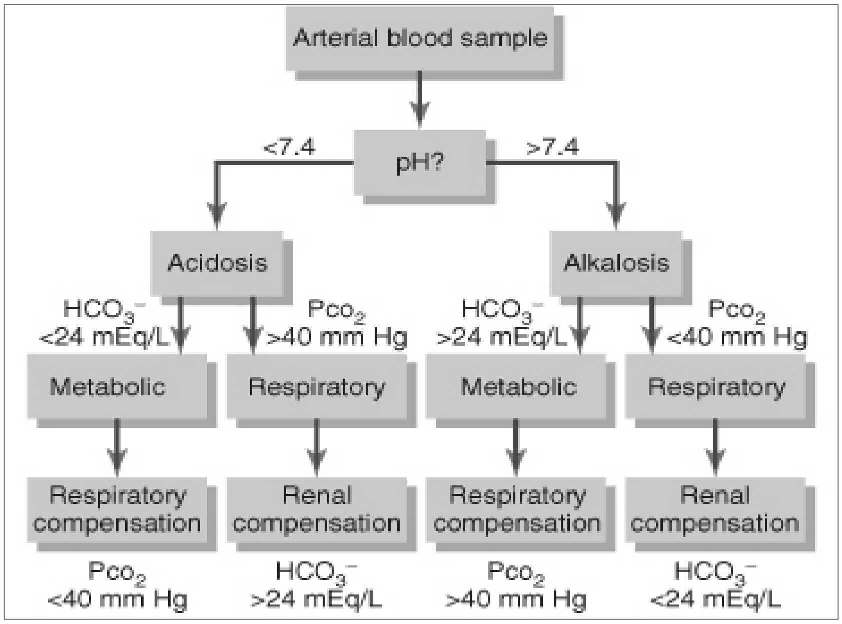
Respiratory Regulation of Acid-Base Balance



Effect of blood pH on the rate of alveolar ventilation.






Arterial blood sample
pH?
<7.4
>7.4
Acidosis
Alkalosis
HCO3−
<24 mEq/L
Pco2
>40 mm Hg
HCO3−
>24 mEq/L
Pco2
<40 mm Hg
Metabolic
Respiratory
Metabolic
Respiratory
Respiratory compensation
Renal compensation
Respiratory compensation
Renal compensation
Pco2
<40 mm Hg
HCO3−
>24 mEq/L
Pco2
>40 mm Hg
HCO3−
<24 mEq/L