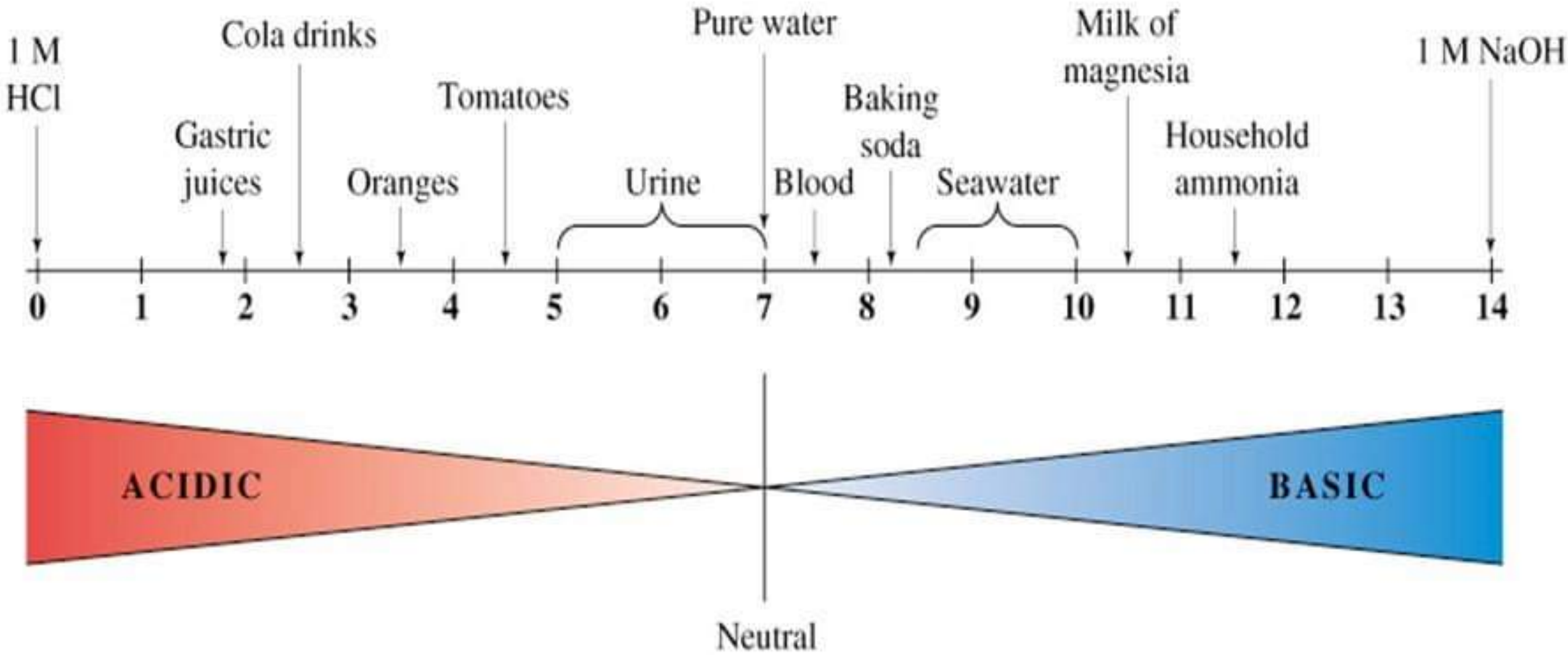
# ACID BASE BALANCE

# Normal acid base values:

| | pH | PCO2 | HCO3- |
|---|---|---|---|
| Range: | 7.35- 7.45 | 36-44 | 22-26 |
| Optimal value | 7.40 | 40 | 24 |

# pH: A Concentration Scale for Acids and Bases



# Definitions

- 1) **Acid**: a substance which can give $H^+$ (proton)
  **Strong acid:** dissociates completely ($H^+$, $H^+$, $H^+$,....) e.g Hcl
  **Weak acid:** dissociates partialy ($H^+$,$H^+$)

  e.g $H_2CO_3 \rightarrow H^+ + HCO_3^-$

  $H_2PO_4 \rightarrow H^+ + HPO_4^-$
- 2) **Base**: can accept proton

  $HCO_3^- + H^+ \rightarrow H_2CO_3$
- 3) **Alkali**: dissociates to produce $OH^+$ group
- 4) **Buffering**: is the process by which a strong acid (or base) is replaced by a weaker one, with a consequent reduction in the number of free hydrogen ions

  $HCl + NaHCO_3 \rightarrow H_2CO_3 + NaCl$

  strong acid  buffer  weak acid  neutral salt
- 5) **Buffer pair**: weak acid and its conjugate base
- 6) **pH**: it is a measure of $H^+$ activity
- **NB**: using pH in measuring $H^+$ concentration is deceiving (makes significant things appear small, 1nm = 0.01pH)

# Acids are continually produced as a by-product of metabolism.

**Volatile acid**
**e.g carbonic acid ($H_2CO_3$),**

(approximately 15,000 to 20,000 mmol per day)

**Nonvolatile acids**

approximately 80 mmol per day

**Organic acids**

sulfuric acid →from sulfur-containing amino acids, from partial metabolism of carbohydrates and fats.
Uric acid →from nucleic acid metabolism,

**Inorganic acids**

Inorganic phosphates →from the metabolism of organic phosphorus compounds.

## Different buffer systems assume dominant roles in different parts of the body

| Extracellular Fluid | Blood | Intracellular Fluid | Urine |
|---|---|---|---|
| **Major Buffer**<br>·Bicarbonate buffer system<br>**Minor Buffers**<br>·Intracellular proteins<br>·Phosphate buffer system | **Major Buffers**<br>·Bicarbonate buffer system<br>·Hemoglobin<br>**Minor Buffers**<br>·Plasma proteins<br>·Phosphate buffer system | **Major Buffers**<br>·Proteins<br>·Phosphate | **Major Buffers**<br>·Ammonia<br>·Phosphate |

# Mechanisms for the Homeostasis of Hydrogen Ions

**Despite the continual metabolic production of acid, the pH of extracellular fluids is normally tightly maintained between 7.35 and 7.45.**

The primary organs that deal with the acid load are the lung (respiratory) and kidneys (metabolic).

Chemical bu... within seconds

**Kidney (24-48h)**

The kidneys maintain the HCO3 buffer system..

**Lungs ( rapid within 1-3 minutes)**

Maintaining a concentration of $CO_2$ by elimination of excess CO2 in the body fluids.

- Acidosis stimulating ventilation

-Alkalosis depressing it.

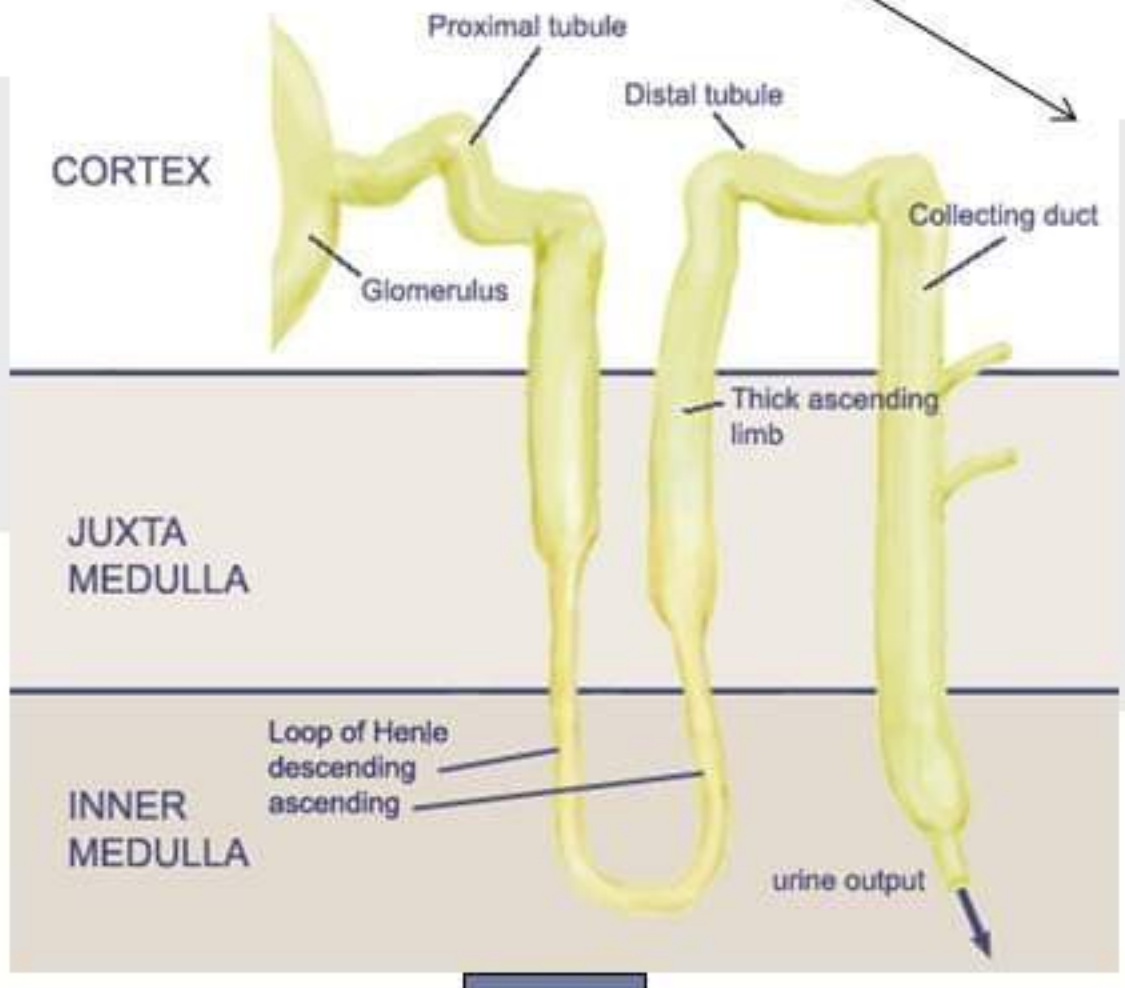
**Buffering**: is the process by which a strong acid (or base) is replaced by a weaker one, with a consequent reduction in the number of free hydrogen ions.

# Physiology of Renal Acidification

The generated acid =50-100 meq/day

**Proximal acidification :**

**➢PCT absorption of HCO3 ( 85%)**




**Distal Urinary acidification.**

- Reabsorption of HCO3 (15%)
- Excretion of fixed acids through buffering & Ammonia recycling and excretion .

The urine PH can be lowered to a max. 4.5-5 in presence of acid load. This maintained the plasma H+ and PH within a narrow limits

Increase PH >7.4

Alkalosis

Decreased PH <7.4

Acidosis

**Normal PH 7.4**

Alkalosis is any abnormality that removes acid or adds base.

**Acidosis is any abnormality that results in addition of acid or removal of alkali from the body fluids**

# Systematic ABG analysis

1. **History taking and physical examination**
2. **Assess accuracy of data (**validity).
3. **Identify the primary disturbance**
    1. Check arterial pH-------- acidosis or alkalosis
    2. $HCO_3^-$ & $pCO_2$ analysis---primary disorder.
4. Compensatory responses
5. Calculate AG
6. Formulate acid-base diagnosis

# I. Some important "Clues" in history

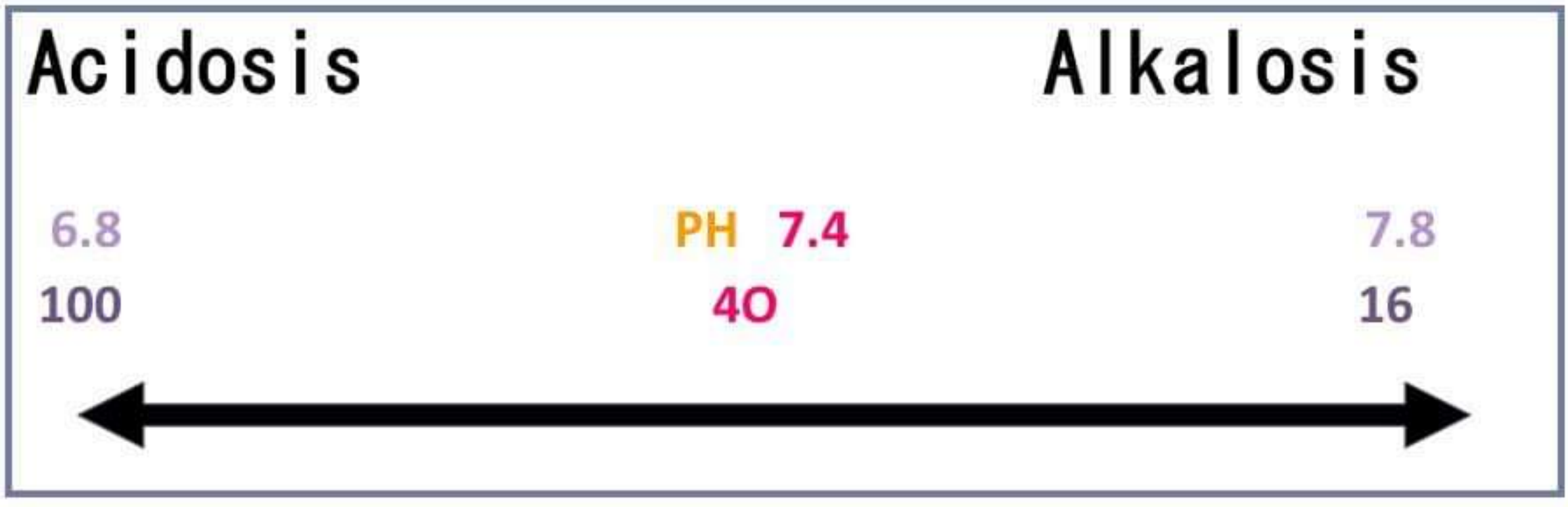
| | |
|---|---|
| Pulmonary embolus | Respiratory alkalosis |
| Cirrhosis | Respiratory alkalosis |
| Dehydration or shock<br>Hyperkalaemia | Metabolic acidosis |
| Vomiting , Hypokalaemia | Metabolic alkalosis |
| Severe diarrhea<br>salisylates or alcohol intoxication | Metabolic acidosis |
| Renal failure | Metabolic acidosis |
| Hyperglycaemia (DKA? if ketones present | suggests metabolic acidosis (high AG |
| Chronic obstructive pulmonary disease | Respiratory acidosis |

# VALIDITY

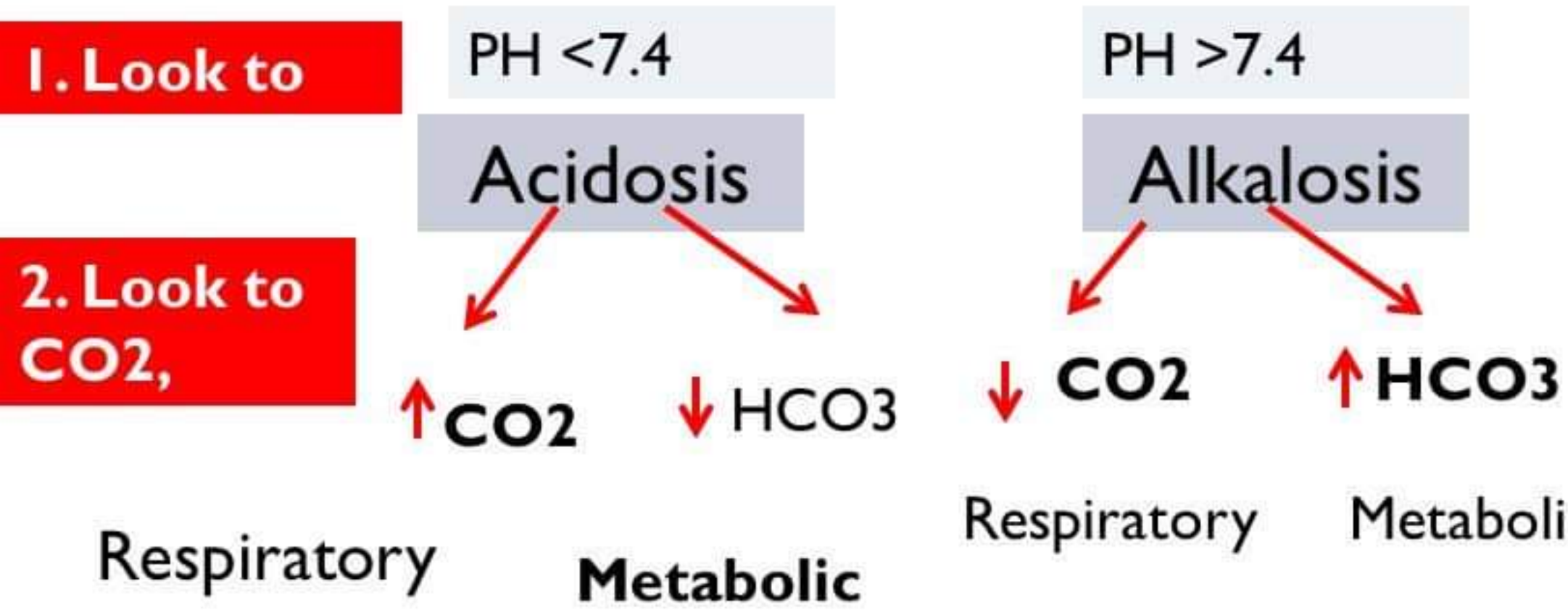
## [H]=24 x Pco2/HCO3 lungs/kidneys

***A modified Henderson-Hasselbalch equation can be used to check the validity of the laboratory values obtained.***

## H = (PCO2/ HCO3) × 24 =PH−7. 8 ×100



# 3. Identify the primary disturbance




- If *PCO2* is the initial chemical change, then process is respiratory **(weak acids).**
- if *HCO3-* is the initial chemical change, then process is metabolic **(weak alkali).**
- Mixed disturbances are possible (e.g., a mixed metabolic acidosis and respiratory alkalosis).
- The term acidemia refers to a decrease in blood pH from normal, whereas alkalemia refers to an abnormal increase in blood pH.

Acidosis ↓↑ PCO2 ↑HCO3

Alkalosis ↑↓ PCO2 ↓ HCO3

Acidosis ↓ HCO3 ↓ PCO2

Alkalosis ↑ HCO3 ↑ PCO2

# The Four Cardinal Acid Base Disorders

| Disorder | pH | $pCO_2$ | $[HCO_3^-]$ |
|---|---|---|---|
| M acidosis | ↓ | ↓ | ↓ |
| M alkalosis | ↑ | ↑ | ↑ |
| R acidosis | ↓ | ↑ | ↑ |
| R alkalosis | ↑ | ↓ | ↓ |

# 4. Compansation

- The body attempts to maintain its pH when confronted with acid–base disturbances.
- The compensatory processes are different for respiratory and renal disturbances.
- The magnitude of an appropriate compensatory response has been determined from empirical observation of the responses in humans and experimental animals.

# Assessment of compensatory responses

## Metabolic

Metabolic acidosis

**Expected pCO2 = 1.5 x [HCO3] + 8 (range: +/- 2)**

Metabolic alkalosis

**Expected pCO2 = 0.7 [HCO3] + 20 (range: +/- 5)**

**"If the actual $pCO_2$ or [$HCO_3^-$] is different from the predicted values,**

**You must suspect a 2nd acid-base disorder"**

# Respiratory

- **Acute Respiratory Acidosis :**

**The [$HCO_3$] will increase by 1 mmol/l for every 10 mmHg elevation in $pCO_2$ above 40 mmHg**

- **Chronic Respiratory Acidosis :**

**The [HCO3] will increase by 4 mmol/l for every 10 mmHg elevation in pCO2 above 40mmHg.**

- **Acute Respiratory Alkalosis:**

**The [HCO3] will decrease by 2 mmol/l for every 10 mmHg decrease in pCO2 below 40 mmHg.**

- **Chronic Respiratory Alkalosis:**

**The [HCO3] will decrease by 5 mmol/l for every 10 mmHg decrease in pCO2 below 40 mmHg.**

# 5. The "Anion Gap"

## Anions and Cations in Serum (Values in mEq/L)

| ANIONS | CATIONS |
|---|---|
| Proteins 15 | Calcium 5 |
| Organic acids 5 | Magnesium 1.5 |
| Phosphates 2 | Potassium 4.5 |
| Bicarbonates 24 | Sodium 140 |
| Sulfates 1 | |
| Chlorides 104 | |
| Total 151 | Total 151 |

**Anion = Cation**

**Anion gap=measured cation- measured anion = $[Na^+]$ – ($[Cl^-]$ + $[HCO_3^-]$)**

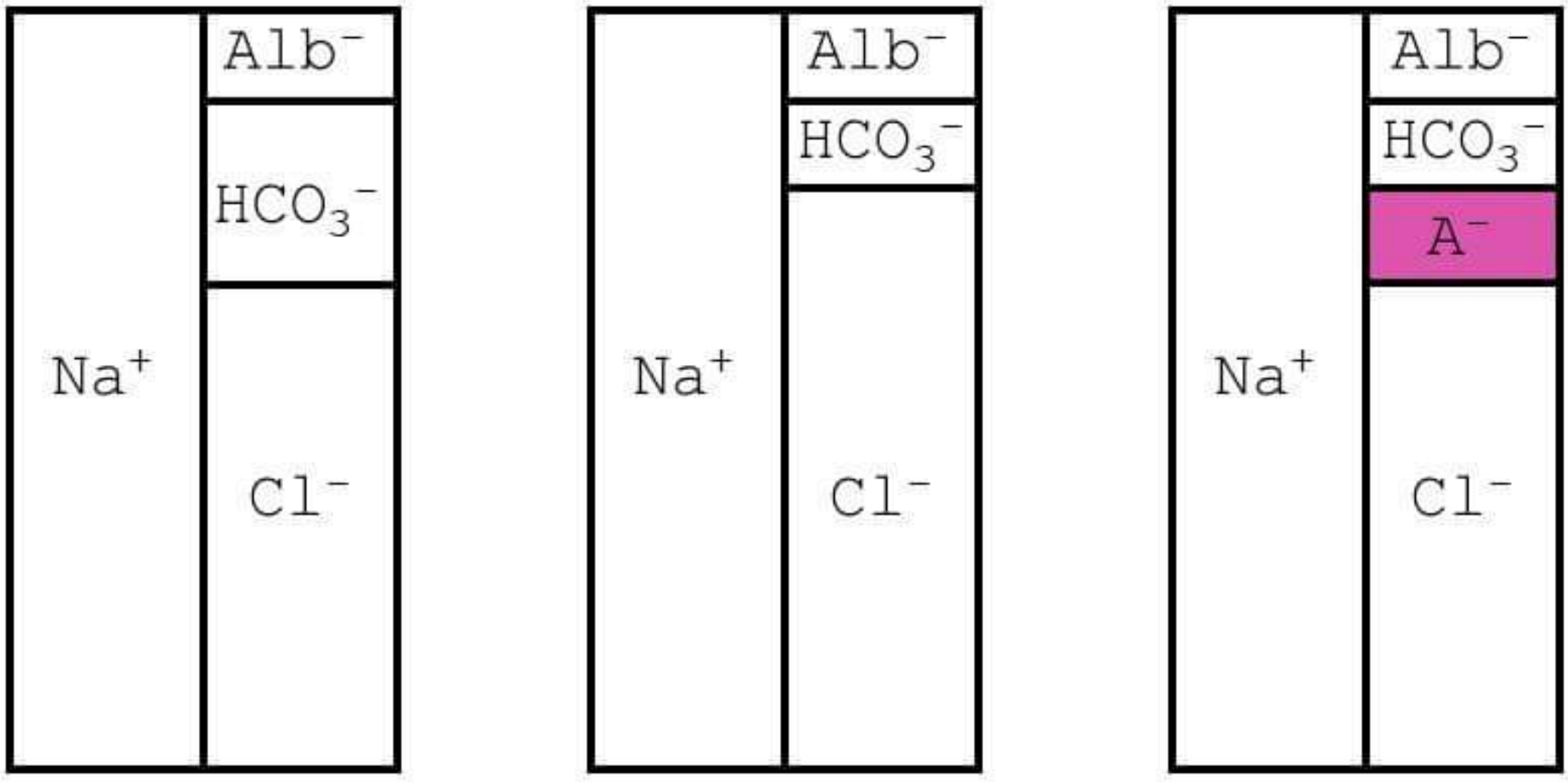
# 5. The "Anion Gap"

$$\text{Anion gap} \equiv [Na^+] - ([Cl^-] + [HCO_3^-])$$

**The gap reflects unmeasured anions, mostly the negative charge on albumin. The gap is used to differentiate metabolic acidosis caused by loss of $HCO_3^-$ (normal gap) from acidosis caused by organic acids like ketoacids, lactic acid, or toxins like ethylene glycol, or methanol**

# Metabolic Acidosis: The "Anion Gap"

$$\equiv [Na^+] - ([Cl^-] + [HCO_3^-])$$




Nl Anion gap M acidosis

High Anion gap M acidosis

# metabolic acidosis

## High Anion Gap

- 1. **Ketoacidosis**
  - Diabetic
  - Alcoholic
  - Starvation
- 2. **Lactic acidosis**
- 3. **Toxicosis**
  - Ethylene glycol
  - Methanol
  - Salicylates
- 4. **Advanced renal failure**

## Normal anion gap

- 1. **GIT $HCO_3^-$ loss**
  - Diarrhea
  - External fistulas
- 2. **Renal $HCO_3^-$ loss**
  - Proximal RTA
  - Distal RTA
  - Hyperkalemic RTA

# Metabolic alkalosis

- Metabolic alkalosis arises by

increased loss of acid (generally from the stomach or kidney).
Volume loss with chloride depletion (vomiting, gastric drainage, diuretics, villous adenoma)

Excess alkali intake (milk-alkali syndrome, bicarbonate administration)

Hypermineralocorticoid states (exogenous steroid treatment, primary aldosteronism, Cushing syndrome, renovascular disease)
Severe potassium deficiency

# Primary respiratory abnormalities

- Failure of respiration, leading to accumulation of carbon dioxide and

## Respiratory Acidosis

1. Acute respiratory failure (drug intoxication, cardiopulmonary arrest)
2. Chronic respiratory failure (chronic obstructive pulmonary disease [COPD], neuromuscular disorders, obesity)

Hyperventilation , leading to a reduction in carbon dioxide and

## Respiratory alkalosis

1. Hypoxia stimulating hyperventilation : (asthma, pulmonary edema, pulmonary fibrosis, high altitude, congenital heart disease)
2. Increased respiratory drive (pulmonary disease, anxiety, salicylate intoxication, cerebral disease, fever)
3. Cirrhosis, pregnancy
4. Excessive mechanical ventilation

# CLINICAL MANIFESTATIONS

- Nonspecific signs such as:
  - Fatigue
  - Mental status changes can be seen along with findings related to the underlying etiologies.
- Some signs and symptoms that can be suggestive are the following:
  - Profound hyperventilation in the setting of acute metabolic acidosis (Kussmaul respiration)
  - Papilledema with severe, acute hypercapnia in the setting of acute respiratory acidosis
  - Neurologic symptoms in acute respiratory alkalosis (paresthesias, numbness, light-headedness

# DIAGNOSTIC EVALUATION

- The diagnosis of acid-base disorders is made by measurement of serum electrolytes and ABGs.
- Measurement of the urine pH and plasma creatinine level can be useful in assessing renal function.

# Renal Tubular Acidosis

Renal tubular acidosis (RTA) is applied to a group of transport defects in the reabsorption of bicarbonate ($HCO_3^-$), the excretion of hydrogen ion ($H^+$), or both.

The RTA syndromes characterized by:

**Relatively normal GFR** .

Hyperchloremia Metabolic Acidosis (with normal plasma anion gap).

# Types of RTA

- Type 1 or distal RTA is associated with a defect in distal hydrogen ion excretion.
- Type 2 or proximal RTA is characterized by a reduction in proximal bicarbonate reabsorptive capacity.
- Type 3 is considered as infantile variant of type 1 RTA.
- Type 4 RTA or hypoaldosteronism is associated with hyperkalemia and a mild metabolic acidosis.

## Features of Classic Distal Renal Tubular Acidosis ("Type I")

Diminished distal $H^+$ secretion (autoimmune)
or backleak of secreted $H^+$ (ampho-B)

Plasma $[HCO_3^-]$ may be below 10 mEq/L

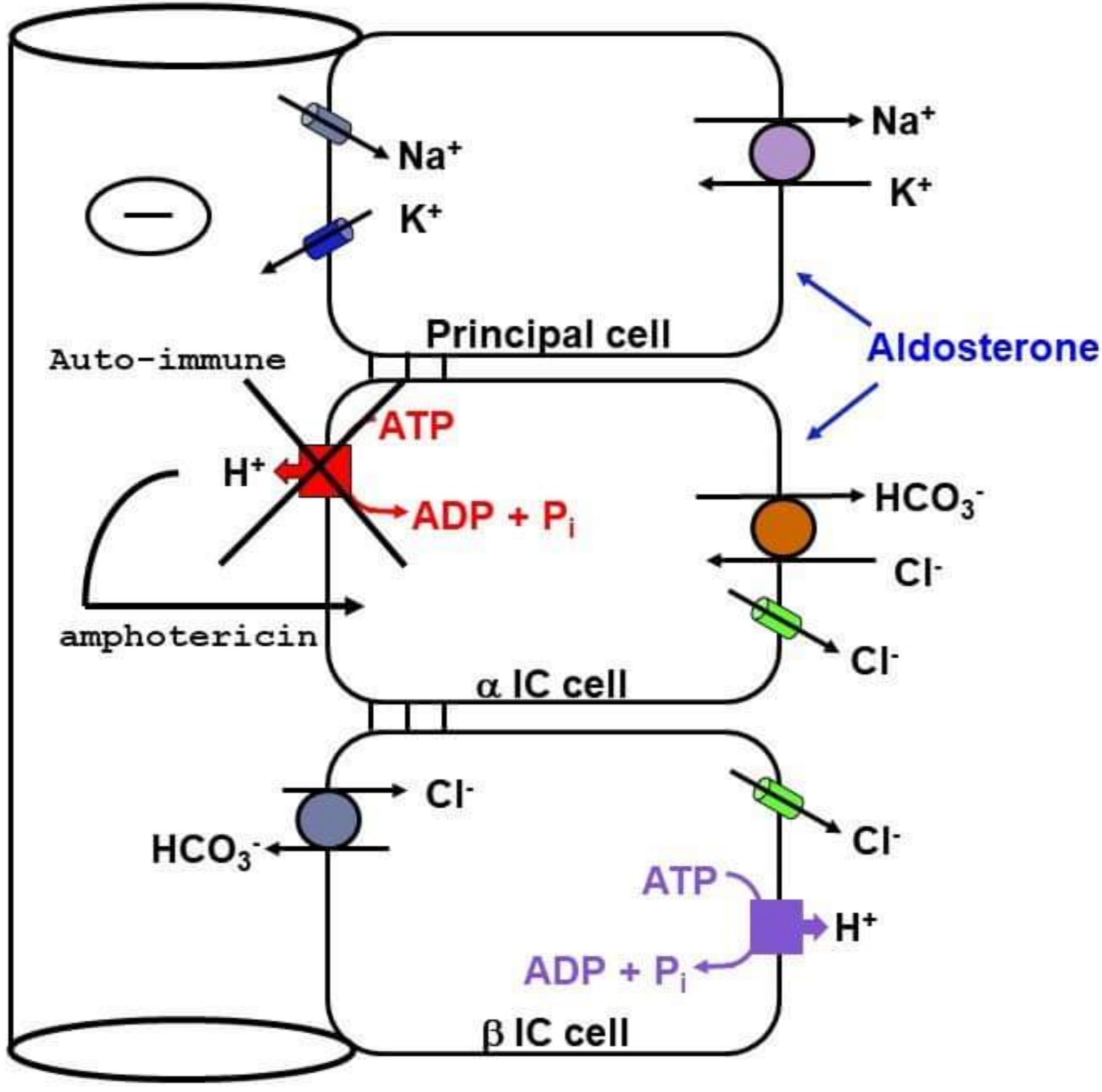
Urine pH always > 5.5

Fractional $HCO_3^-$ <3% plasma $[HCO_3^-]$

Plasma $[K^+]$ reduced

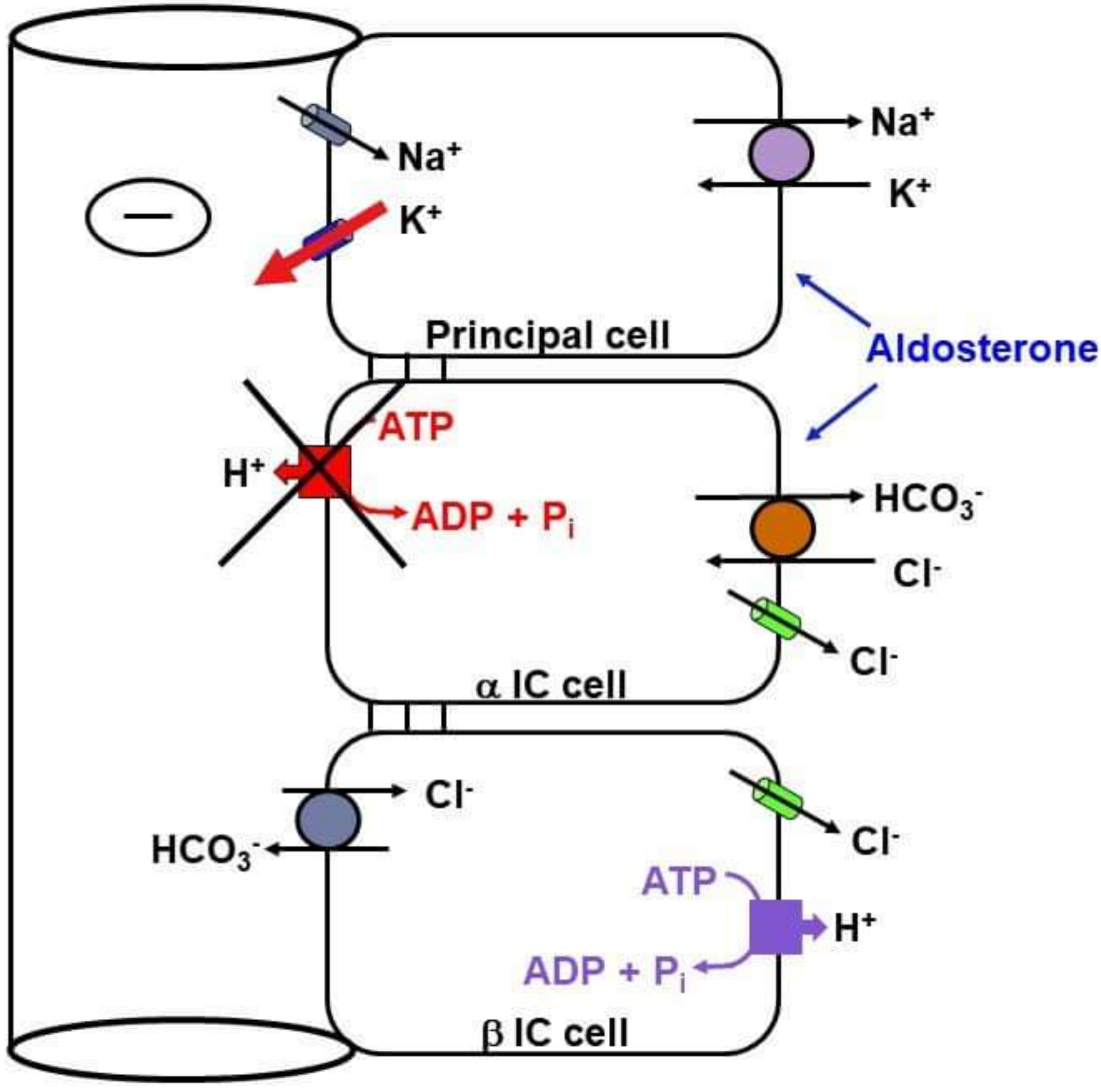
Dose of daily $HCO_3^-$ required: 1-2 mEq/kg/d

# Distal RTA

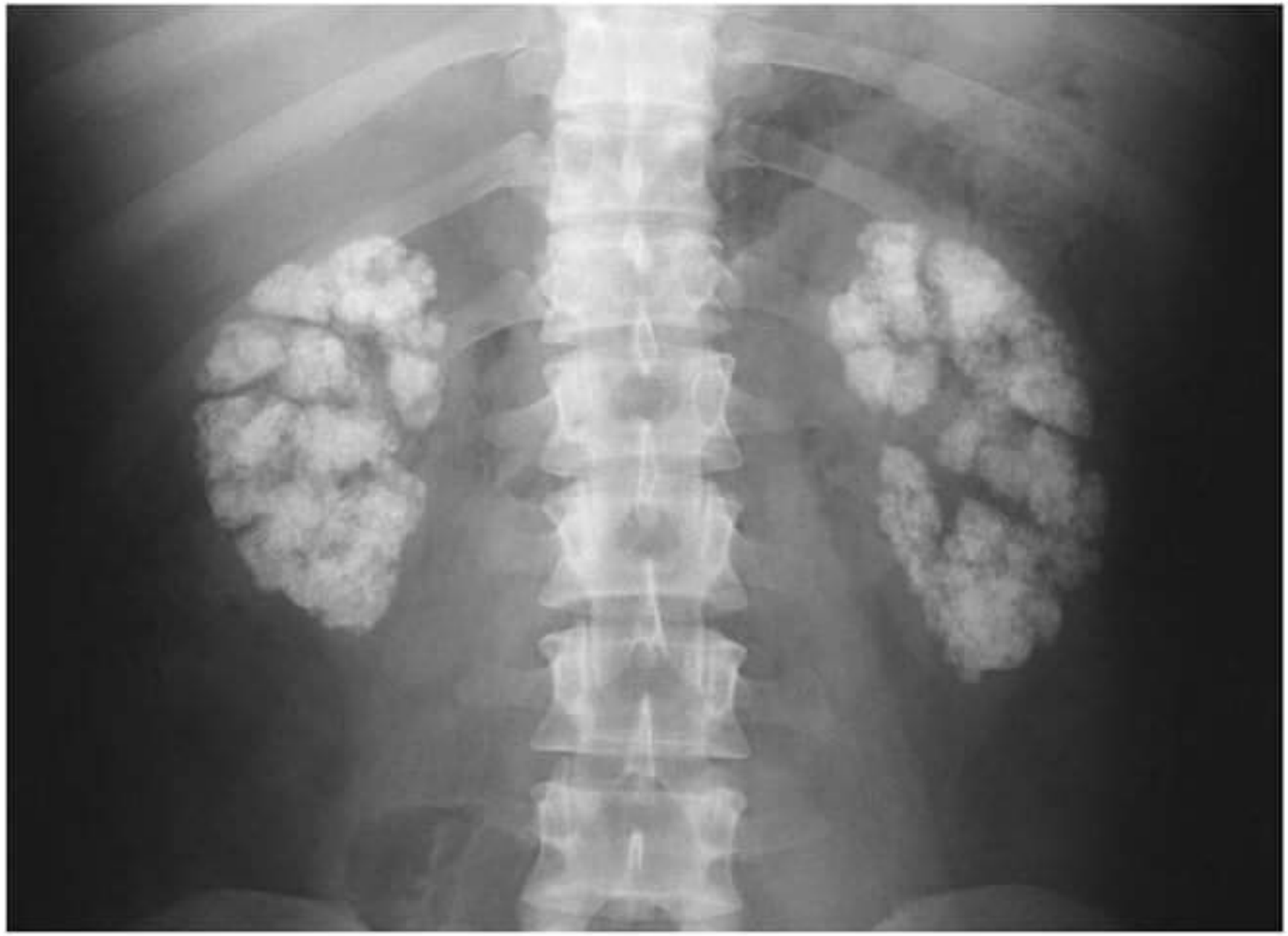

Na+
K+
Na+
K+
Principal cell
Aldosterone
Auto-immune
ATP
H+
ADP + Pi
HCO3-
Cl-
amphotericin
Cl-
α IC cell
Cl-
HCO3-
Cl-
ATP
H+
ADP + Pi
β IC cell

**Hypo-kalemia in distal RTA:**

**$H^+$ no longer shunts $Na^+$ current so $K^+$ must do so**



**A 37-year-old man was referred for evaluation of distal renal tubular acidosis**



Serrano A and Batlle D. N Engl J Med 2008;359:e1

# Type 1 distal RTA

**Causes**:

- Primary
  - Idiopathic, sporadic
  - Familial – AD, AR
- Secondary –
  - Autoimmune (SLE, Sjogren's, RA)
  - Hereditary hypercalciuria, hyperparathyroidism, Vit D intoxication
  - Hypergammaglobulinemia
  - Drugs (Amphotericin B, Ifosfamide, Lithium)
  - Chronic hepatitis
  - Obstructive uropathy
  - Sickle cell anemia
  - Renal transplantation

# Features of Proximal Renal Tubular Acidosis ("Type II")

Diminished proximal resorption of $HCO_3^-$

Plasma [$HCO_3^-$] 10-15 mEq/L

Urine pH depends on plasma [$HCO_3^-$]

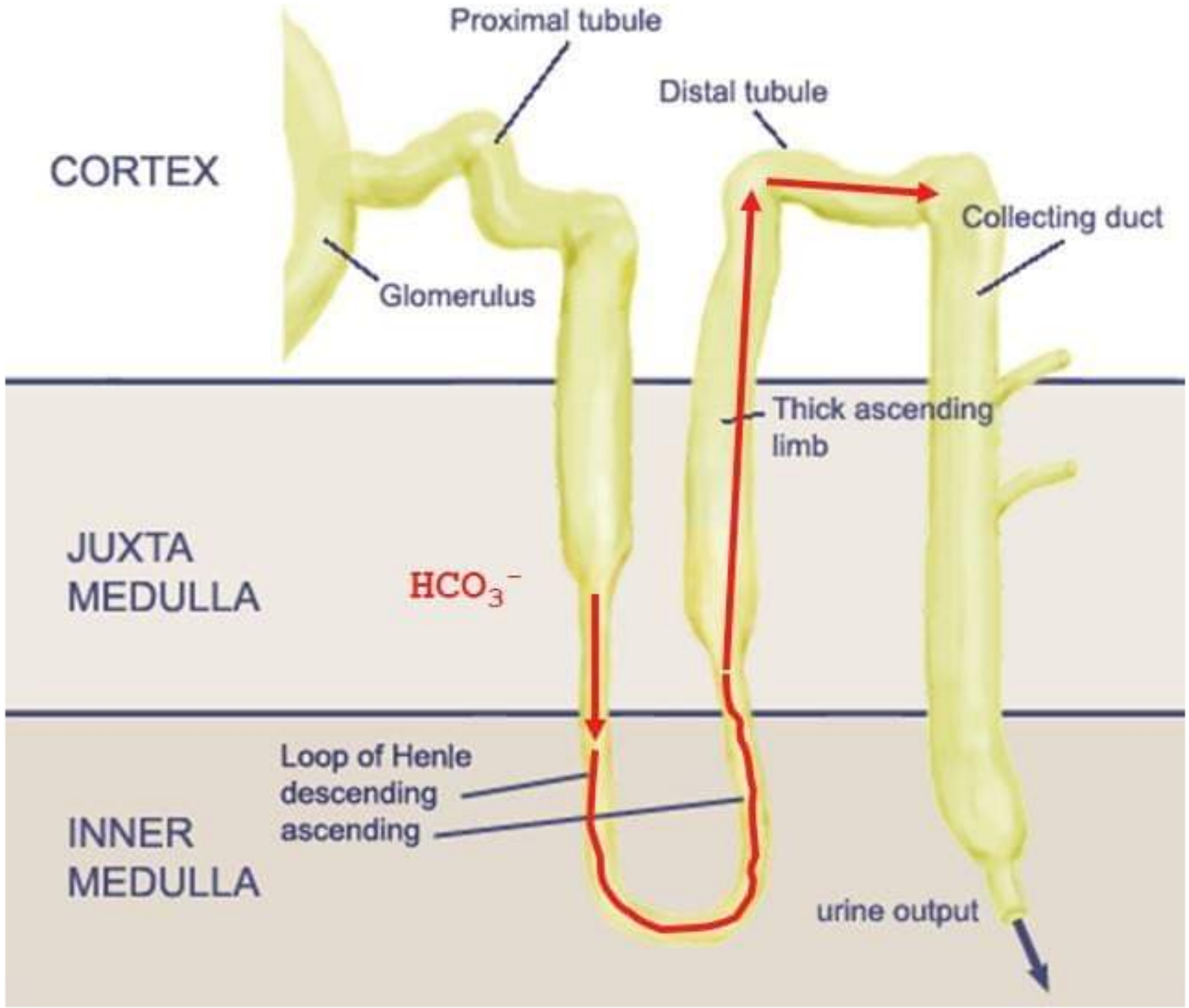
Fractional $HCO_3^-$ excretion high (15-20%)
at normal plasma [$HCO_3^-$]

Plasma [$K^+$] reduced, worsens with $HCO_3^-$ therapy

Dose of daily $HCO_3^-$ required: 10-15 mEq/kg/d

Non-renal: rickets or osteomalacia

# Type II Renal Tubular Acidosis ("RTA")



# Type 2 RTA

## Causes:

- Primary
  - Idiopathic, sporadic
  - Familial: Cystinosis, Tyrosinemia, Hereditary Fructose intolerance, Galactosemia, Glycogen storage disease (type 1), Wilson's disease, Lowe's syndrome
- Fanconi's Syndrome
  - Generalized proximal tubule dysfunction
  - Proximal loss of phos, uric acid, glucose, AA
- Acquired
  - Multiple Myeloma
  - Carbonic anhydrase inhibitors (Acetazolamide)
  - Other drugs (Ampho B, 6-mercaptopurine)
  - Heavy Metal Poisonings (Lead, Copper, Mercury, Calcium)
  - Amyloidosis
  - Disorders of protein, Carb, AA metabolism

→ Hypophosphatemia, hypouricosuria, renal glycosuria with normal serum glucose

# Features of the Hyperkalemic Distal RTAs

- Aldosterone deficiency or resistance ("voltage")

- Plasma [$HCO_3^-$] usually above 15 mEq/L

- Urine pH depends:
  - generally < 5.5 in hypoaldosteronism
  - generally > 5.5 in voltage defect

- Fractional $HCO_3^-$ excretion <3% at normal plasma [$HCO_3^-$]

- Plasma [$K^+$] elevated

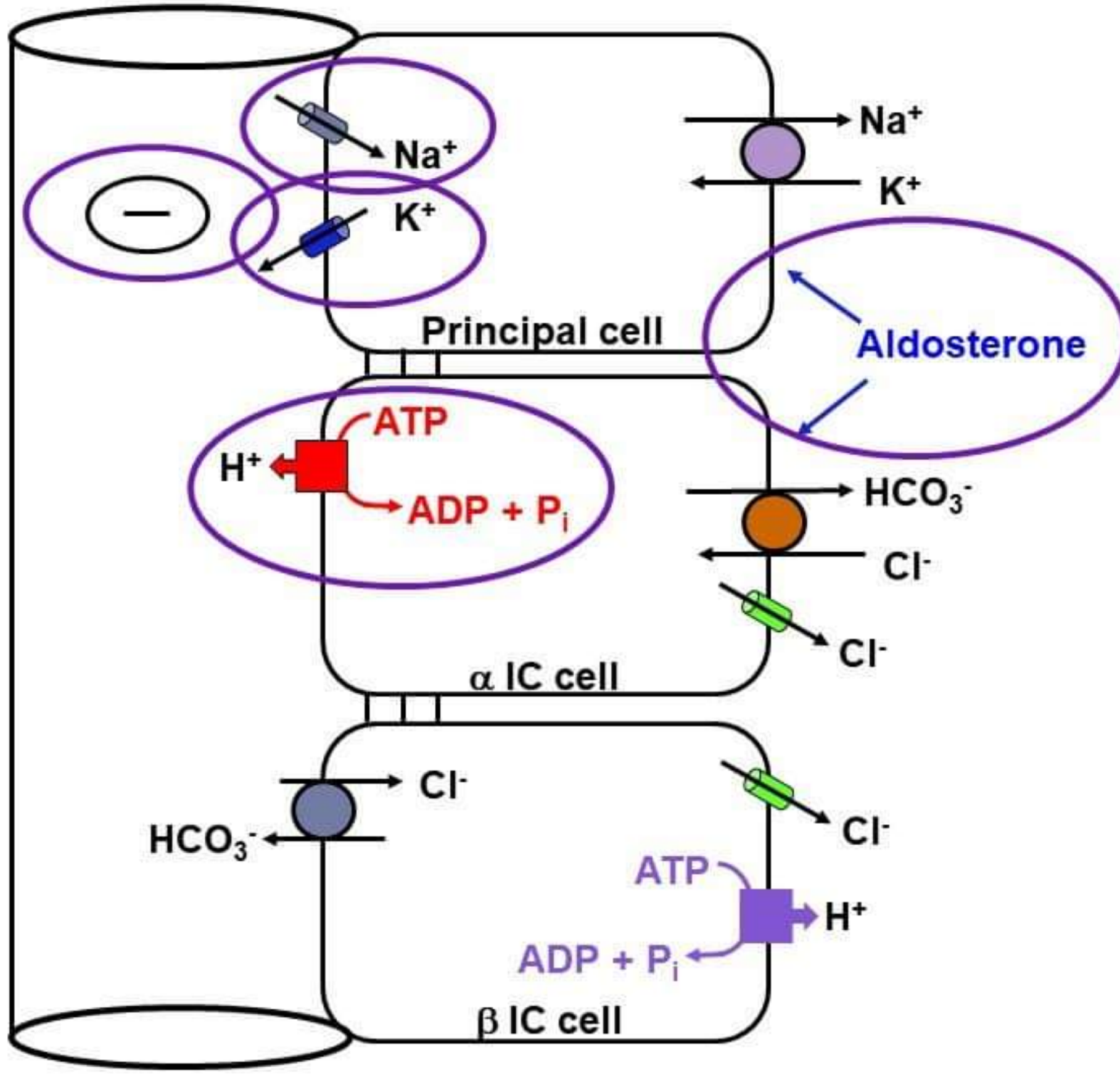
- Dose of daily $HCO_3^-$ required: 1-3 mEq/kg/d

- Non-renal: none

Hyporenin-
hypo
aldosteronism

Diabetes
is the main
cause

Other causes include NSAIDS, ACE inhibitors, adrenal insufficiency etc.



# Type 4 RTA

## Acquired Causes

- ↓ Renin:
  - Diabetic nephropathy
  - NSAIDS
  - Interstitial Nephritis
- Normal renin, ↓Aldo:
  - ACEs, ARBs
  - Heparin
  - Primary adrenal response
- ↓response to Aldo:
  - Medications: K+ sparing drugs (Sprinolactone), TMP-SMX, pentamidine, tacrolimus
  - Tubulointerstitial ds: sickle cell, SLE, amyloid, diabetes

# Characteristics of types 1,2,4 RTA

| | Type 1 | Type 2 | Type 4 |
|---|---|---|---|
| Primary defect | Impaired distal acidification of urine | Decreased proximal HCO3 reabsorption | Aldosterone def. or resistance |
| Urine PH | >5.3 | Variable >5.3 if HCO3 > reaborbed threshold and < 5.3 if below | ≤5.3 |
| Plasma HCO3 | May be <10meq/L | Above 12meq/L | Above 17meq/L |
| Plasma K | Usually reduced rarely elevated | Normal or reduced worsen by alkali | elevated |

| | Type 1<br>Distal | Type 2<br>Proximal | Type 4 |
|---|---|---|---|
| Fractional excretion of bicarbonate<br>When plasma HCO3-<br>>20meq/L | <3% | >15-20% | <3% |
| Diagnosis | Response to NaHCO3 or ammonium chloride | Response to NaHCO3 | Measurement of plasma aldosterone |
| Therapeutic amount of NaHCO3 required | 1-3 meq/kg/d | 10-15 meq/kg/d | 1-3 meq/kg/d |
| Non-electrolyte complications | Nephrocalcinosis and renal stones;<br>Osteomalacia uncommon | Rickets in children and Osteomalacia in adults; calculi is rare. | None |

# TREATMENT

- Several conditions may require specific therapeutic interventions:
  - metabolic acidosis in the setting of chronic renal failure (administration of oral bicarbonate), severe uncorrectable metabolic acidosis in the setting of acute renal failure (temporary hemodialysis).
- Metabolic alkalosis from volume and chloride loss (fluid replacement with saline solution).

Arterial Blood Sample

pH

< 7.4 ACIDOSIS

> 7.4 ALKALOSIS

$[HCO_3^-]$

< 24mM

METABOLIC

Respiratory compensation

$pCO_2$

< 40mmHg

$pCO_2$

> 40mmHg

RESPIRATORY

Renal compensation

$[HCO_3^-]$

> 24mM

$[HCO_3^-]$

> 24mM

METABOLIC

Respiratory compensation

$pCO_2$

> 40mmHg

$pCO_2$

< 40mmHg

RESPIRATORY

Renal compensation

$[HCO_3^-]$

< 24mM

# Diagnosis

- Clues to diagnosis of A/B disorder:
- 1. Serum $HCO3^-$:
  - ↑ → M.alkalosis
    - R.acidosis
  - ↓ → M.acidosis
    - R.alkalosis
- 2. Serum K:
  - ↑ $K^+$ → hypekalemic distal renal tubular acidosis
    - ( hyporenenemic hypoaldosteronism)
  - ↓ $K^+$ → M.alkalosis
    - Renal tubular acidosis

# KEY POINTS

- Metabolic acid exists as either carbonic acid or nonvolatile acids (which are buffered by the blood bicarbonate system).
- The lungs serve to eliminate carbonic acid as $CO_2$, and the kidneys are responsible for maintenance of the bicarbonate buffer system.
- Acidemia is a decrease in normal blood pH; alkalemia is an abnormal increase in blood pH.
- Disturbance in the acid-base balance can be classified as acidosis (addition of acid or loss of base) or alkalosis (loss of acid or addition of base). If the primary abnormality is related to bicarbonate balance, the disturbance is said to be metabolic. If the primary abnormality is related to $CO_2$ handing, the disturbance is said to be respiratory.
- For each primary acid-base disturbance, there is an appropriate compensatory response that attempts to counteract the primary change.
- To treat alkalemia or acidemia successfully, the underlying abnormality or abnormalities need to be identified and corrected. This permits the kidneys and lungs to restore acid-base balance.