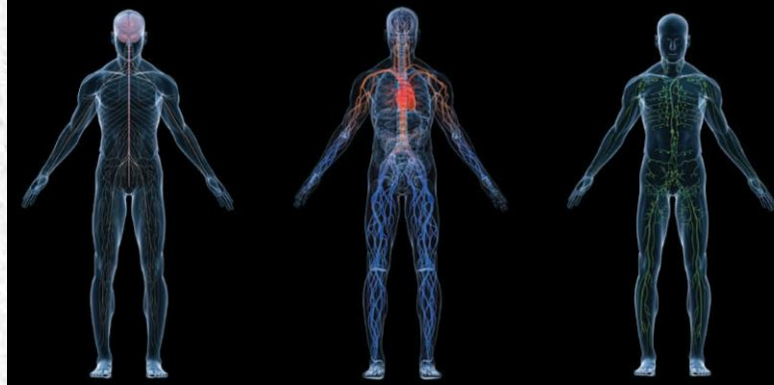


GUYTON AND HALL *Textbook of*
Medical Physiology

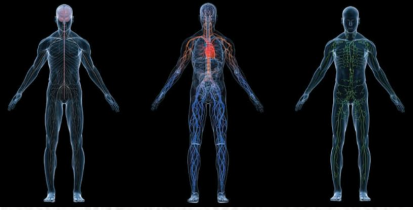
TWELFTH EDITION



Chapter 30:

Acid-Base Regulation in the Kidney

Chapter 30



Mechanisms of Hydrogen Ion Regulation

$[H^+]$ is precisely regulated at $3-5 \times 10^{-8}$ moles/L
(pH range 7.2 -7.4)

1. Body fluid chemical buffers (rapid but temporary)

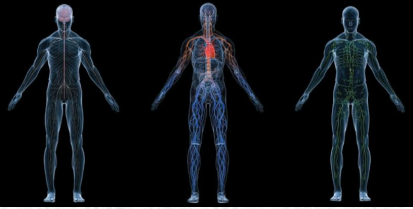
- bicarbonate - ammonia
- proteins - phosphate

2. Lungs (rapid, eliminates CO_2)

$\uparrow [H^+] \longrightarrow \uparrow \text{ventilation} \longrightarrow \uparrow CO_2 \text{ loss}$

3. Kidneys (slow, powerful); eliminates non-volatile acids

- secretes H^+
- reabsorbs HCO_3^-
- generates new HCO_3^-



Buffer Systems in the Body

Bicarbonate : most important ECF buffer



Phosphate : important renal tubular buffer



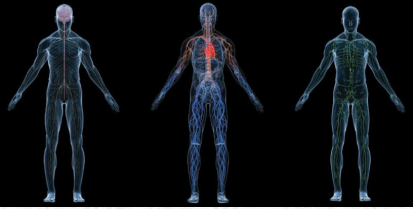
Ammonia : important renal tubular buffer



Proteins : important intracellular buffers



(60-70% of buffering is in the cells)



Importance of Buffer Systems

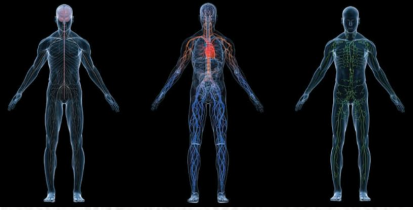
Normal H^+ concentration = 0.00004 mmol/L

Amount of non-volatile acid produced
~ 60-80 mmol/day

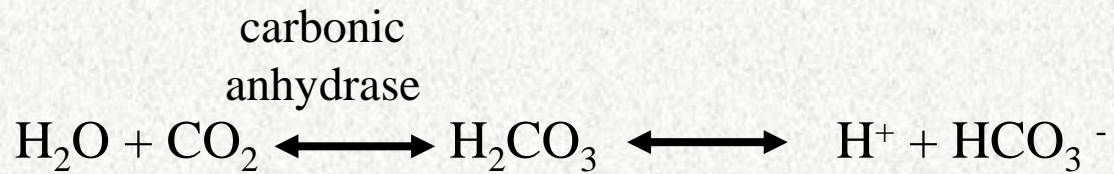
80 mmol /42 L = 1.9 mmol/L

= 47,500 times > normal H^+ concentration

PH ----6.8-8 lives for hours



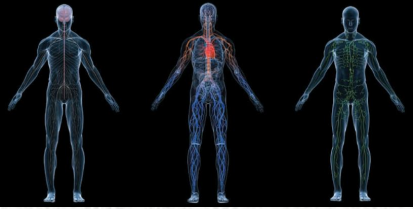
Bicarbonate Buffer System



$$\text{pH} = \text{pK} + \log \frac{\text{HCO}_3^-}{\alpha \text{ pCO}_2} \quad \begin{array}{l} \alpha = 0.03 \\ \text{pK} = 6.1 \end{array}$$

Effectiveness of buffer system depends on:

- concentration of reactants
- pK of system and pH of body fluids



Titration curve for bicarbonate buffer system.

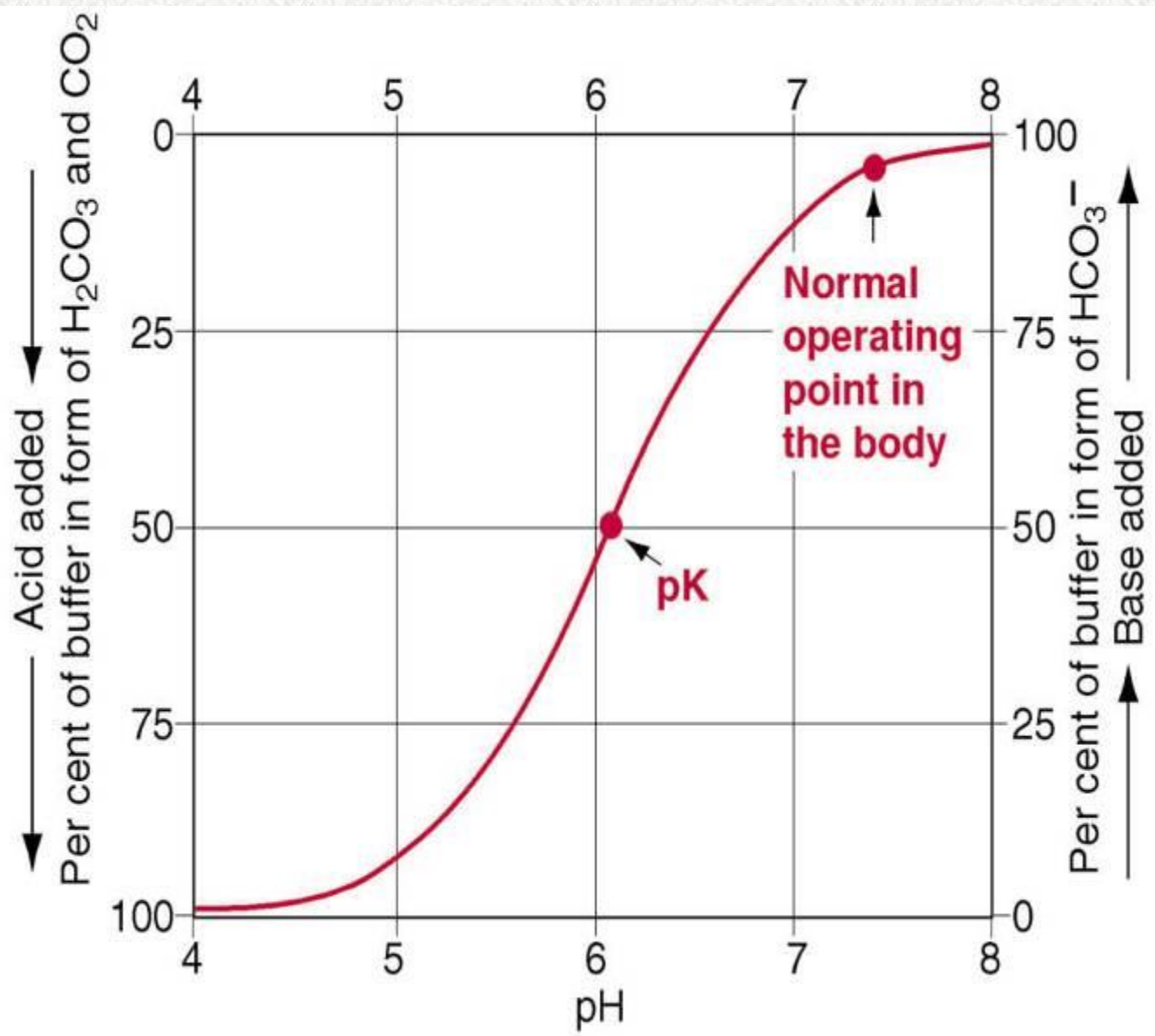
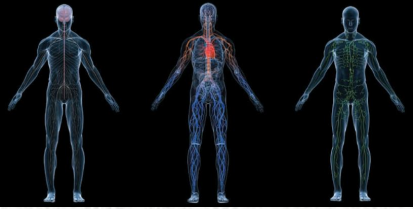


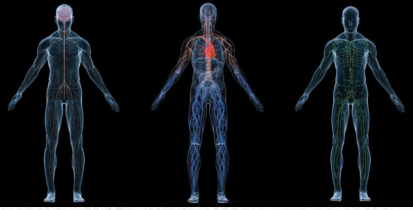
Figure 30-1.



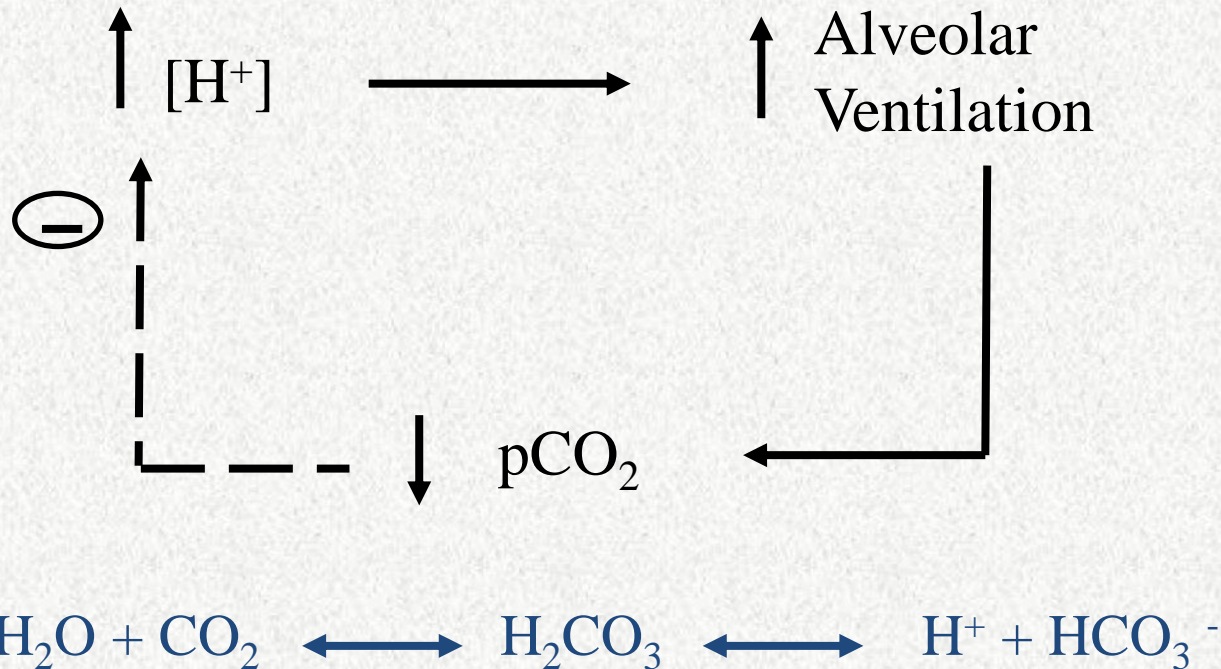
Bicarbonate Buffer System

Is the most important buffer in extracellular fluid even though the concentration of the components are low and pK of the system is 6.1, which is not very close to normal extracellular fluid pH (7.4).

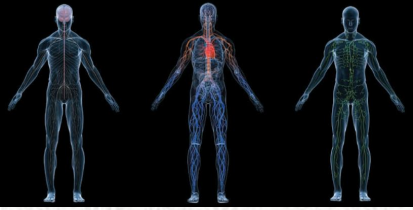
Reason: the components of the system (CO_2 and HCO_3^-) are closely regulated by the lungs and the kidneys



Respiratory Regulation of Acid-Base Balance



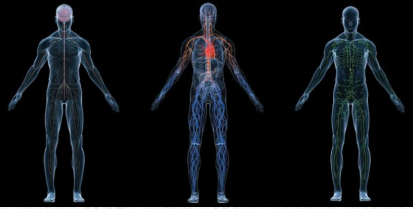
Feedback Gain = 1.0 to 3.0
(corrects 50 to 75 %)



Renal Regulation of Acid-Base Balance

- Kidneys eliminate non-volatile acids (H_2SO_4 , H_3PO_4) (~ 80 mmol/day)
- Filtration of HCO_3^- (~ 4320 mmol/day)
- Secretion of H^+ (~ 4400 mmol/day)
- Reabsorption of HCO_3^- (~ 4319 mmol/day)
- Production of new HCO_3^- (~ 80 mmol/day)
- Excretion of HCO_3^- (1 mmol/day)

Kidneys conserve HCO_3^- and excrete acidic or basic urine depending on body needs



Reabsorption of bicarbonate (and H^+ secretion) in different segments of renal tubule.

Key point:
For each HCO_3^- reabsorbed, there must be a H^+ secreted

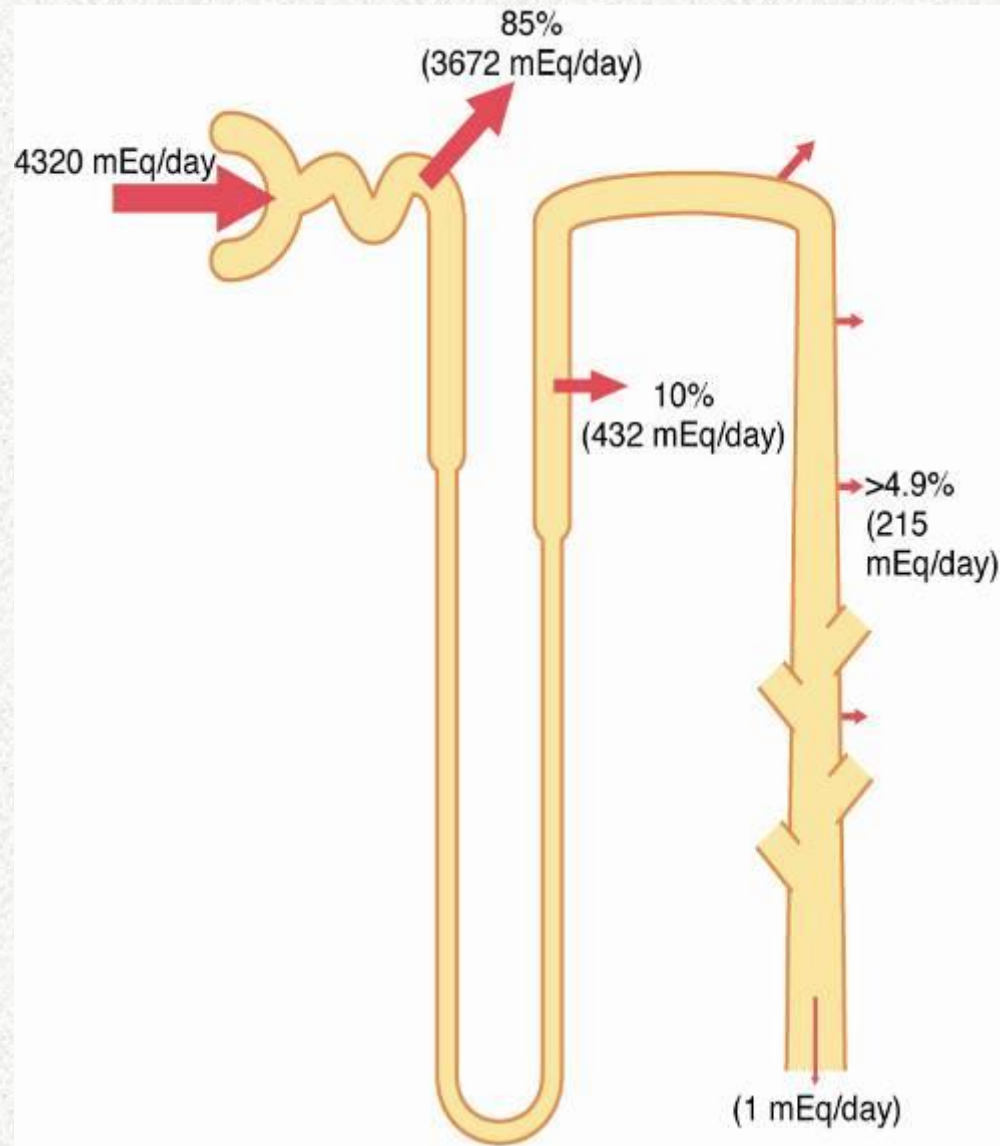
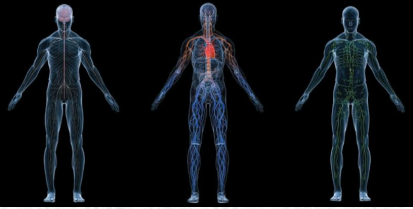


Figure 30-4.



Mechanisms for HCO_3^- reabsorption and $\text{Na}^+ - \text{H}^+$ exchange in proximal tubule and thick loop of Henle

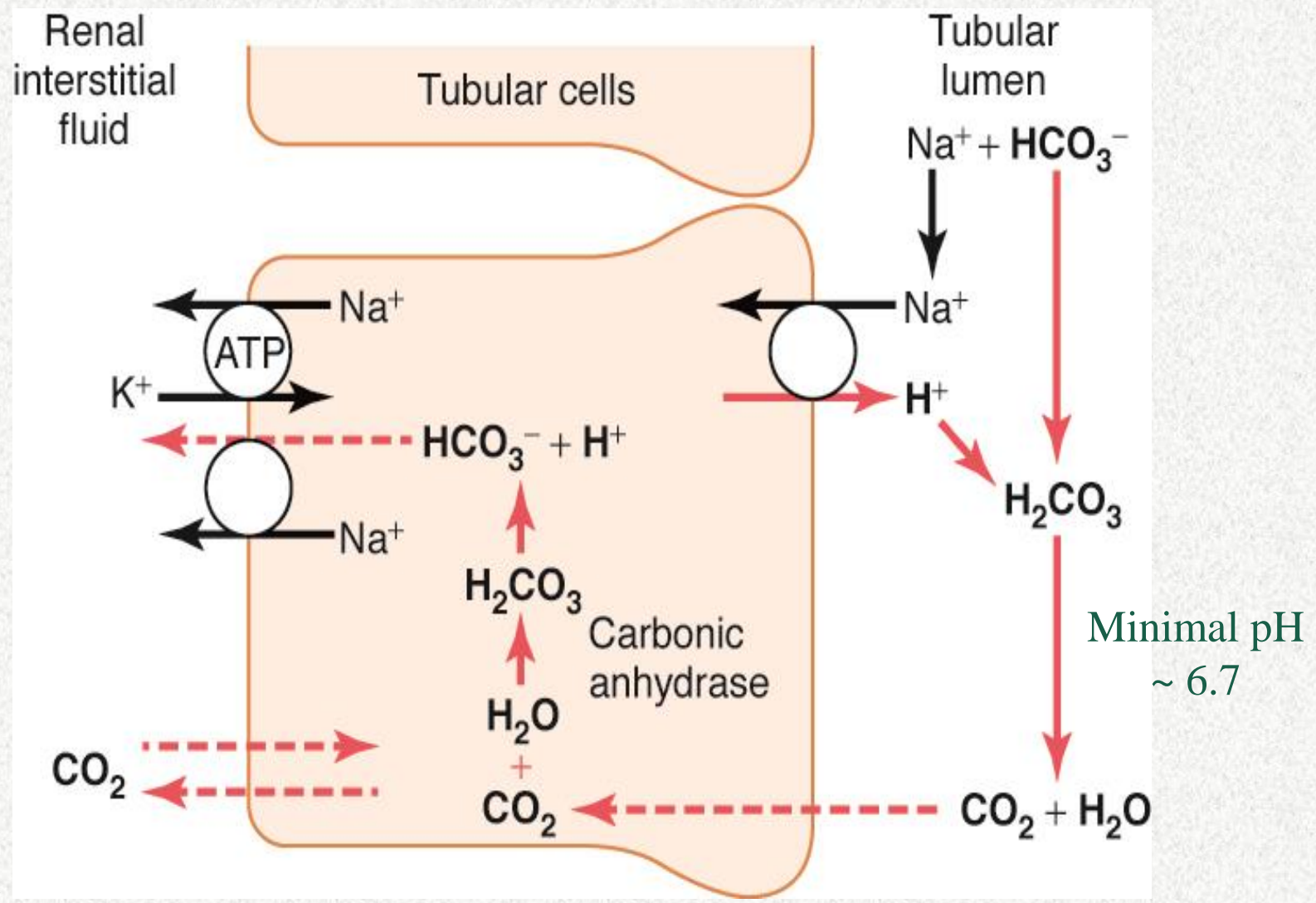
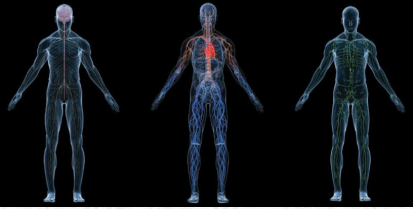
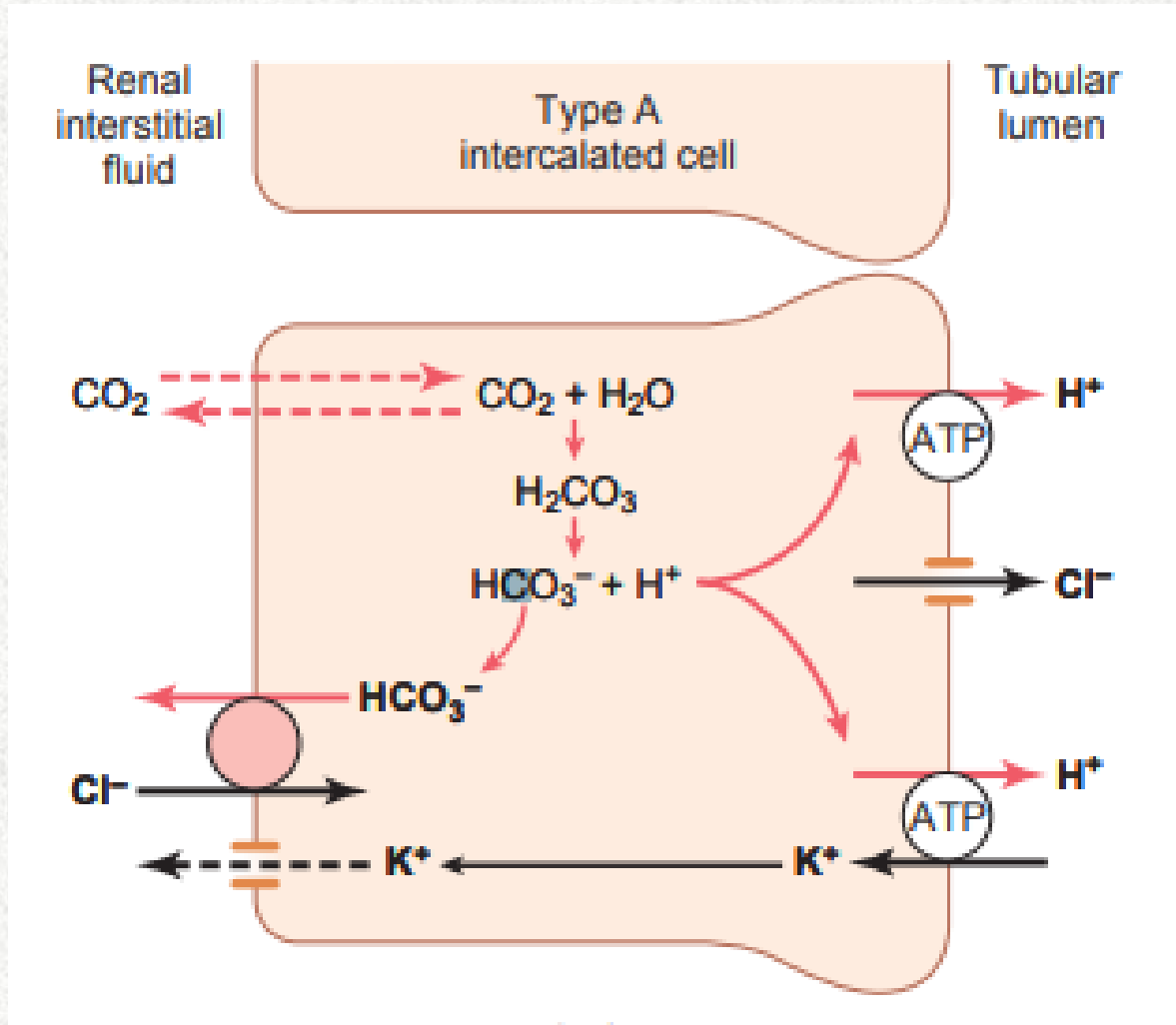


Figure 30-5.

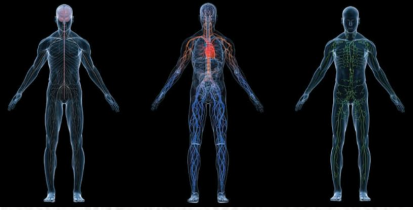


HCO_3^- reabsorption and H^+ secretion in intercalated cells of late distal and collecting tubules



Minimal
pH ~4.5

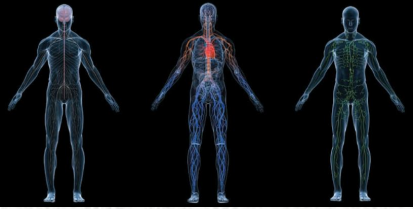
Figure 30-6.



Renal Regulation of Acid-Base Balance

- Kidneys eliminate non-volatile acids (H_2SO_4 , H_3PO_4) (~ 80 mmol/day)
- Filtration of HCO_3^- (~ 4320 mmol/day)
- Secretion of H^+ (~ 4400 mmol/day)
- Reabsorption of HCO_3^- (~ 4319 mmol/day)
- Production of new HCO_3^- (~ 80 mmol/day)
- Excretion of HCO_3^- (1 mmol/day)

Kidneys conserve HCO_3^- and excrete acidic or basic urine depending on body needs

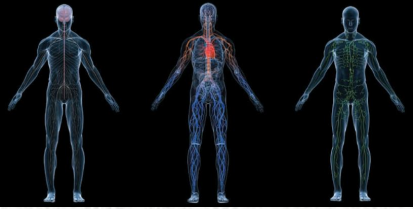


Regulation of H⁺ secretion



$$\text{pH} = \text{pK} + \log \frac{\text{HCO}_3^-}{\alpha \text{ pCO}_2}$$

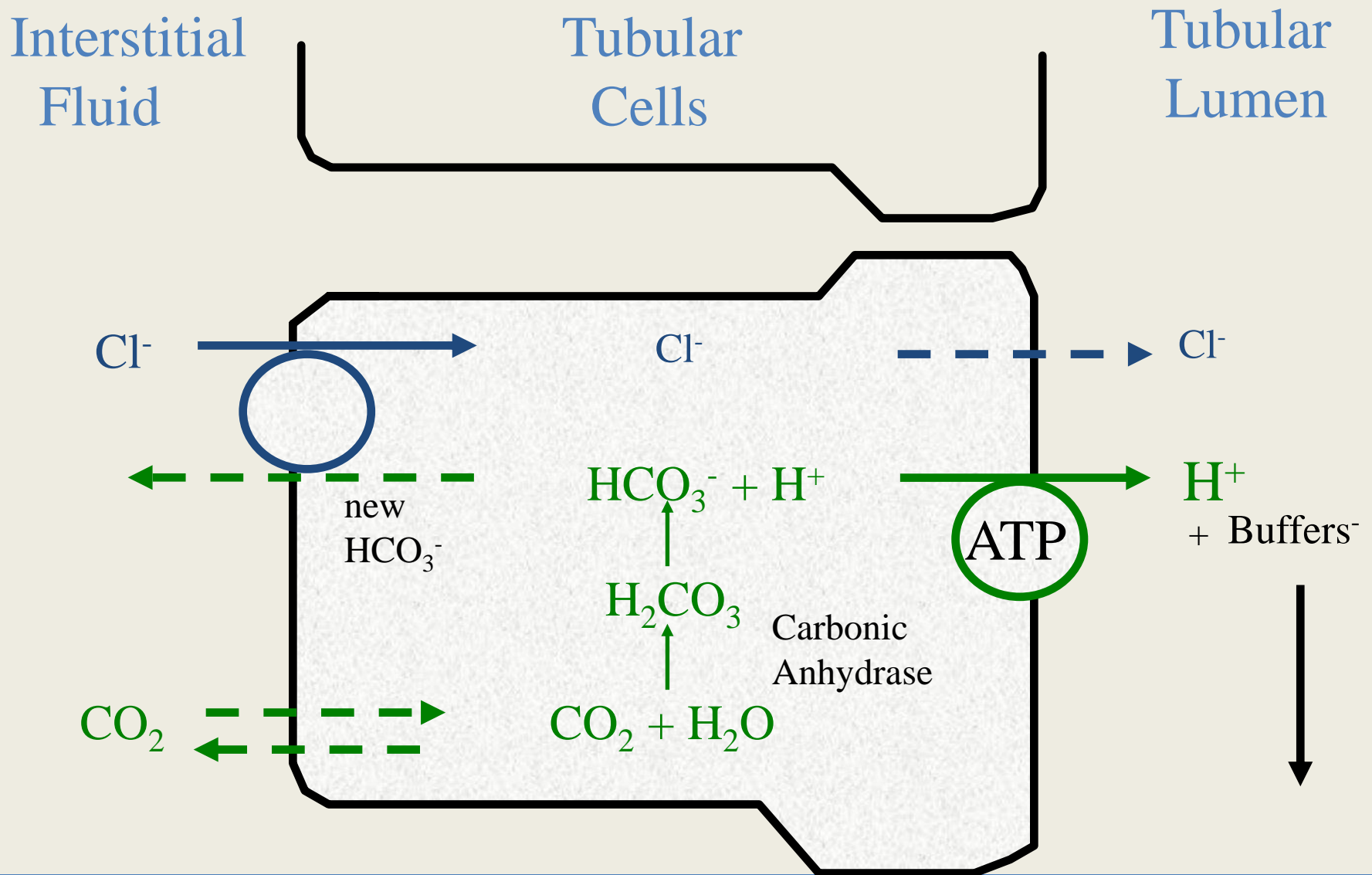
- Increased pCO₂ increases H⁺ secretion
i.e. respiratory acidosis
- Increased extracellular H⁺ increases H⁺ secretion
i.e. metabolic or respiratory acidosis
- Increased tubular fluid buffers increases H⁺ secretion
i.e. metabolic or respiratory acidosis

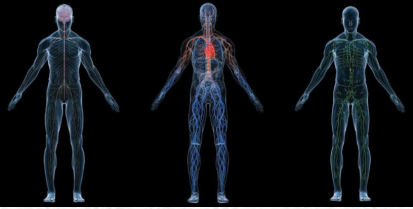


Renal Compensations for Acid-Base Disorders

- **Acidosis:**
 - increased H^+ secretion
 - increased HCO_3^- reabsorption
 - production of new HCO_3^-
- **Alkalosis:**
 - decreased H^+ secretion
 - decreased HCO_3^- reabsorption
 - loss of HCO_3^- in urine

In acidosis all HCO_3^- is titrated and excess H^+ in tubule is buffered





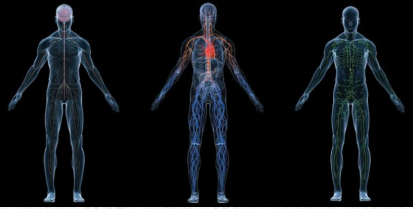
Importance of Renal Tubular Buffers

$$\begin{aligned}\text{Minimum urine pH} &= 4.5 \\ &= 10^{-4.5} \\ &= 3 \times 10^{-5} \text{ moles/L}\end{aligned}$$

i.e. the maximal $[\text{H}^+]$ of urine is 0.03 mmol/L

Yet, the kidneys must excrete, under normal conditions, at least 60 mmol non-volatile acids each day. To excrete this as free H^+ would require :

$$\frac{60 \text{ mmol}}{0.03 \text{ mmol/L}} = 2000 \text{ L per day !!!}$$



Buffering of secreted H^+ by filtered phosphate ($NaHPO_4^-$) and generation of “new” HCO_3^-

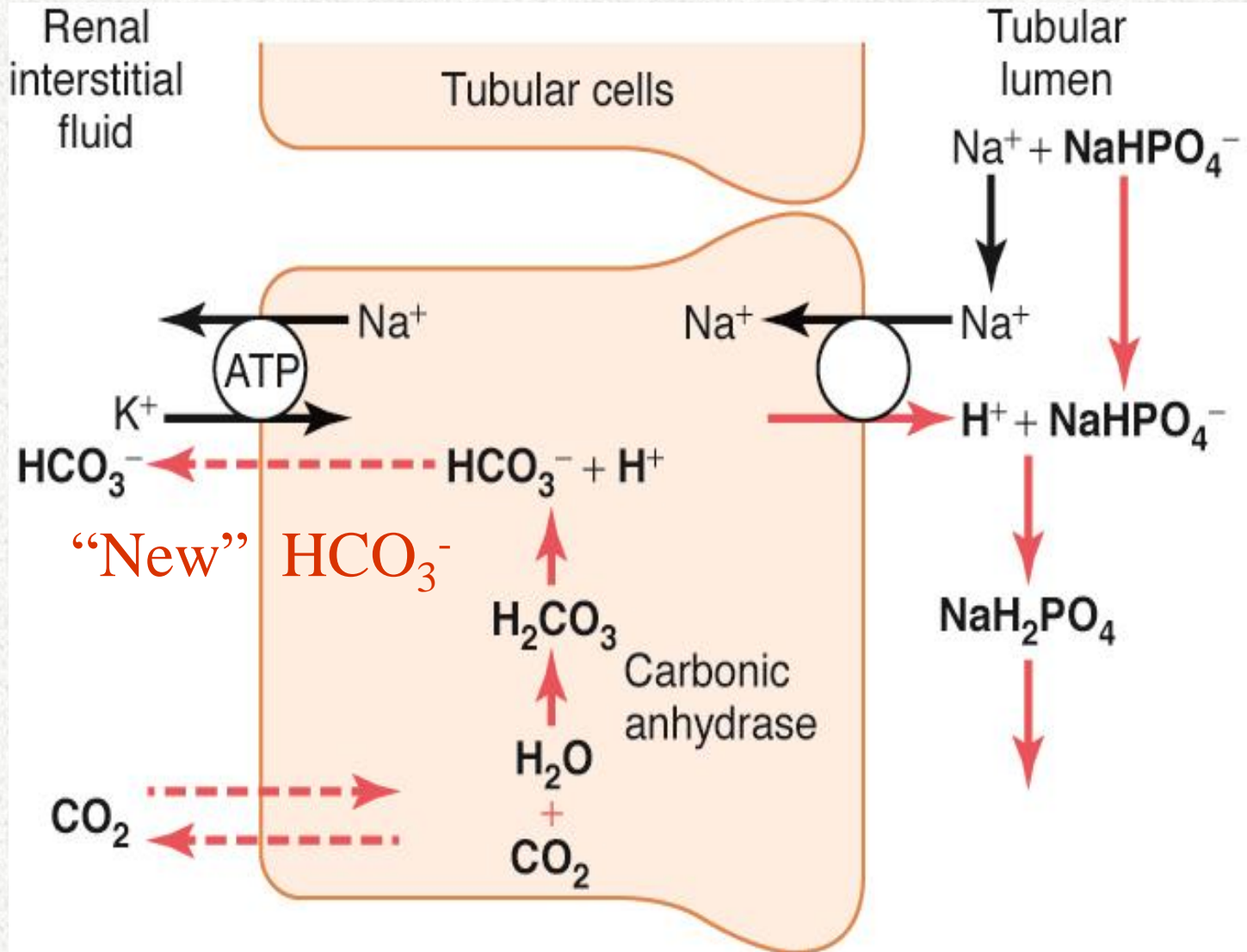
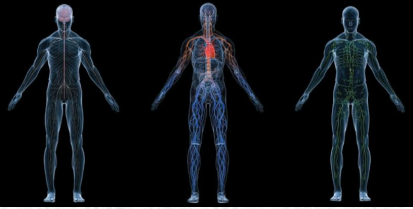


Figure 30-7.



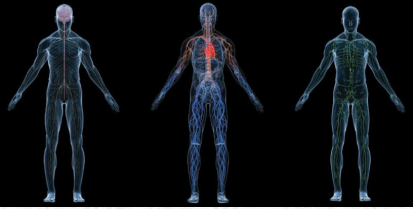
Phosphate as a Tubular Fluid Buffer

There is a high concentration of phosphate in the tubular fluid; $pK = 6.8$

Phosphate normally buffers about 30 mmol/day H^+ (about 100 mmol/day phosphate is filtered but 70 % is reabsorbed)

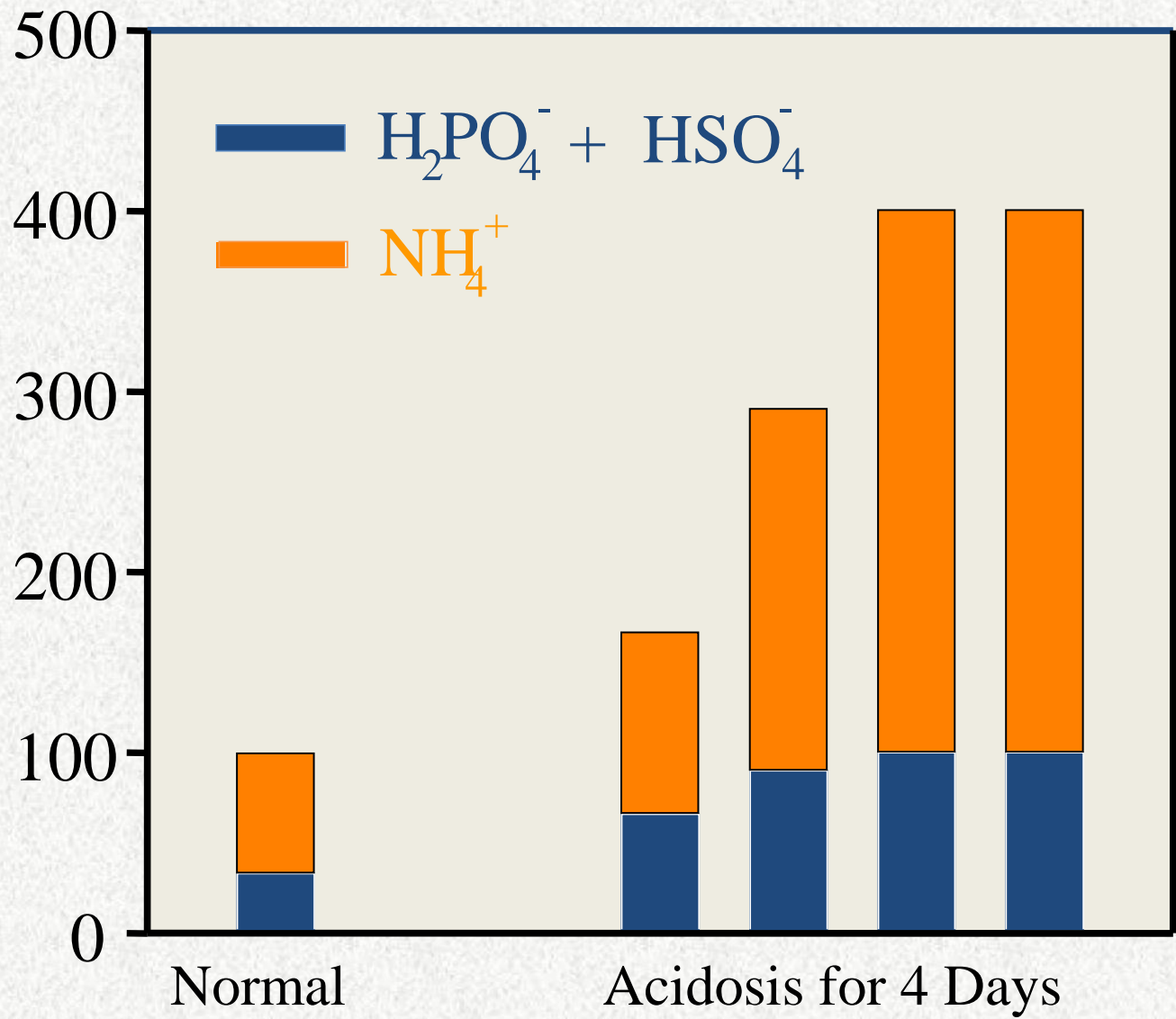
Phosphate buffering capacity does not change much with acid-base disturbances (phosphate is not the major tubular buffer in chronic acidosis)

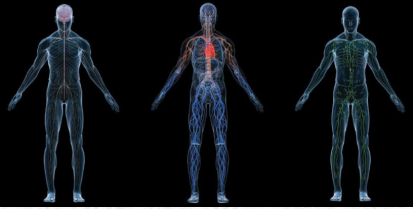




Phosphate and Ammonium Buffering In Chronic Acidosis

Acid Excretion (mmoles/day)





Production and secretion of NH_4^+ and HCO_3^- by proximal, thick loop of Henle, and distal tubules

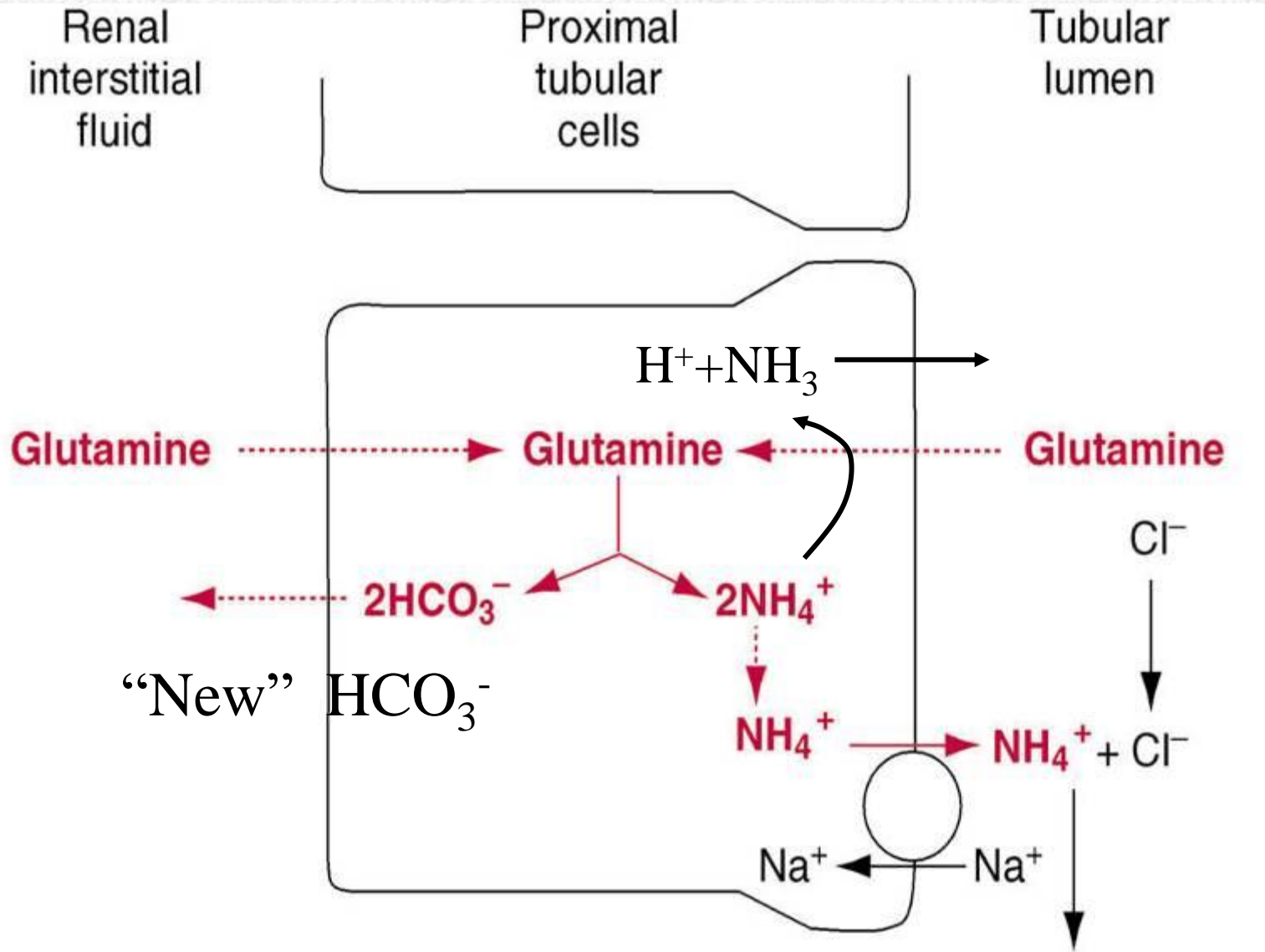
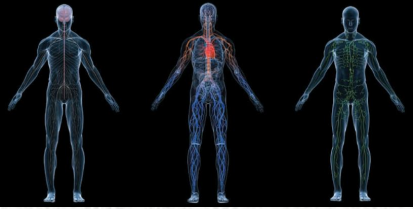


Figure 30-8.



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

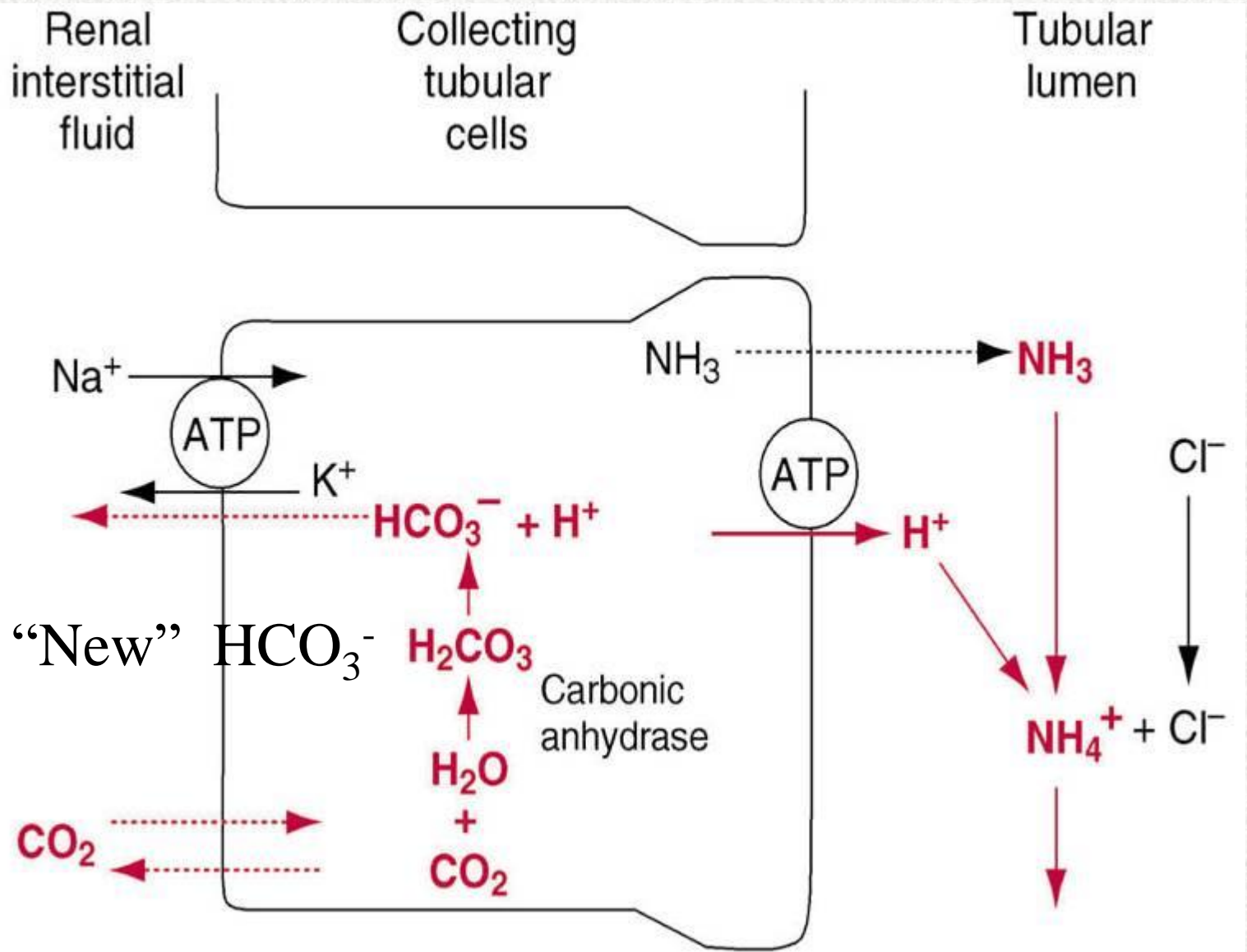
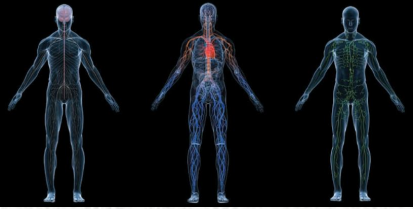


Figure 30-9.



Quantification of Normal Renal Acid-Base Regulation

Total H⁺ secretion

$$= 4320 \text{ mEq of H}^+ \text{ secreted (HCO}_3^-) + 60 \text{ mEq of H}^+ \text{ non-volatile} = 4380$$

Total H⁺ secretion = 4380 mmol/day

= HCO₃⁻ reabsorption (4320 mmol/d)

+ titratable acid (NaHPO₄⁻) (30 mmol/d)

+ NH₄⁺ excretion (30 mmol/d)

Net H⁺ excretion =

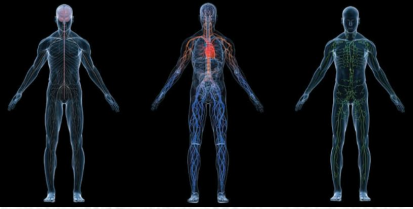
H⁺ excreted by buffers not bicarbonate (=new bicarb) - new H⁺ added to blood (=HCO₃⁻ excreted)

Net H⁺ excretion = 59 mmol/day

= titratable acid (30 mmol/d)

+ NH₄⁺ excretion (30 mmol/d)

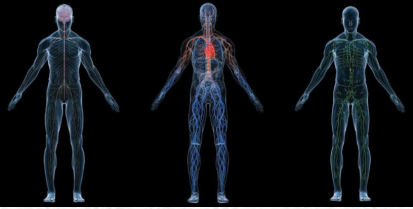
- HCO₃⁻ excretion (1 mmol/d) (or new H to blood)



Normal Renal Acid-Base Regulation

Net addition of HCO_3^- to body
(i.e. net loss of H^+)

Titratable acid	= 30 mmol/day
+ NH_4^+ excretion	= 30 mmol/day
- HCO_3^- excretion	= 1 mmol/day
Total	= 59 mmol/day

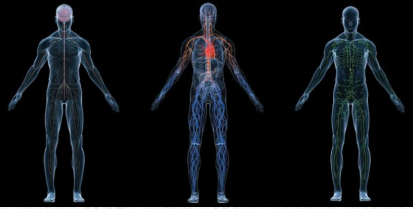


Renal Compensation for Acidosis

Increased addition of HCO_3^- to body by kidneys
(increased H^+ loss by kidneys)

Titratable acid	= 35 mmol/day (small increase)
NH_4^+ excretion	= 165 mmol/day (increased)
HCO_3^- excretion	= 0 mmol/day (decreased)
Total	= 200 mmol/day

This can increase to as high as 500 mmol/day

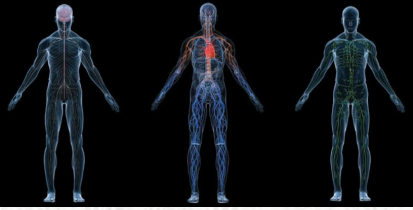


Renal Compensation for Alkalosis

Net loss of HCO_3^- from body
(i.e. decreased H^+ loss by kidneys)

Titratable acid	= 0 mmol/day (decreased)
NH_4^+ excretion	= 0 mmol/day (decreased)
HCO_3^- excretion	= 80 mmol/day (increased)
Total	= 80 mmol/day

HCO_3^- excretion can increase markedly in alkalosis



Classification of Acid-Base Disorders from plasma pH, pCO₂, and HCO₃⁻



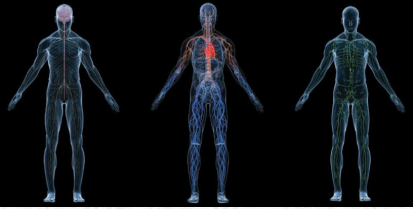
$$\text{pH} = \text{pK} + \log \frac{\text{HCO}_3^-}{\alpha \text{ pCO}_2}$$

Acidosis : pH < 7.4

- metabolic : ↓ HCO₃⁻
- respiratory : ↑ pCO₂

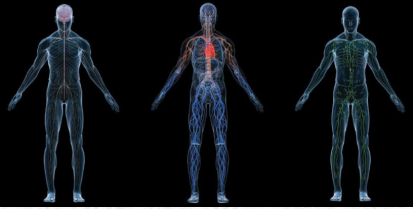
Alkalosis : pH > 7.4

- metabolic : ↑ HCO₃⁻
- respiratory : ↓ pCO₂



Renal Compensations for Acid-Base Disorders

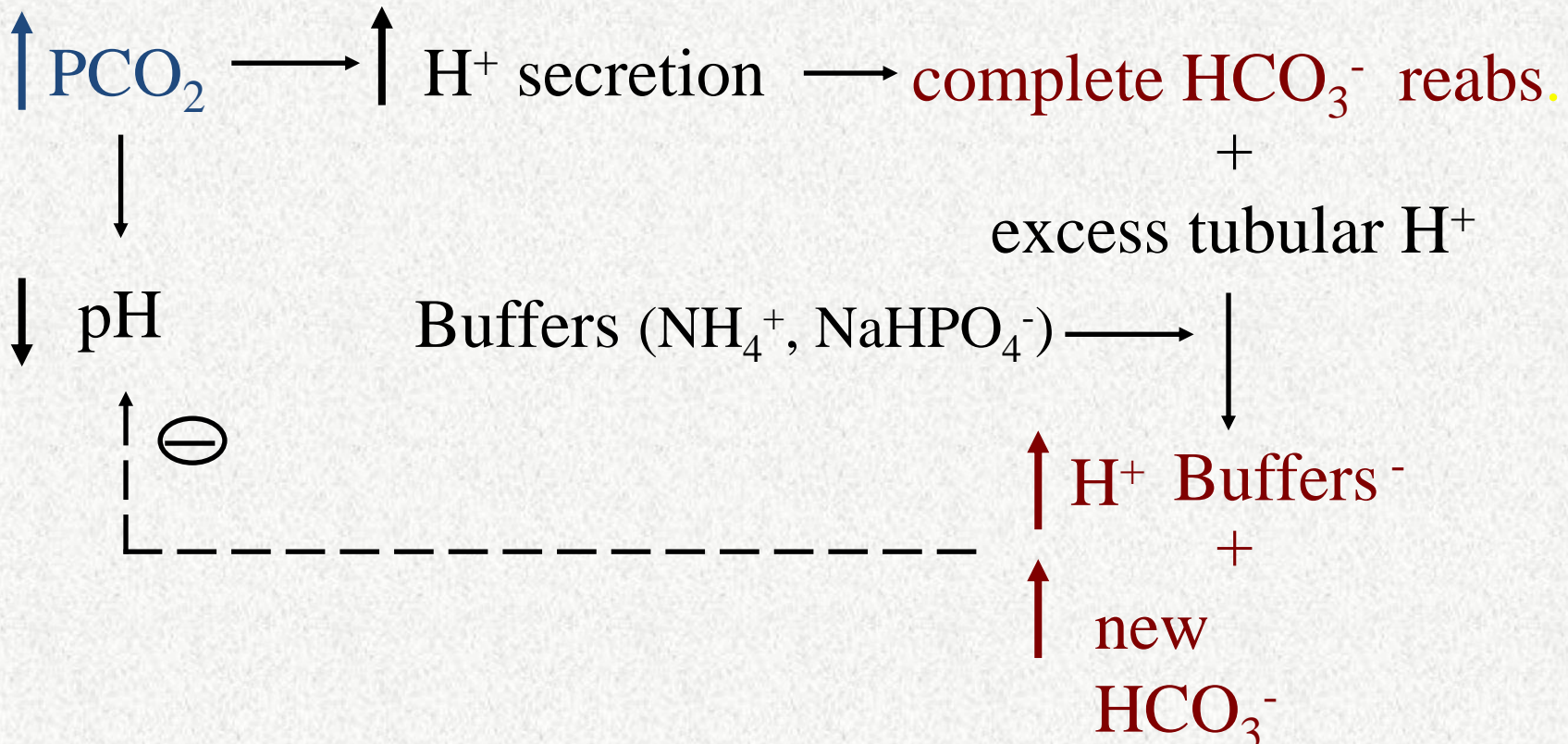
- **Acidosis:**
 - increased H^+ excretion
 - increased HCO_3^- reabsorption
 - production of new HCO_3^-
- **Alkalosis:**
 - decreased H^+ excretion
 - decreased HCO_3^- reabsorption
 - loss of HCO_3^- in urine

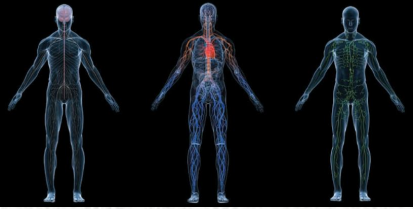


Renal Responses to Respiratory Acidosis



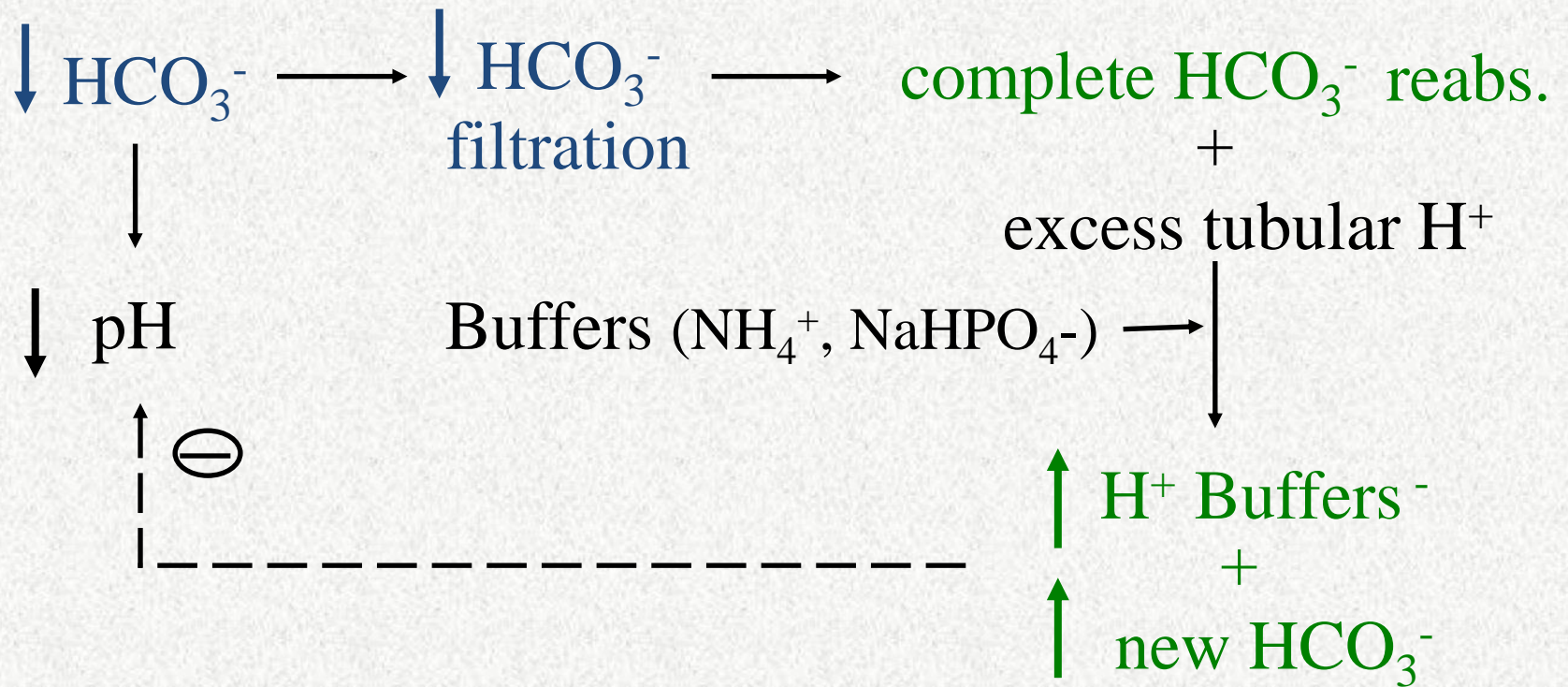
Respiratory acidosis : \downarrow pH \uparrow pCO₂ \uparrow HCO₃⁻

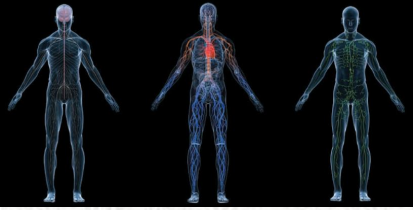




Renal Responses to Metabolic Acidosis

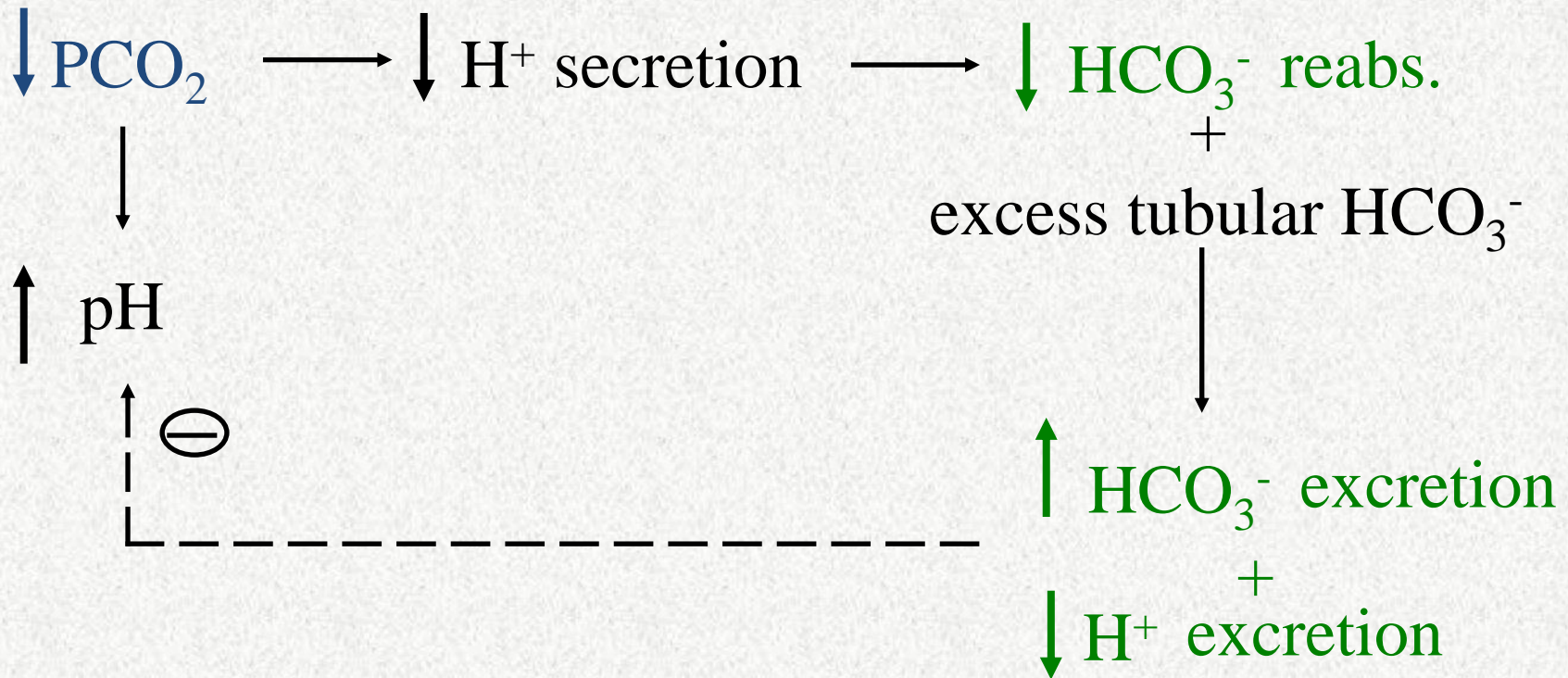
Metabolic acidosis : \downarrow pH \downarrow pCO₂ \downarrow HCO₃⁻

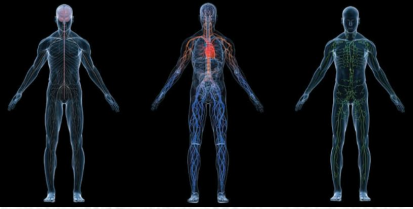




Renal Responses to Respiratory Alkalosis

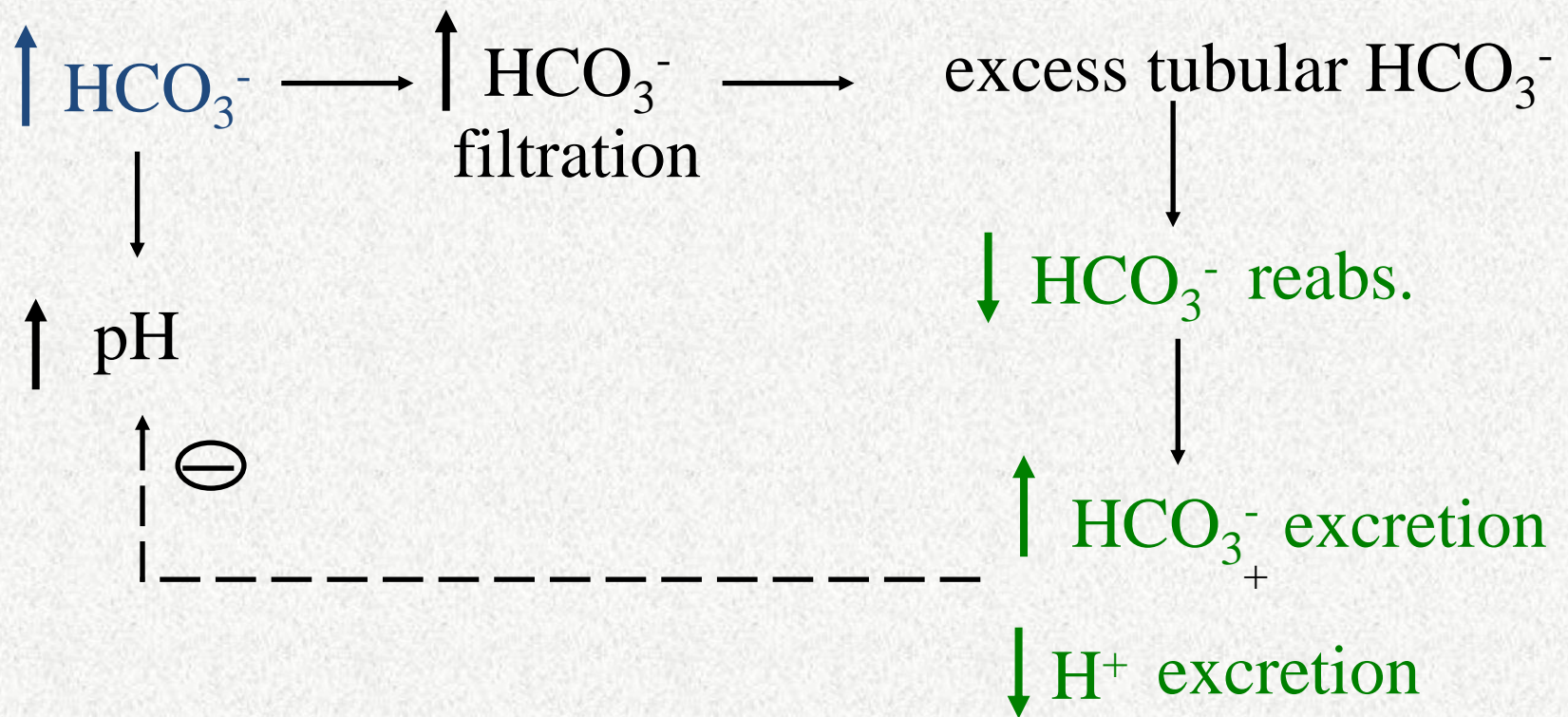
Respiratory alkalosis : \uparrow pH \downarrow pCO₂ \downarrow HCO₃⁻

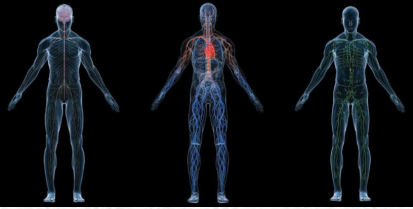




Renal Responses to Metabolic Alkalosis

Metabolic alkalosis : \uparrow pH \uparrow pCO₂ \uparrow HCO₃⁻





Question

The following data were taken from a patient:

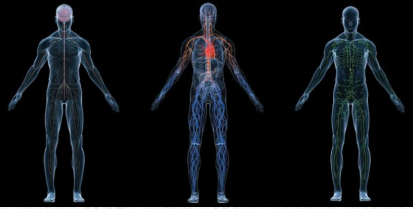
urine volume = 1.0 liter/day

urine HCO_3^- concentration = 2 mmol/liter

urine NH_4^+ concentration = 15 mmol/liter

urine titratable acid = 10 mmol/liter

- What is the daily net acid excretion in this patient ?
- What is the daily net rate of HCO_3^- addition to the extracellular fluids ?



Answer

The following data were taken from a patient:

urine volume = 1.0 liter/day

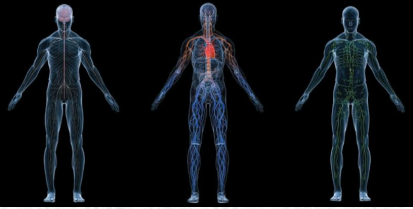
urine HCO_3^- concentration = 2 mmol/liter

urine NH_4^+ concentration = 15 mmol/liter

urine titratable acid = 10 mmol/liter

$$\begin{aligned}\text{net acid excretion} &= \text{Titr. Acid} + \text{NH}_4^+ \text{ excret} - \text{HCO}_3^- \\ &= (10 \times 1) + (15 \times 1) - (1 \times 2) \\ &= 23 \text{ mmol/day}\end{aligned}$$

$$\text{net rate of HCO}_3^- \text{ addition to body} = 23 \text{ mmol/day}$$



Classification of Acid-Base Disorders from plasma pH, pCO₂, and HCO₃⁻



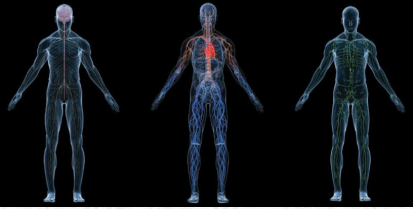
$$\text{pH} = \text{pK} + \log \frac{\text{HCO}_3^-}{\alpha \text{ pCO}_2}$$

Acidosis : pH < 7.4

- metabolic: ↓ HCO₃⁻
- respiratory: ↑ pCO₂

Alkalosis : pH > 7.4

- metabolic: ↑ HCO₃⁻
- respiratory: ↓ pCO₂



Classification of Acid-Base Disturbances

Plasma

Disturbance

pH

HCO_3^-

pCO_2

Compensation

metabolic
acidosis



↑ ventilation
↑ renal HCO_3^-
production

respiratory
acidosis



↑ renal HCO_3^-
production

metabolic
alkalosis

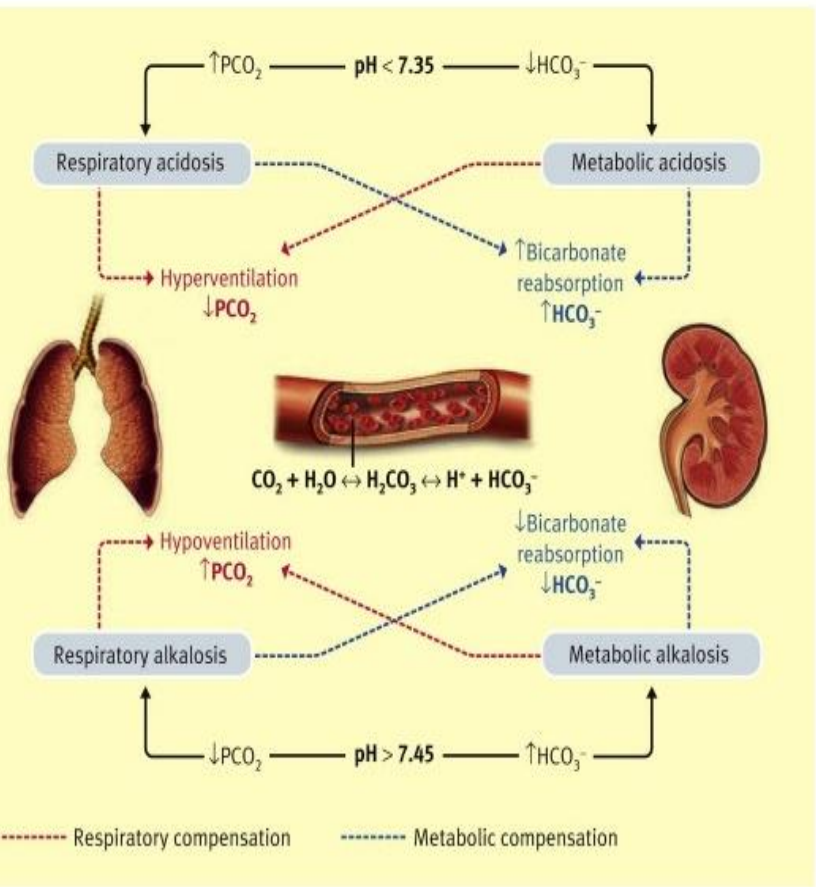
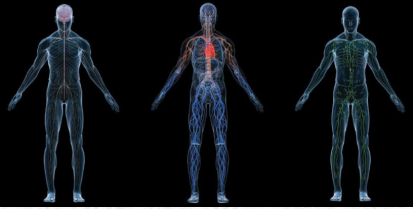


↓ ventilation
↑ renal HCO_3^-
excretion

respiratory
alkalosis



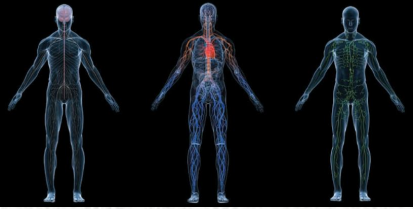
↑ renal HCO_3^-
excretion



	pH	HCO ₃ ⁻	CO ₂
Metabolic acidosis	↓	↓	Normal
Metabolic alkalosis	↑	↑	Normal
Metabolic acidosis with respiratory compensation	↓	↓	↓
Metabolic alkalosis with respiratory compensation	↑	↑	↑

Test	Normal	Decrease Value	Increase Value
pH	7.35-7.45	Acidosis	Alkalosis
PaCO ₂	35-45	Alkalosis	Acidosis
HCO ₃	22-26	Acidosis	Alkalosis
PaO ₂	80-100	Hypoxemia	O ₂ therapy
SaO ₂	95-100%	Hypoxemia	----- -





Question

A plasma sample revealed the following values
in a patient: norm for PCO_2 35-45, HCO_3^- 22-26

$$\text{pH} = 7.12$$

$$\text{PCO}_2 = 50$$

$$\text{HCO}_3^- = 18$$

diagnose this patient's acid-base status :

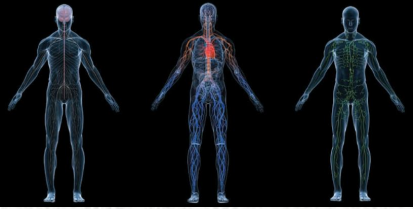
acidotic or alkalotic ?

Acidotic

respiratory, metabolic, or both ?

Both

Mixed acidosis: metabolic and respiratory acidosis



Mixed Acid-Base Disturbances

Two or more underlying causes of acid-base disorder.

pH= 7.60

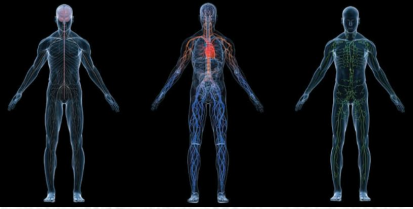
pCO₂ = 30 mmHg

plasma HCO₃⁻ = 29 mmol/L

What is the diagnosis?

Mixed Alkalosis

- Metabolic alkalosis : increased HCO₃⁻
- Respiratory alkalosis : decreased pCO₂



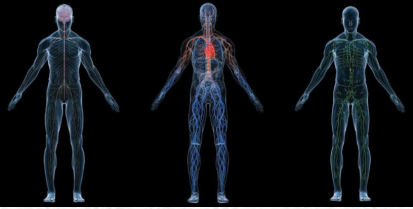
Question

A patient presents in the emergency room and the following data are obtained from the clinical labs:

plasma pH= 7.15, $\text{HCO}_3^- = 8 \text{ mmol/L}$, $\text{pCO}_2 = 24 \text{ mmHg}$

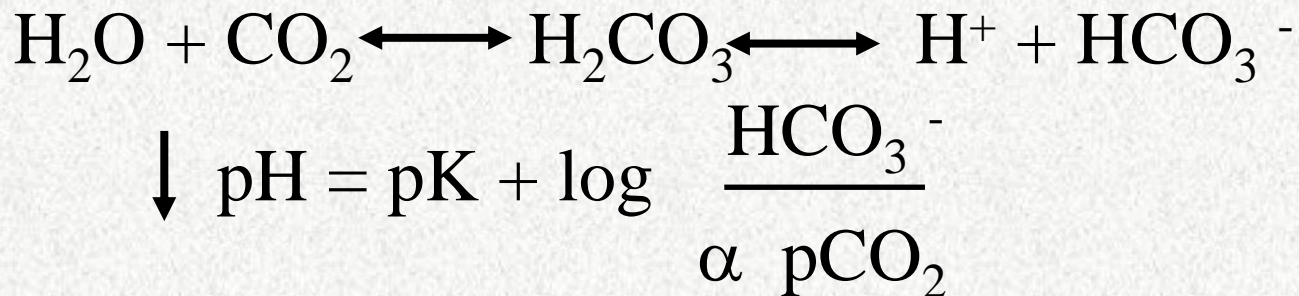
This patient is in a state of:

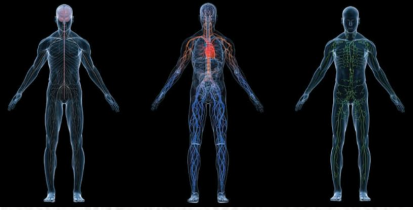
1. metabolic alkalosis with partial respiratory compensation
2. respiratory alkalosis with partial renal compensation
3. metabolic acidosis with partial respiratory compensation
4. respiratory acidosis with partial renal compensation



Acid-Base Disturbances

- **Metabolic Acidosis** : $\downarrow \text{HCO}_3^- / \text{pCO}_2$ in plasma
($\downarrow \text{pH}, \downarrow \text{HCO}_3^-$)
 - aspirin poisoning ($\uparrow \text{H}^+$ intake)
 - diabetes mellitus ($\uparrow \text{H}^+$ production)
 - diarrhea (HCO_3^- loss)
 - renal tubular acidosis ($\downarrow \text{H}^+$ secretion, $\downarrow \text{HCO}_3^-$ reabs.)
 - carbonic anhydrase inhibitors ($\downarrow \text{H}^+$ secretion)





Anion Gap as a Diagnostic Tool

In body fluids: total cations = total anions

Cations (mEq/L)

Na⁺ (142)

K⁺ (4)

Ca⁺⁺ (5)

Mg⁺⁺ (2)

Total (153)

Anions (mEq/L)

Cl⁻ (108)

HCO₃⁻ (24)

Proteins (17)

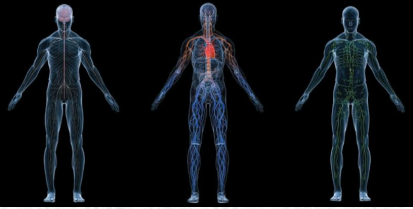
Phosphate,

Sulfate,

lactate, etc (4)

(153)

Unmeasured



Anion Gap as a Diagnostic Tool

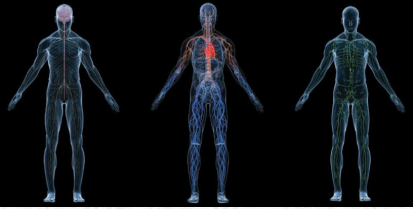
In body fluids: total cations = total anions

$$\text{Na}^+ = \text{Cl}^- + \text{HCO}_3^- + \text{unmeasured anions}$$

$$\text{unmeasured anions} = \text{Na}^+ - \text{Cl}^- - \text{HCO}_3^- = \text{anion gap}$$

$$= 142 - 108 - 24 = 10 \text{ mEq/L}$$

$$\text{Normal anion gap} = 8 - 16 \text{ mEq / L}$$



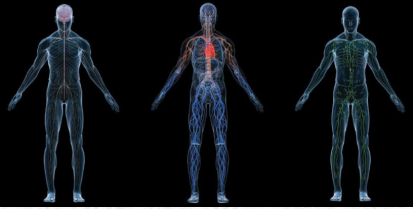
Anion Gap in Metabolic Acidosis

- loss of HCO_3^- = normal anion gap

↔ anion gap = Na^+ - ↑ Cl^- - ↓ HCO_3^-
hyperchloremic metabolic acidosis

- ↑ unmeasured anions = ↑ anion gap

↑ anion gap = Na^+ - ↔ Cl^- - ↓ HCO_3^-
normochloremic metabolic acidosis
i.e. diabetic ketoacidosis, lactic acidosis,
salicylic acid, etc.



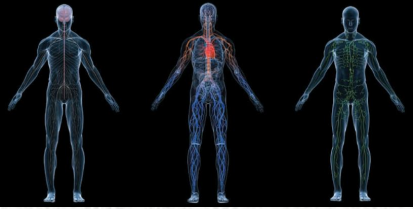
Use of “Anion Gap” as a Diagnostic Tool for Metabolic Acidosis

Increased Anion Gap (normal Cl^-)

- diabetes mellitus (ketoacidosis)
- lactic acidosis
- aspirin (acetylsalicylic acid) poisoning
- methanol poisoning
- starvation

Normal Anion Gap (increased Cl^- , hyperchloremia)

- diarrhea
- renal tubular acidosis
- Addison’ disease
- carbonic anhydrase inhibitors



Laboratory values for an uncontrolled diabetic patient include the following:

arterial pH = 7.25

Plasma $\text{HCO}_3^- = 12$

Plasma $\text{P}_{\text{CO}_2} = 28$

Plasma $\text{Cl}^- = 102$

Plasma $\text{Na}^+ = 142$

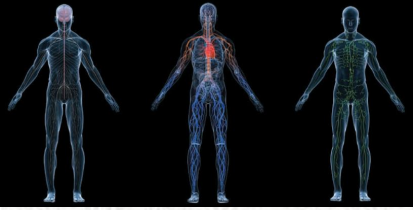
Metabolic Acidosis

Respiratory Compensation

What type of acid-base disorder does this patient have?

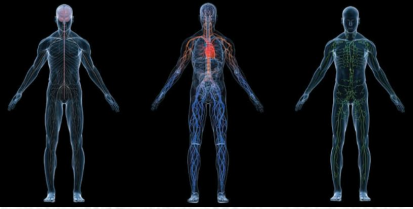
What is his anion gap ?

$$\text{Anion gap} = 142 - 102 - 12 = 28$$



Which of the following are the most likely causes of his acid-base disorder?

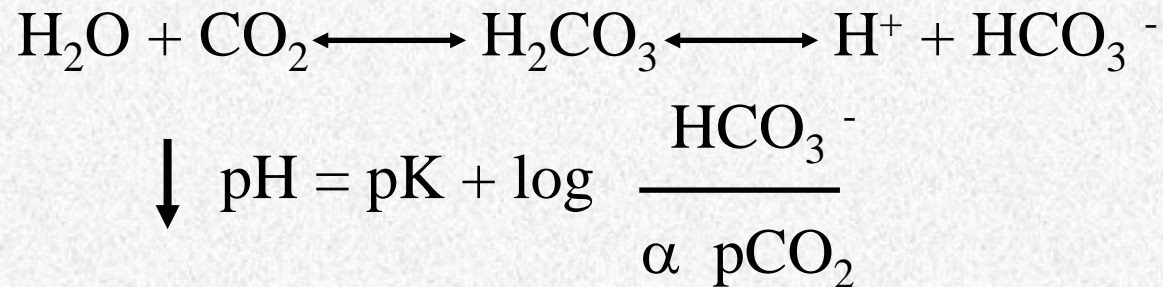
- a. diarrhea
- b. diabetes mellitus
- c. Renal tubular acidosis
- d. primary aldosteronism

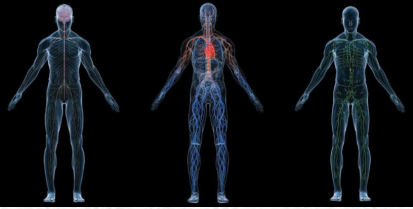


Acid-Base Disturbances

- Respiratory Acidosis : $\downarrow \text{HCO}_3^- / \text{pCO}_2$ in plasma
($\downarrow \text{pH}, \uparrow \text{pCO}_2$)

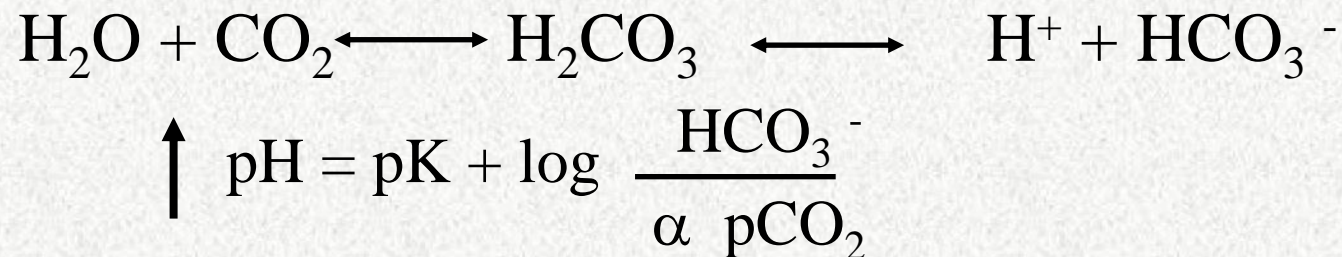
- brain damage
- pneumonia
- emphysema
- other lung disorders

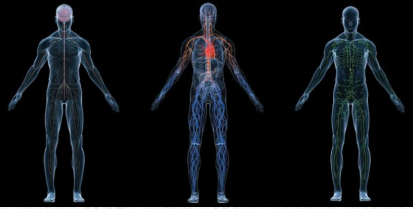




Acid-Base Disturbances

- Metabolic Alkalosis : $\uparrow \text{HCO}_3^- / \text{pCO}_2$ in plasma
($\uparrow \text{pH}$, $\uparrow \text{HCO}_3^-$)
 - increased base intake (e.g. NaHCO_3)
 - vomiting gastric acid
 - mineralocorticoid excess
 - overuse of diuretics (except carbonic anhydrase inhibitors)





↑ Aldosterone

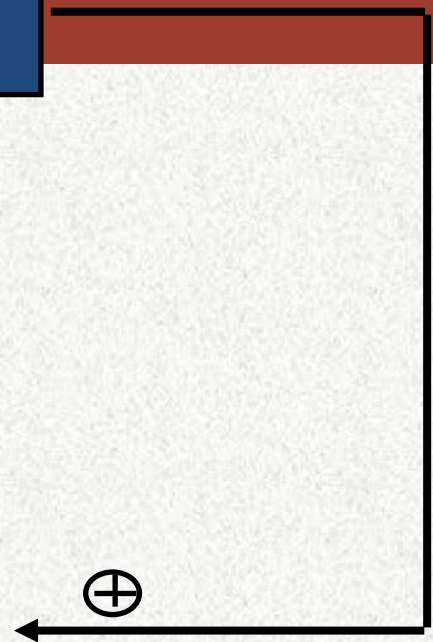
↑ tubular K^+ secretion

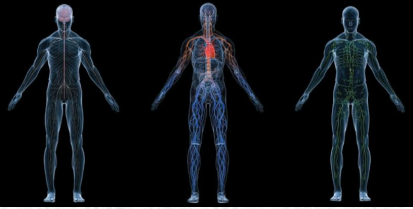
K^+ depletion

↑ H^+ secretion

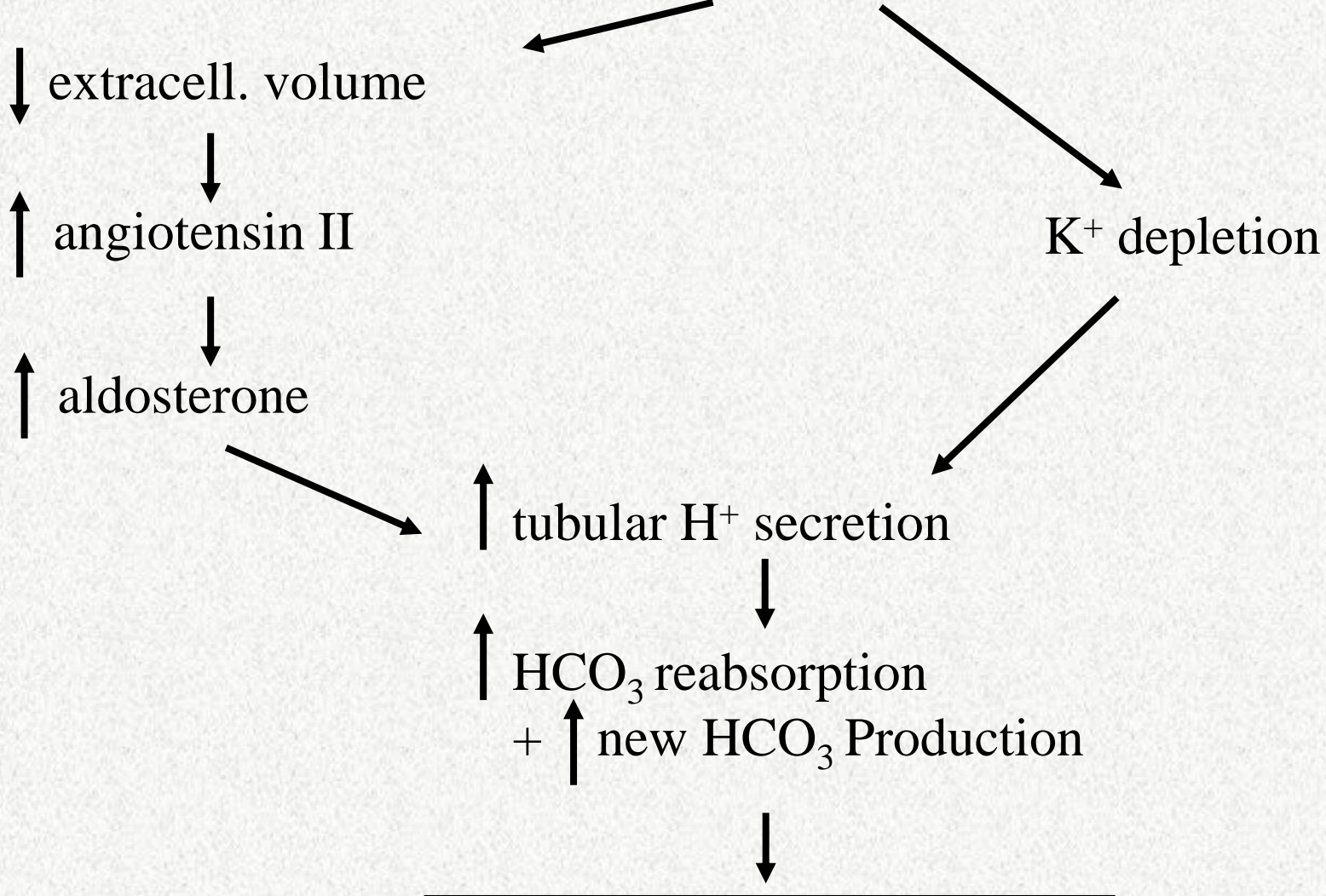
↑ HCO_3^- reabsorption
+ ↑ new HCO_3^- Production

Metabolic Alkalosis

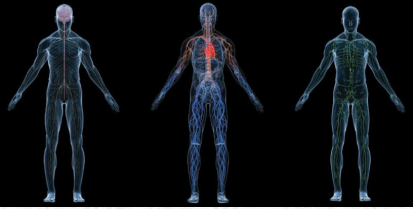




Overuse of Diuretics



Metabolic Alkalosis

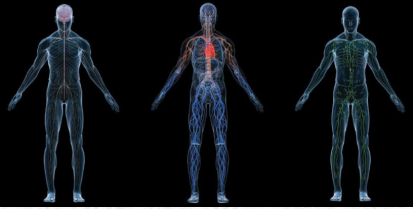


Acid-Base Disturbances

- Respiratory Alkalosis : $\uparrow \text{HCO}_3^- / \text{pCO}_2$ in plasma
($\uparrow \text{pH}$, $\downarrow \text{pCO}_2$)
 - high altitude
 - psychic (fear, pain, etc)



$$\uparrow \text{pH} = \text{pK} + \log \frac{\text{HCO}_3^-}{\alpha \text{pCO}_2}$$



Laboratory values for a patient include the following:

arterial pH = 7.34

Plasma $\text{HCO}_3^- = 15$

Plasma $\text{P}_{\text{CO}_2} = 29$

Plasma $\text{Cl}^- = 118$

Plasma $\text{Na}^+ = 142$

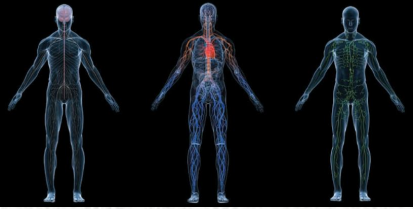
Metabolic Acidosis

Respiratory Compensation

What type of acid-base disorder does this patient have?

What is his anion gap ?

$$\text{Anion gap} = 142 - 118 - 15 = 9 \quad (\text{normal})$$



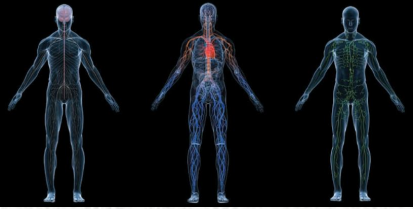
Which of the following are the most likely causes of his acid-base disorder?

a. diarrhea

b. diabetes mellitus

c. aspirin poisoning

d. primary aldosteronism



Indicate the Acid -Base Disorders in Each of the Following Patients

pH	HCO_3^-	PCO_2	Acid-Base Disorder ?
7.34	15	29	Metabolic acidosis
7.49	35	48	Metabolic alkalosis
7.34	31	60	Respiratory acidosis
7.62	20	20	Respiratory alkalosis
7.09	15	50	Acidosis: respiratory + metabolic