

## Acid Base Balance and its Disturbances: Acidosis and Alkalosis

[See online here](#)

**Acid-base balance in the body is necessary for the proper functioning of body organs. Even a slight alteration in the level of acid or base may severely impact many organs. The balance between acid and base is controlled by different mechanisms occurring in the lungs, kidneys, and buffer systems. Acid-base disturbances are classified into metabolic acidosis, metabolic alkalosis, respiratory acidosis, and respiratory alkalosis based on the variations of blood pH and carbon dioxide exhalations, respectively. They are diagnosed through a blood test and lung function test after evaluation of respective symptoms and etiology.**



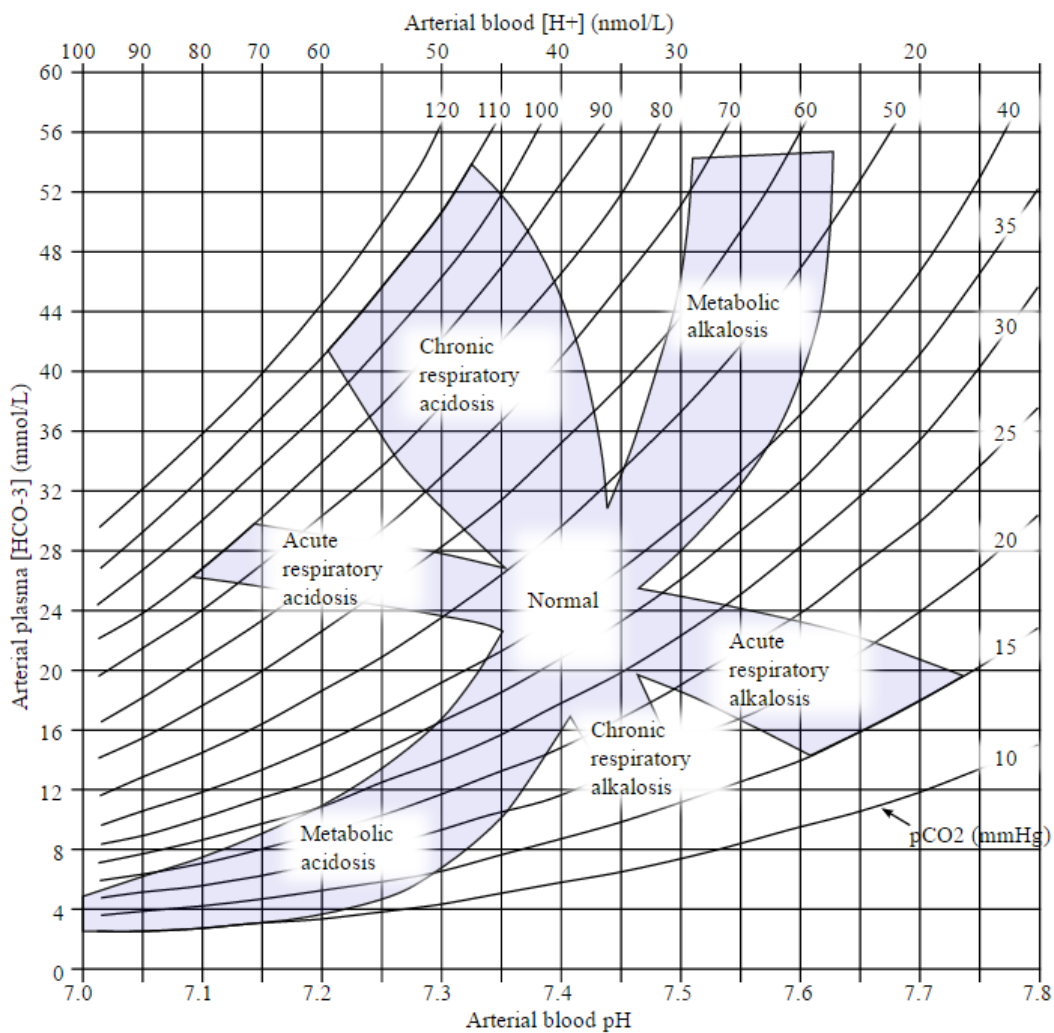
### Definition and Introduction

Acid-Base disorders are characterized by abnormal pH levels, the partial pressure of carbon dioxide ( $pCO_2$ ), and bicarbonate ( $HCO_3^-$ ) in the blood.

1. **Acidemia**- state of blood in which pH is  $< 7.35$ .
2. **Alkalemia**- state of blood with serum pH  $> 7.45$ .

**Acidosis** defines all processes in which acid accumulation or alkali loss leads to a reduction in pH level. Alkalosis is characterized by all processes resulting in excess production of alkali or excess acid loss.

**Physiologic compensatory mechanisms** are activated in the body; change in pH levels depends on the degree of these compensatory mechanisms.

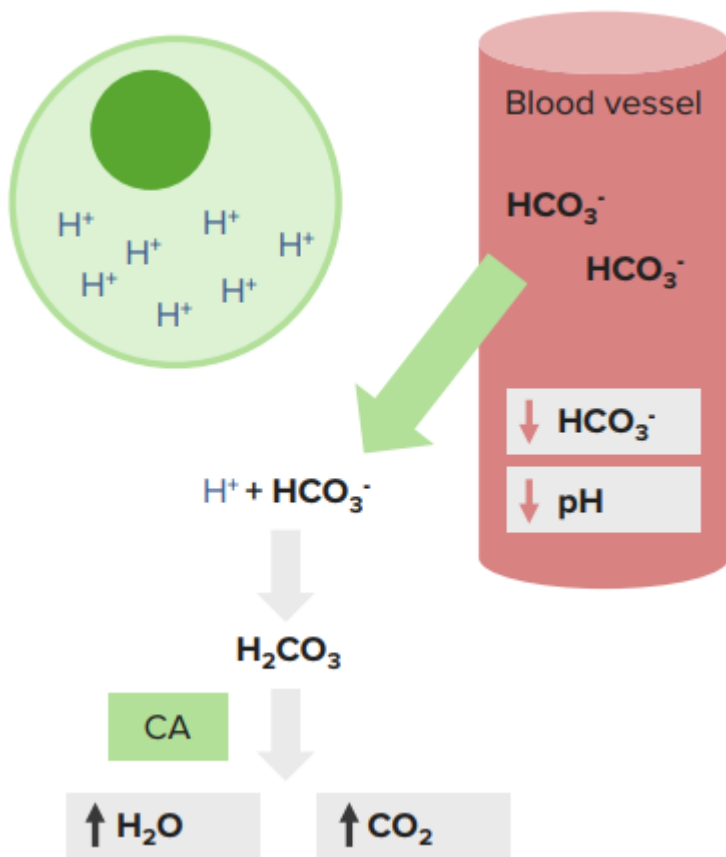


**Image:** "An acid base nomogram for human plasma, showing the effects on the plasma pH when carbonic acid (partial pressure of carbon dioxide) or bicarbonate occur in excess or are deficient in the plasma" by Huckfinne - Own work. License: [Public Domain](#)

## Volatile and Non-Volatile Acids

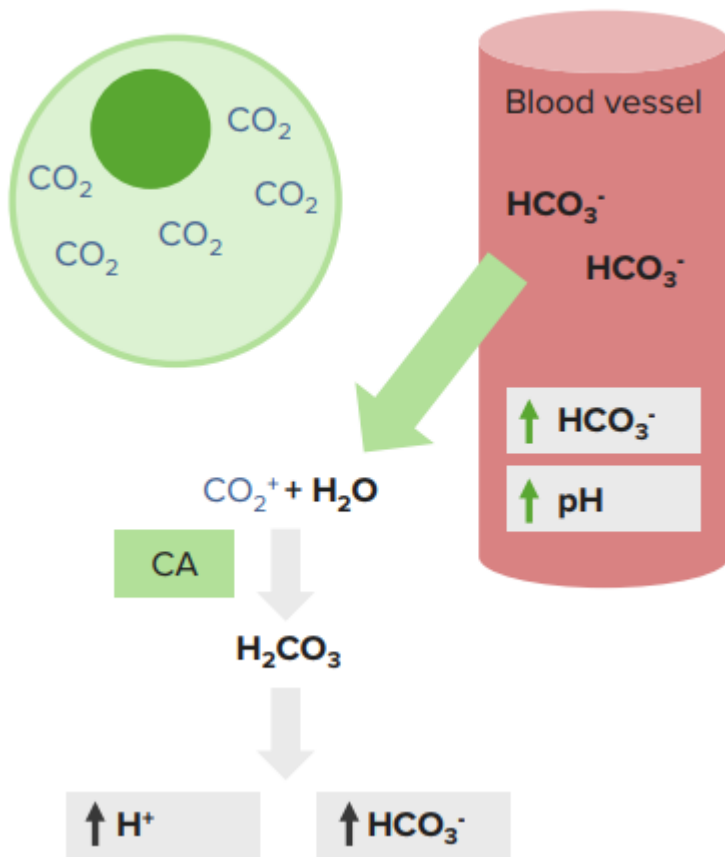
### Volatile Acids

1. CO<sub>2</sub>

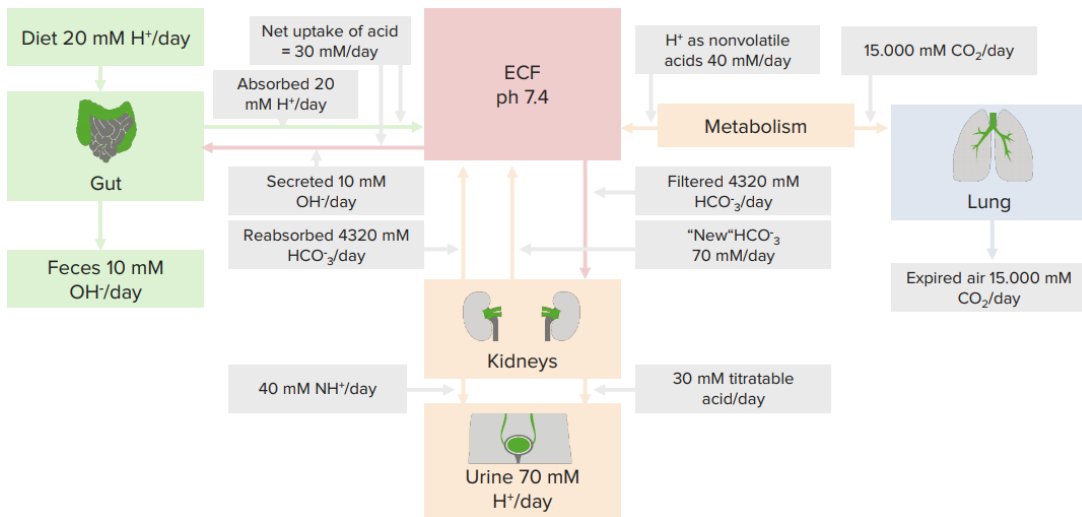


## Non-volatile acids

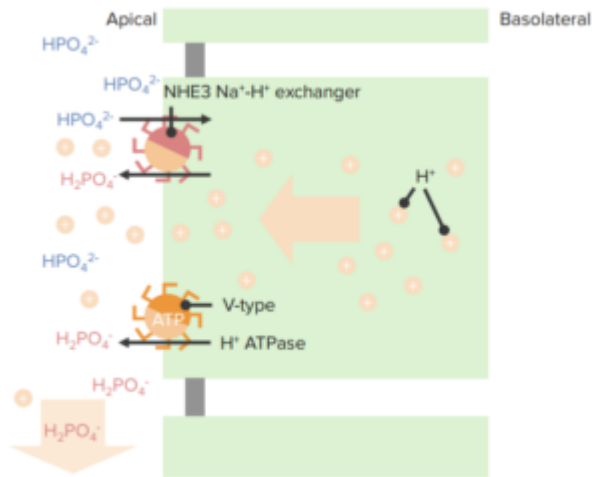
1. Sulfur-containing amino acid (e.g., cysteine)
2. Phosphorus-containing compounds
3. Cationic amino acid (e.g., lysine)
4. Uric acid
5. Lactic acid
6. Keto acids



### Typical daily acid handling



### Titratable acids



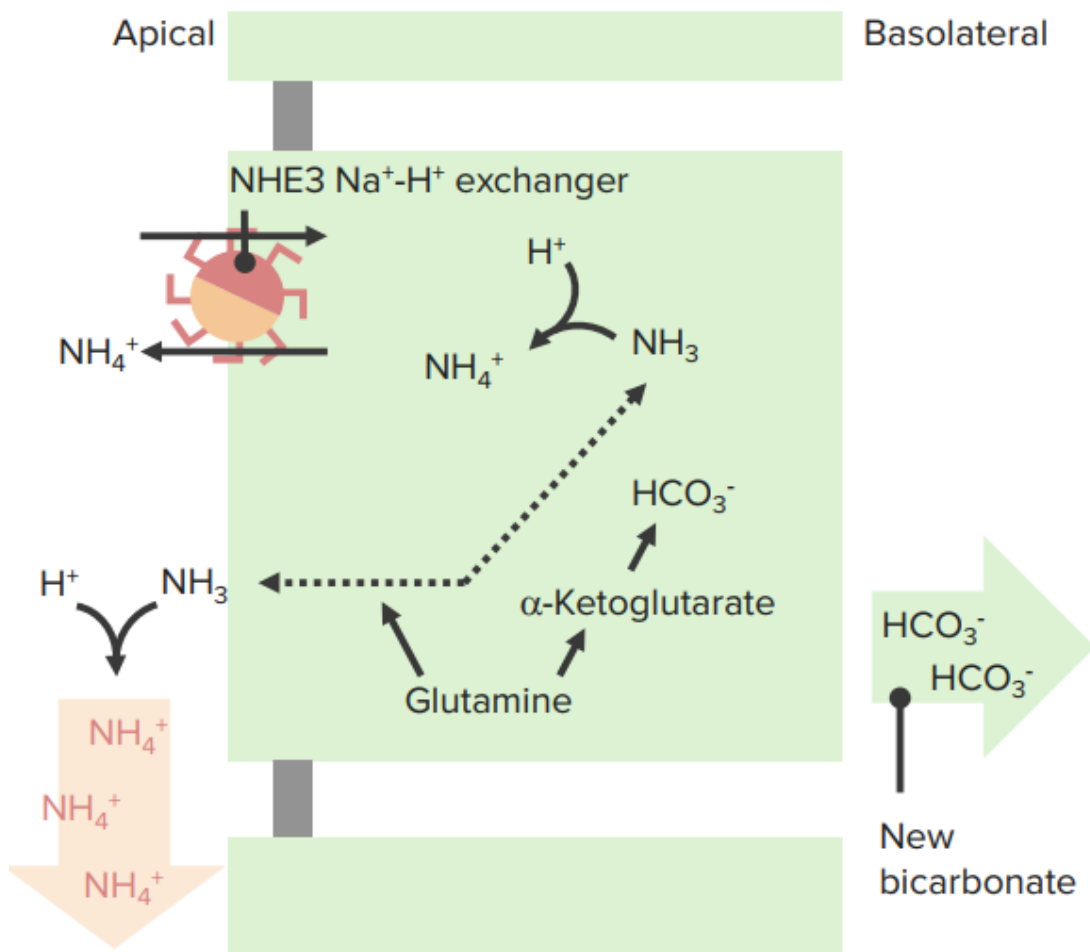
Phosphate (pK = 6.8)

- 1.
2. Urate (pK = 5.8)
3. Creatinine (pK = 5.0)
4. Lactate (pK = 3.9)\*
5. Pyruvate (pK = 2.5)\*

\* minor roles

$\text{NH}_3/\text{NH}_4^+$

- $\text{NH}_3$  is membrane permeable
- "New"  $\text{HCO}_3^-$  ~ 60 % in PT



# Classification of Acid-Base Balance Disorders

Clinically, the primary causes of acid-base imbalance responsible for changes in pH, (and thus changes in serum  $\text{HCO}_3^-$  or  $\text{pCO}_2$  ) are:

- Metabolic
- Respiratory

Metabolic acidosis and metabolic alkalosis are caused by an imbalance in the production of acids or bases and their excretion by the kidneys.

Respiratory acidosis and respiratory alkalosis are caused primarily by changes in carbon dioxide exhalation due to lung or breathing disorders.

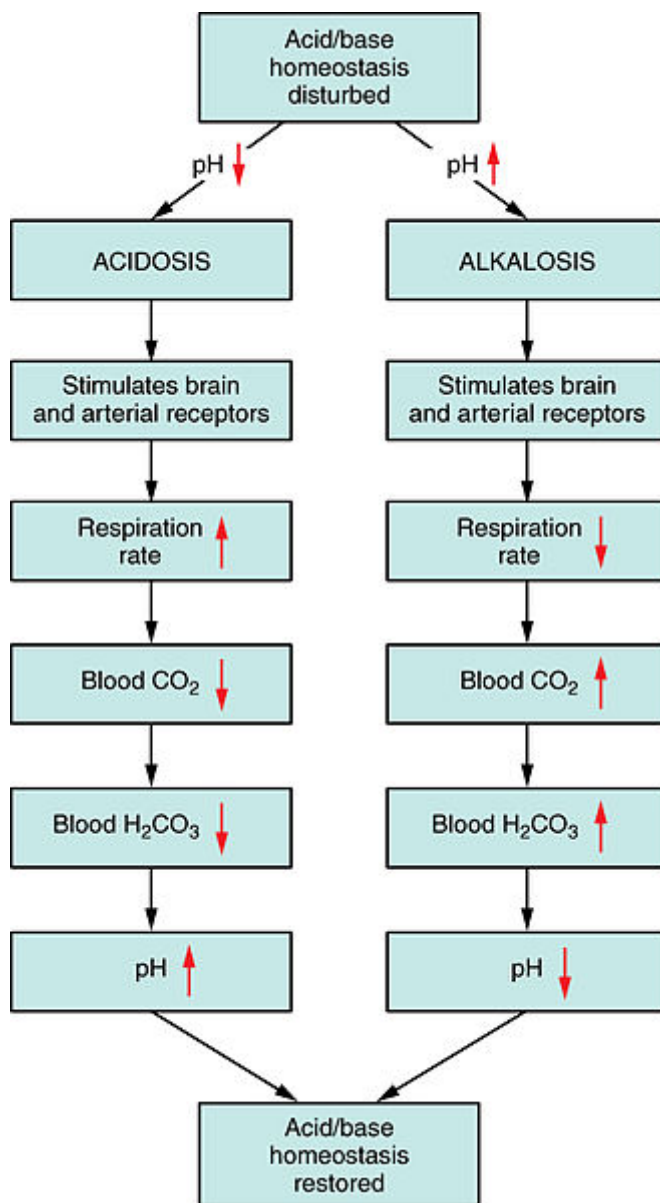


Image: "Respiratory Regulation of Blood." by Anatomy & Physiology, Connexions. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

# Metabolic Acidosis

If serum  $\text{HCO}_3^-$  is less than 24 mEq/L, it is classified as metabolic acidosis. The body compensates by hyperventilation, i.e., the rate of breathing increases and  $\text{CO}_2$  is lost from the body. The body tries to maintain pH through compensatory mechanisms. It initiates a high or normal anion gap where anions may or may not be present.

## Causes

Causes of metabolic acidosis are an increase in acid production, excess acid intake, reduced excretion of acid by kidneys, or loss of negatively charged bicarbonates by the GI and kidneys.

Before discussing the causes of acidosis, we need to learn about the anion gap.

**Anion gap:** It is the sum of the concentrations of all the major cations (sodium + potassium ion concentration) minus the sum of the concentrations of all the anions (chloride + bicarbonate ions). Positive ion concentration is higher than the negative ions by roughly 14 mmol/L. The normal anion gap is 8–16 mmol/L without potassium in the equation, and 10–20 mmol/L with potassium.

The anion gap exists because there are more unmeasured anions (phosphates, lactate, and sulfate) than cations (potassium, calcium, and magnesium).

The anion gap exists because there are more unmeasured anions (mostly albumin, but others include lactate and sulfate) than cations (calcium and magnesium).

Metabolic acidosis is divided into an increased and normal anion gap.

### Increased anion gap:

1. Lactic acidosis: [shock](#), infection, [hypoxia](#)
2. [Renal failure](#)
3. Raised ketones ([diabetes mellitus](#) (DKA), alcohol)
4. [Drugs or toxins](#): salicylates, metformin, ethylene glycol, methanol, cyanide

### Normal anion gap (due to loss of bicarbonate or ingestion of hydrogen ions):

1. Renal tubular acidosis
2. [Addison's disease](#)
3. Pancreatic fistulae
4. Drugs or toxins: acetazolamide, ammonium chloride

DKA is a complication of uncontrolled type I diabetes mellitus in which surplus ketone bodies are produced as a result of [gluconeogenesis](#).

Lactic acidosis is due to surplus lactic acid production in the body as a result of:

- Prolonged exercise and lack of oxygen
- Low blood sugar, or hypoglycemia
- [Alcohol use](#)
- [Liver failure](#)
- Severe [dehydration](#) or [shock](#)

**Hyperchloremic acidosis** occurs after the loss of bicarbonate through the stools in severe watery [diarrhea](#).

## SYMPTOMS OF ACIDOSIS

### Central Nervous System

Headache  
Sleepiness  
Confusion  
Loss of consciousness  
Coma

### Respiratory System

Shortness of breath  
Coughing

### Heart

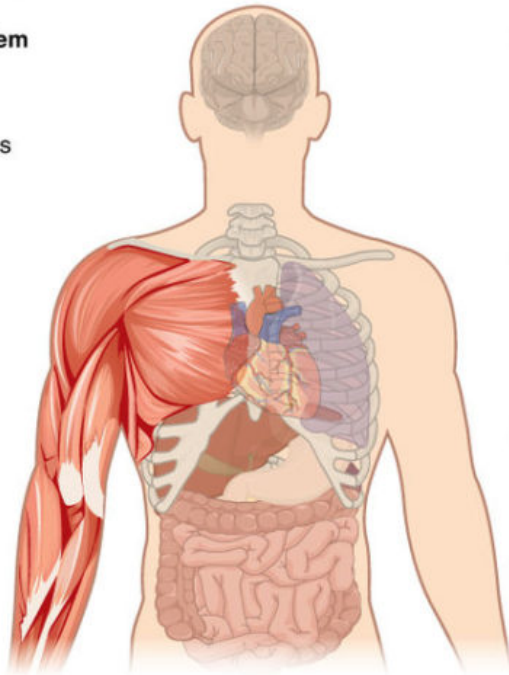
Arrhythmia  
Increased heart rate

### Muscular System

Seizures  
Weakness

### Digestive System

Nausea  
Vomiting  
Diarrhea



## SYMPTOMS OF ALKALOSIS

### Central Nervous System

Confusion  
Light-headedness  
Stupor  
Coma

### Peripheral Nervous System

Hand tremor  
Numbness or tingling in  
the face, hands, or feet

### Muscular System

Twitching  
Prolonged spasms

### Digestive System

Nausea  
Vomiting

Image: "Symptoms of Acidosis and Alkalosis." by Anatomy & Physiology, [Connexions](#). License: [CC BY-SA 3.0](#)

## Clinical Symptoms

In mild metabolic acidosis, people may have no symptoms but usually experience:

1. **Nausea**
2. **Vomiting**
3. **Fatigue**

Kussmaul breathing is a typical breathing pattern in metabolic acidosis, i.e., deeper and slightly faster (the body tries to correct acidosis by removing CO<sub>2</sub>). In extreme cases, cardiac issues may develop, and the blood pressure falls, leading to shock, coma, and even death.

## Metabolic Alkalosis

If the arterial blood gas and electrolytes show alkalemia and serum HCO<sub>3</sub><sup>-</sup> is more than 24 mEq/L, it will be labeled as metabolic alkalosis.

## Causes

1. Vomiting
2. [Hypokalemia](#)—e.g., [diuretics](#). See also the separate article on hypokalemic alkalosis
3. Excessive alkali drugs, such as for acid dyspepsia
4. Burns

A major cause of metabolic alkalosis is the loss of stomach acid after persistent vomiting.

The body compensates by reducing the respiratory rate and retaining CO<sub>2</sub> to try and



maintain body pH.

The symptoms of metabolic alkalosis are headache, lethargy, and tetany.

Figure 11

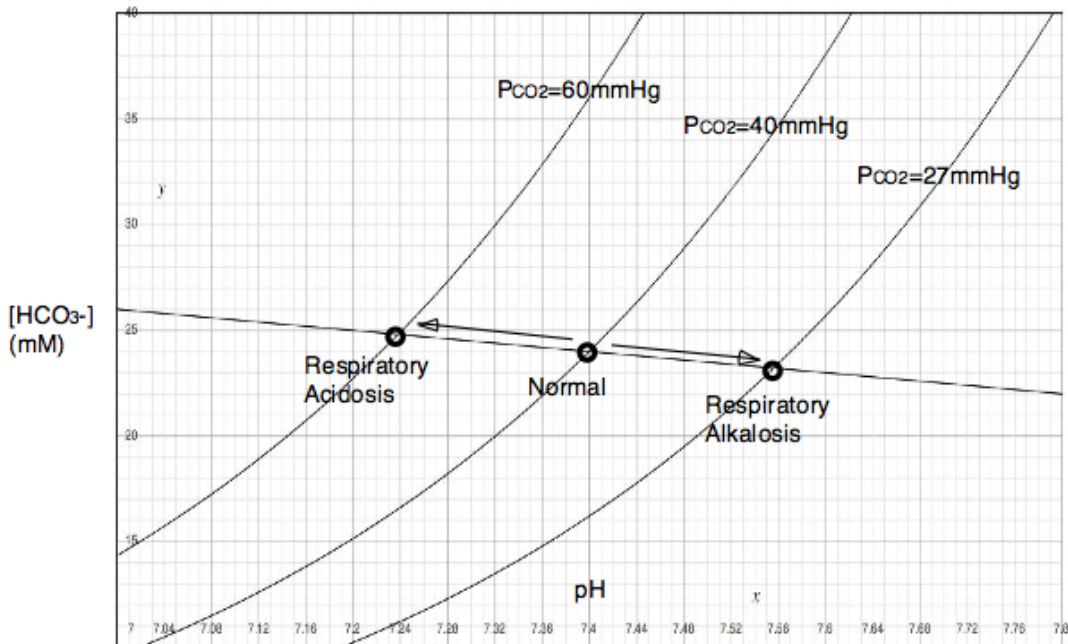


Image: "Davenport diagram." by K90 - Own work. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

## Respiratory Acidosis

Respiratory acidosis is a state of the body in which partial pressure of the CO<sub>2</sub> is more than 40 mm Hg ([hypercapnia](#)), along with acidic arterial pH.

## Causes

### Acute Onset Acidosis:

1. Depression of the central respiratory center by cerebrovascular disease or drugs ([coma](#))
2. Inability to ventilate adequately due to neuromuscular disease e.g., [myasthenia gravis](#), [amyotrophic lateral sclerosis](#), [Guillain-Barré syndrome \(GBS\)](#), [muscular dystrophy](#)
3. Airway obstruction related to [asthma](#) or exacerbation of [chronic obstructive pulmonary disease \(COPD\)](#)

Acute acidosis is worse than respiratory acidosis. It has symptoms like headache, confusion, stupor, drowsiness with signs like tremors, myoclonic jerks, and asterixis.

### Chronic Onset Acidosis:

Chronic respiratory acidosis can occur secondary to [COPD](#), [obesity hypoventilation syndrome \(Pickwickian syndrome\)](#), [neuromuscular disorders](#), and restrictive ventilatory defects, such as in [interstitial fibrosis](#) or thoracic deformities. Chronic acidosis is asymptomatic.

# Respiratory Alkalosis

When  $p\text{CO}_2$  falls below 40 mm Hg (hypocapnia) along with alkalemia in the arterial blood, it is called respiratory alkalosis.

pH level may be near normal or high. Respiratory alkalosis may be acute or chronic in onset. The symptoms of acute respiratory alkalosis are light-headedness, confusion, cramps, paresthesia, and syncope with the signs of hyperpnea or tachypnea and spasms. Chronic respiratory alkalosis remains asymptomatic.

## Causes

Increase in minute ventilation (persistent hyperventilation) due to any cause like anxiety, [stroke](#), meningitis, altitude, and pregnancy can lead to respiratory alkalosis.

Figure 11

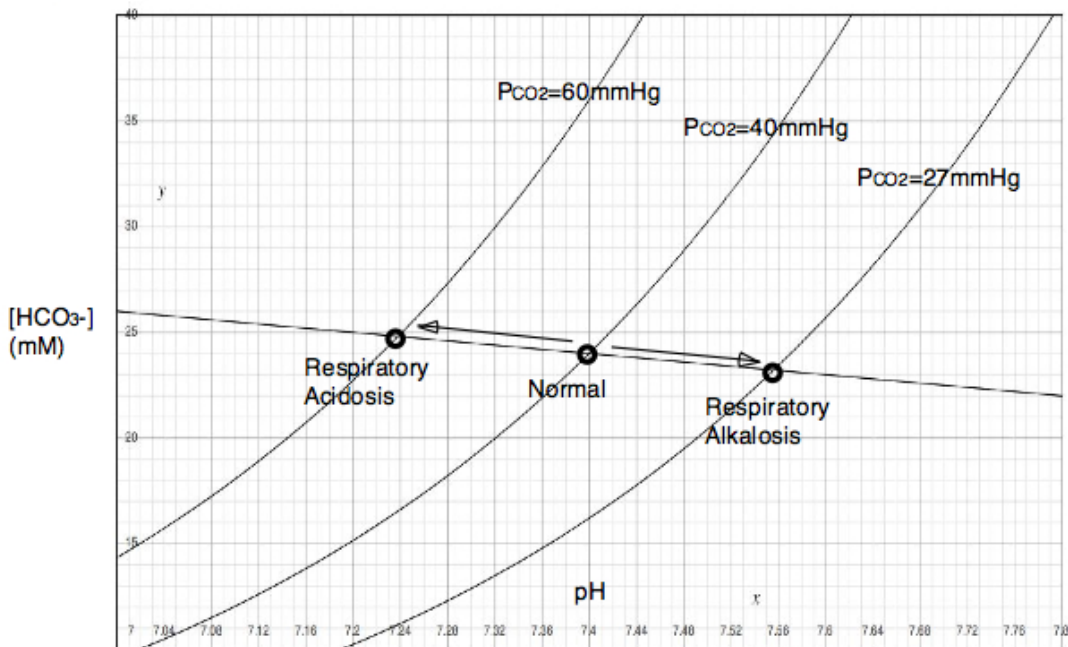


Image: "Davenport diagram." by K90 - Own work. License: [CC BY-SA 3.0](#)

## Diagnosis of Acid-Base Disturbances

For the diagnosis of acidosis or alkalosis, the following investigations are needed:

1. **Arterial blood Gases—ABG with pH,  $\text{Pco}_2$ ,  $\text{Po}_2$**
2. **Serum electrolytes**
3. **Anion gap calculated**

The ABG directly measures arterial pH and  $p\text{CO}_2$ . In cases of CVS failure, venous blood gasses (VBG) may more accurately reflect conditions at the tissue level and may be a more useful guide to bicarbonate administration and adequacy of ventilation. Bicarbonate levels on ABG are directly measured and calculated using the Henderson-Hasselbalch equation.

# Renal Tubular Acidosis

Renal tubular acidosis (RTA) is a type of acidosis in which an electrolyte disturbance in the body leads to chronic metabolic acidosis with a normal anion gap. RTA can occur after abnormal renal H<sup>+</sup> ion excretion (type 1 RTA), impaired bicarbonate resorption (type 2 RTA), or abnormal aldosterone production/ response (type 4 RTA). Type 3 RTA is a very rare condition, so it is not discussed. RTA, if not managed properly, can complicate chronic renal failure (CRF).

## Type 1—Distal Renal Tubular Acidosis (RTA)

H<sup>+</sup> ion secretion into the distal tubule by the alpha-intercalated cells of the medullary collecting duct is impaired in type I RTA, resulting in a high urine pH (> 5.5) and metabolic acidosis. In distal RTA, serum HCO<sub>3</sub><sup>-</sup> < 15 mEq/L along with hypokalemia, hypercalciuria, and decreased citrate excretion. Nephrocalcinosis and nephrolithiasis are possible complications and present in many distal RTA patients.

## Causes

It can be primary or secondary. Familial cases manifest in childhood and are autosomal dominant (AD).

### Secondary causes include:

- Autoimmune disease with hypergammaglobulinemia, particularly Sjögren syndrome or RA
- [Kidney transplantation](#)
- Nephrocalcinosis
- Medullary sponge kidney
- Chronic obstructive uropathy
- Drugs (mainly amphotericin B, ifosfamide, and lithium)
- Cirrhosis
- [Sickle cell anemia](#)

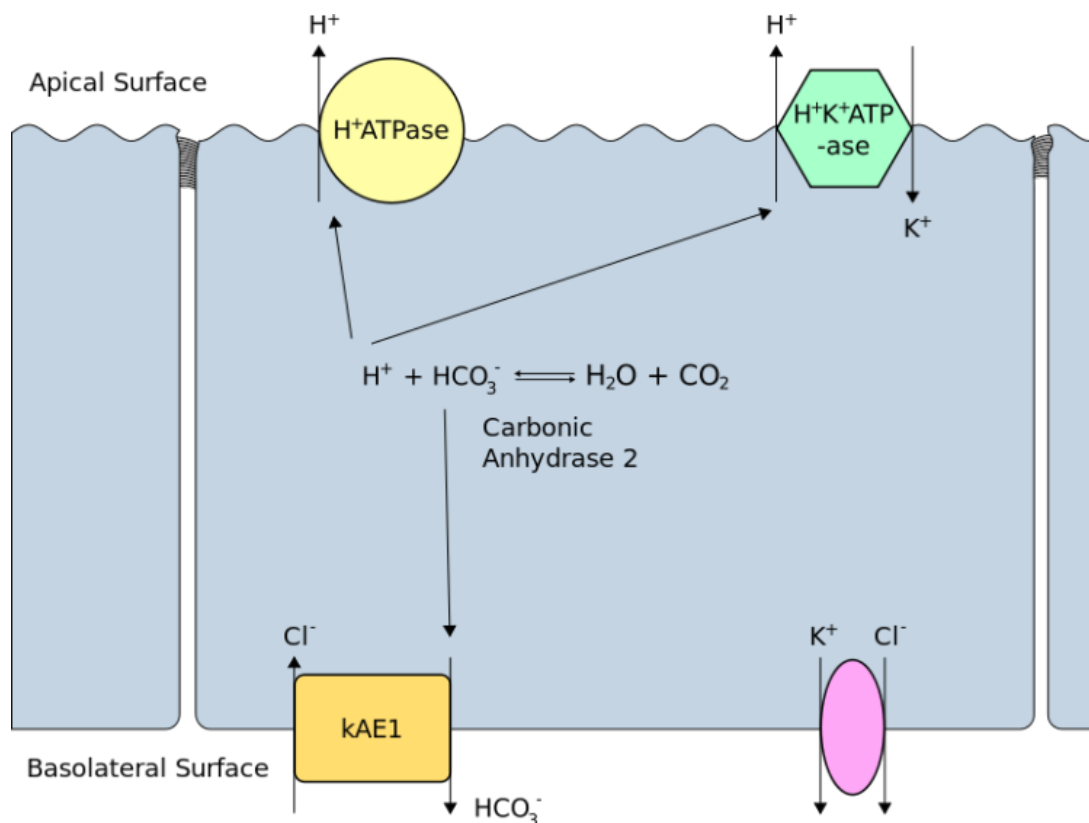


Image: "Alpha intercalated cell with the apical proton pump and basolateral band." by Rswarbrick. License: [CC BY 3.0](https://creativecommons.org/licenses/by/3.0/)

## Type 2—Proximal Renal Tubular Acidosis (RTA)

The main etiology behind this is the inability to reabsorb bicarbonate in the proximal tubules with a urine pH > 7 if the plasma bicarbonate concentration is normal, and a urine pH < 5.5 if the plasma bicarbonate concentration is already depleted due to ongoing losses. The generalized inadequate function of proximal tubules contributes to this syndrome. These patients can have an increased urinary excretion of glucose, uric acid, phosphate, amino acids, citrate, calcium, potassium, and proteins as well.

Patients develop [osteomalacia or osteopenia \(rickets in children\)](#). Hypercalciuria, hyperphosphaturia, [disturbed vitamin D metabolism](#), and secondary hyperparathyroidism are the major complications.

### Causes

- [Fanconi syndrome](#)
- Light chain nephropathy due to multiple myeloma
- Various drug exposures (usually acetazolamide, sulfonamide, ifosfamide, outdated tetracycline or streptozotocin)

## Type 4—Renal Tubular Acidosis (RTA)

Aldosterone deficiency or loss of sensitivity of the collecting ducts to aldosterone is the main cause of type 4 RTA. Reduced potassium excretion leads to hyperkalemia and reduced acid excretion leading to mild metabolic acidosis with a normal anion gap (i.e., a

hyperchloremic acidosis) because of the renal ability to compensate. This is the most common type of RTA. Urine pH is usually similar to serum pH. It is < 5.5 when there is serum acidosis.

It's secondary to impairment in the renin-aldosterone-renal tubule axis in:

**It's secondary to impairment in the renin-aldosterone-renal tubule axis in:**

- [Diabetic nephropathy](#)
- Chronic [interstitial nephritis](#)

**Other factors that can contribute to type 4 RTA include the following:**

- [ACE inhibitor use](#)
- Aldosterone synthase type I or II deficiency
- Angiotensin II receptor blocker use
- [Chronic kidney disease](#), usually due to diabetic nephropathy or chronic interstitial nephritis
- [Congenital adrenal hyperplasia](#), particularly a 21-hydroxylase deficiency
- HIV nephropathy (due, possibly in part, to infection with Mycobacterium avium complex or cytomegalovirus)
- Interstitial renal damage (e.g., due to SLE, obstructive uropathy, or sickle cell disease)
- Potassium-sparing diuretics (e.g., amiloride, eplerenone, spironolactone, triamterene)
- Obstructive uropathy
- Primary adrenal insufficiency
- Aldosterone deficiency is the most frequently seen form of hyperkalemic metabolic acidosis in adults
- Pseudohypoaldosteronism (type I or II)
- Volume expansion (e.g., in acute glomerulonephritis or chronic kidney disease)

## Different Types of Renal Tubular Acidosis

Feature	Type 1	Type 2	Type 3
<b>Incidence</b>	Rare	Very rare	Common
<b>Mechanism</b>	Impaired hydrogen ion excretion	Impaired bicarbonate resorption	Decrease in aldosterone secretion or activity
<b>Plasma bicarbonate (mEq/L)</b>	Frequently < 15, occasionally < 10	Usually 12—20	Usually > 17
<b>Plasma potassium</b>	Usually low but tends to normalize with alkalinization	Usually low and decreased further by alkalinization	High
<b>Urine pH</b>	> 5.5	> 7 if plasma bicarbonate is normal < 5.5 if plasma bicarbonate is depleted (e.g., < 15 mEq/L)	< 5.5

## References

*Acid-Base Balance*. Retrieved March 12, 2018, from

<https://www.healthline.com/health/acid-base-balance>

Lewis, J. L. *Overview of Acid-Base Balance – Hormonal and Metabolic Disorders*. Retrieved March 12, 2018, from

<https://www.msdmanuals.com/home/hormonal-and-metabolic-disorders/acid-base-balance/overview-of-acid-base-balance>

Lewis, J. L. *Acid-Base Disorders – Endocrine and Metabolic Disorders*. Retrieved March 12, 2018, from

<https://www.merckmanuals.com/professional/endocrine-and-metabolic-disorders/acid-base-regulation-and-disorders/acid-base-disorders>

Lewis, J. L. *Acidosis – Hormonal and Metabolic Disorders*. Retrieved March 12, 2018, from

**Legal Note:** Unless otherwise stated, all rights reserved by Lecturio GmbH. For further legal regulations see our [legal information page](#).

Notes