🧪 Acids vs. Bases

- **Normal Acid:Base ratio ≈ 1:20** → Meaning for every 1 acid molecule, there are 20 base molecules to maintain balance.
- **Acid** = a substance that **donates protons** (H^+ ions).
- **Base** = a substance that **receives protons** (H^+ ions).
- **Strength** of an acid or base depends on how **easily** it **gives** or **takes** hydrogen ions (H^+) in water.

In water = the biological solvent.

🧪 pH Concept

- **pH** tells **how much H^+** is in a solution.
- **pH is an *indirect measure* of $[H^+]$**.

Formula: → $pH = -\log[H^+]$ (as H^+ increases, pH drops)

- **Important detail:**

Hydrogen ions **do not float free** — they are **linked to adjacent water molecules** by hydrogen bonds (H_3O^+).

- **If $[H^+]$ doubles**, pH **drops by 0.3**.
- **Normal plasma pH** = **7.36–7.44** (slightly alkaline, not exactly neutral).

pH 7.0 is chemically neutral, but in the body it's **fatal**.

pH	$[H^+]$
7.40	40 nM
7.36	44 nM
7.44	36 nM
7.00	100 nM

🧪 Buffers Overview

Buffers = substances that **stabilize pH** by accepting or donating H^+ ions.

- **Extracellular buffers** (in plasma):

Main: **Carbonic acid/Bicarbonate (H_2CO_3/HCO_3^-) system**.

- **Intracellular buffers** (inside cells):

Proteins (like Albumin).

Phosphoric acid / Hydrogen phosphate system ($H_3PO_4/H_2PO_4^-/HPO_4^{2-}$).

- **Special buffer:**

Hemoglobin binds or releases H^+ depending on needs.

- **Equation to relate them: → Henderson–Hasselbalch equation** → $pH = 6.1 + \log([HCO_3^-]/(0.03 \times PCO_2))$

(Modified form: $[H^+] = 24 \times PCO_2 \div [HCO_3^-]$)

- **Lungs** control **CO_2** (fast).
- **Kidneys** control **HCO_3^-** (slow).

🧪 Plasma pH Balance Diagram

H^+ input comes from:

- **Diet** (Fatty acids, Amino acids).
- **Metabolism** (CO_2, Lactic acid, Ketoacids).

Buffers work to neutralize:

- **HCO_3^-** in plasma.
- **Proteins, Hemoglobin, Phosphates** inside cells.
- **Phosphates and Ammonia** in urine.

H^+ output:

- **Respiration** removes CO_2 (lungs).
- **Kidneys** excrete H^+ (urine).

Organs Involved in Acid-Base Balance

🫀 **Blood and Plasma**:

- Blood stays balanced with plasma (the liquid part of blood).
- Blood has **high buffer capacity** (this means it can resist changes in pH).

✅ **Haemoglobin** (inside red blood cells):

- It's the **main buffer** for **CO_2** (carbon dioxide).
- It **stops pH from changing too much**.
- Other buffers: bicarbonate (HCO_3^-) and proteins/phosphates.

✏️ *Side note: Bicarbonate is the major extracellular buffer system.*

🫁 **Lungs (Ventilation)**:

- Lungs get rid of CO_2 by breathing.
- We normally remove **about 12,000 mmol of CO_2 every day**.

✏️ **If you breathe faster** → You throw out more CO_2 → You get rid of H^+ ions → **Less acidic** (prevent acidosis). ✏️ **If you breathe slower** → CO_2 builds up → H^+ ions build up → **More acidic** (causes acidosis).

🛑 Important:

- ↓ **Breathing = Hypoventilation** = Acidosis.
- ↑ **Breathing = Hyperventilation** = Alkalosis.

🛁 **Kidneys**:

- Kidneys **reabsorb bicarbonate (HCO_3^-)** — about **4,000–5,000 mmol/day**.
- They **excrete fixed acids** like sulfuric acid and phosphoric acid.
- About **100 mmol/day** of fixed acid is removed.

🆚 Compare:

- Lungs remove **volatile acid** (CO_2).
- Kidneys remove **fixed acids** (that can't evaporate).

Liver and Bone in Acid-Base Balance

🫀 **Liver**:

- Makes **CO_2** by **complete oxidation** of carbs, fats, proteins.
- About **20% of your body's daily CO_2** is made by the liver.
- Liver also handles:
- **Metabolism of organic acids** (like lactate, ketones, amino acids).
- **Metabolism of ammonium (NH_4^+)**:
- When liver changes NH_4^+ to urea → H^+ is made → adds to acid load.
- **Production of plasma proteins** (mainly albumin).

✏️ *Albumin helps maintain the anion gap (important for acid-base balance).*

🦴 **Bones**:

- Bones have a mineral called **hydroxyapatite** [$Ca_{10}(PO_4)_6(OH)_2$].
- It acts like a **buffer**!
- Bone can **absorb H^+** to help when there is too much acid.
- Bone exchanges H^+ for calcium (Ca^{2+}), sodium (Na^+), and potassium (K^+).

😢 **Chronic acidosis** (too much acid for a long time):

- Bone loses minerals → **Bone becomes weaker** → **Fracture risk increases**.

Metabolism Produces Acids Continuously

🎂 **Metabolism = Acid production non-stop**.

Sources:

- **Volatile acids** (like CO_2, H_2CO_3): 12,000–24,000 mmol/day → removed by lungs.
- **Fixed acids** (lactate, phosphate, sulfate, etc.): 70–100 mmol/day → removed by kidneys.

⚡ **Buffering System**:

- $CO_2 + H_2O \rightleftarrows H_2CO_3 \rightleftarrows H^+ + HCO_3^-$
- Hemoglobin helps buffer CO_2 inside red blood cells.

⚡ **Excretion**:

- Lungs remove CO_2 by breathing.
- Kidneys remove H^+ and reabsorb bicarbonate (HCO_3^-).

✏️ *pCO_2 (pressure of CO_2) is regulated by breathing rate.*

- **Faster breathing = lower pCO_2**
- **Slower breathing = higher pCO_2**

🧱 **Total CO_2 =**

- [Bicarbonate] + [Carbonic Acid] + [Carbamino CO_2] + [Dissolved CO_2].

Intracellular pH Is Critical

🏥 Inside the cells, pH control is **most important** for survival.

- Plasma pH affects intracellular pH.
- Doctors use **blood (plasma) tests** to understand what's happening **inside the cells** because direct measurement is hard.

🧪 Examples:

- **Low plasma pH (acidosis)** → means intracellular acid is high.
- **High plasma pH (alkalosis)** → less intracellular acid.

🔎 We look at extracellular results to guess about intracellular conditions.

More Details about Intracellular vs Extracellular pH

🧪 **Intracellular pH** (inside cells):

- Around **6.8 at 37°C** (slightly acidic compared to blood).
- This keeps metabolic processes working properly.

🧪 **Extracellular pH** (blood and plasma):

- Around **7.4**.
- It's **higher by 0.5–0.6 units** than intracellular pH.
- Creates a **fourfold gradient**: pushes H^+ out of cells (to protect cells from acid overload).

🛡️ How body maintains intracellular pH:

- **Intracellular buffering** (chemical/metabolic).
- **Arterial pCO_2 control** (through breathing).
- **Loss of fixed acids** from cells to extracellular fluid.

Respiratory System and pH Control

🫁 **CO_2 and breathing**:

- pCO_2, H^+, and pO_2 control breathing rate.

📈 **Acidemia** (low pH = more H^+):

- Stimulates brain center → **breathing rate increases** → get rid of CO_2.

📉 **Alkalemia** (high pH = less H^+):

- Suppresses brain center → **breathing rate decreases** → retain CO_2.

✏️ *Normal ventilation keeps pCO_2 around 40 mmHg.*

- **Hyperventilation** → CO_2 decreases → causes alkalosis.
- **Hypoventilation** → CO_2 builds up → causes acidosis.

Renal System and pH Control

🛁 **Kidneys do 2 big jobs**:

🧪 **Proximal tubules**:

- Reabsorb **bicarbonate (HCO_3^-)** to prevent its loss.
- Produce **ammonium (NH_4^+)** to help buffer acid.

🧪 **Distal tubules**:

- Excrete **H^+ directly**.
- Make **titratable acidity** (TA) using phosphate and ammonium.
- Add NH_4^+ into urine.

🚽 **Urine can become very acidic (pH = 4.5)**:

- This allows kidneys to excrete **1000x more acid** if needed!

✅ Summary:

- Bicarbonate reabsorption prevents alkalosis.
- Ammonium production removes extra acid.
- Low urine pH = extreme acid removal if necessary.

Proximal Tubule - $NaHCO_3$ Reabsorption

🛁 **Main Function**:

- Reabsorb **bicarbonate (HCO_3^-)** to **help maintain blood pH**.

🧪 **How it works** (step-by-step):

1. **Na^+/H^+ exchanger (NHE3)**:
- **Pushes Na^+ in** and **pushes H^+ out** into the urine (lumen).
2. The **H^+** in the urine **combines with HCO_3^-** → forms **$CO_2 + H_2O$** (using the enzyme **carbonic anhydrase**).
3. **CO_2** then **diffuses** (moves) **back into the cell** easily.
4. Inside the cell, $CO_2 + H_2O$ are turned back into **HCO_3^-**.
5. **HCO_3^- is sent into the blood** → keeps blood from becoming too acidic.

🔵 **Important**:

- Without this reabsorption, you would lose too much HCO_3^- in urine → blood would get acidic!

Thick Ascending Limb (TAL) Transport

🛁 **Main Function**:

- Reabsorb **Na^+, K^+, and Cl^-** ions → helps create the **concentration gradient** needed to concentrate urine.

🧪 **How it works**:

1. **$Na^+/K^+/2Cl^-$ cotransporter (NKCC2)** pulls these ions into the cell from urine.
2. **Some K^+ leaks back out** into the urine → makes the urine **positively charged**.
3. This positive charge helps **pull Ca^{2+} and Mg^{2+}** (calcium and magnesium) into the blood.

🧠 *Big idea*: this area is **very important for saving salts and water**.

Secretion of H^+ in α-Intercalated Cells (Cortical Collecting Duct)

🛁 **Main Function**:

- **Secrete acid (H^+)** into the urine → **regulates blood pH**.

🧪 **How it works**:

1. **H^+-ATPase** pumps **H^+ out into urine**.
2. Inside the cell, $CO_2 + H_2O$ are made into **H^+ and HCO_3^-**.
3. **HCO_3^- goes to the blood** (via Cl^-/HCO_3^- exchanger).

✅ This way:

- Acid is thrown into the urine.
- Bicarbonate is kept inside the blood (prevents acidosis).

Secretion of HCO_3^- in β-Intercalated Cells (Cortical Collecting Duct)

🛁 **Main Function**:

- Secrete **bicarbonate (HCO_3^-)** when you have **alkalosis** (blood is too basic).

🧪 **How it works**:

1. **HCO_3^-** is pushed **into the urine** (via Pendrin exchanger).

2. **H^+ is kept inside the blood**.

✅ This fixes the problem by **getting rid of extra base (bicarbonate)** → helping **lower blood pH**.

Principal Cell - Sodium (Na^+) Transport (Cortical Collecting Duct)

🛁 **Main Function**:

- Reabsorb **Na^+** and **secrete K^+** — controlled by **aldosterone** hormone.

🧪 **How it works**:

1. **ENaC channel** lets Na^+ come inside the cell.
2. **Na^+/K^+ ATPase** pumps Na^+ into blood and K^+ out into urine.

✅ This controls **salt and water balance**, and **potassium levels**.

Summary of Bicarbonate Reabsorption in the Kidney

🛁 **Goal**:

- Reabsorb almost **all filtered HCO_3^-** back into blood.
- Excrete acid (H^+) in urine.

📊 Numbers:

- 85% reabsorbed in **proximal tubule**.
- 10% in **loop of Henle**.
- 5% in **distal tubule and collecting duct**.

✅ **Very little bicarbonate is lost in urine** — kidney saves it to protect blood pH.

Proximal Tubule - H^+ Secretion and HCO_3^- Reabsorption

🧪 **Simple steps**:

1. **H^+ is secreted** into urine.
2. It **combines with HCO_3^-** to form **H_2CO_3 (carbonic acid)**.
3. H_2CO_3 breaks down into **CO_2 + H_2O**.
4. **CO_2 diffuses back** into the cell.
5. Inside the cell: CO_2 + H_2O make new **HCO_3^-**, which is sent to the blood.

✅ This **saves bicarbonate** and **throws out acid**.

Distal Tubule - Final H^+ Secretion

🛁 **Main Function**:

- Excrete **the last bit of acid (H^+)** that wasn't excreted earlier.

🧪 **How it works**:

1. **H^+ is actively pumped** into the urine.
2. H^+ combines with HCO_3^- inside the cell → H_2CO_3 → CO_2 + H_2O.
3. Very strong **acidic urine pH (4.5)** can be achieved!

✅ This removes the final acid and protects blood from becoming too acidic.

Phosphate Buffering

🛁 **Main Function**:

- Helps **trap H^+** safely in the urine without making the urine extremely acidic.

🧪 **How it works**:

1. H^+ binds to **phosphate (HPO_4^{2-})** → forms **$H_2PO_4^-$** (which is excreted).
2. This helps remove H^+ without hurting urine too much.

✅ **Bicarbonate is made at the same time and returned to blood**.

Ammonia (NH_3) Buffering

🛁 **Main Function**:

- Helps **remove acid** when acid levels are very high.

🧪 **How it works**:

1. Cells make **ammonia (NH_3)**.
2. **NH_3 diffuses into urine** and binds to secreted **H^+** → forms **NH_4^+**.
3. **NH_4^+ is trapped** in urine and removed.

✅ Each time NH_4^+ is made, **new bicarbonate (HCO_3^-)** is made and sent into the blood.

Part	Main Function	Key Transport/Action	Goal
Proximal Tubule	Reabsorb HCO_3^-	Na^+/H^+ exchanger (NHE3), Carbonic Anhydrase	Save bicarbonate, remove H^+
Thick Ascending Limb (TAL)	Reabsorb Na^+, K^+, Cl^-	NKCC2 cotransporter	Create salt gradient for urine concentration
α-Intercalated Cells (Collecting Duct)	Secrete H^+ into urine	H^+ ATPase	Remove acid, reabsorb HCO_3^-
β-Intercalated Cells (Collecting Duct)	Secrete HCO_3^- into urine (in alkalosis)	Pendrin (Cl^-/HCO_3^- exchanger)	Remove extra base
Principal Cells (Collecting Duct)	Reabsorb Na^+, secrete K^+	ENaC + Na^+/K^+ ATPase (Aldosterone control)	Maintain salt, water, potassium balance
Distal Tubule + Collecting Duct	Final acid secretion	Active H^+ transport	Create very acidic urine (pH 4.5)
Phosphate Buffering	Trap H^+ safely	H^+ binds to HPO_4^{2-} → $H_2PO_4^-$	Excrete H^+ without making urine too acidic
Ammonia (NH_3) Buffering	Remove large amounts of H^+	NH_3 binds H^+ → NH_4^+	Excrete H^+ and make new HCO_3^-

🫁 **Respiratory Alkalosis**

Definition:

- It's a **primary disorder** where **pH goes up** (alkalosis) because of **low $PaCO_2$** (carbon dioxide pressure falls below 35 mmHg).
- This is called **hypocapnia** (low CO_2 in the blood).

Time Course:

- **Acute:**
- pH rises immediately because of a sudden drop in CO_2.
- **Chronic:**
- Over 3–4 days, the **kidneys compensate** by **excreting bicarbonate (HCO_3^-)** to lower the pH back closer to normal.

Causes:

- **CNS Disease** (e.g., brain tumor — affects breathing control)
- **Toxins** (e.g., salicylates — early phase causes hyperventilation)
- **High Altitude** (low oxygen → hyperventilation)
- **Pulmonary Embolism or Pneumonia** (breathing faster due to lung problem)
- **Sepsis** (infection → changes in breathing)

- **Liver Cirrhosis** (affects metabolism → breathing changes)

Acute: High pH now
Chronic: Kidneys remove HCO_3^- to bring pH back

🫁 **Respiratory Alkalosis Summary Table**
- If **pH > 7.45**, think **respiratory alkalosis**.
- The **primary problem** = ↓ $PaCO_2$.
- The **compensatory response** = ↓ HCO_3^-.

Compensation:
- **Acute:**
- **1–2 mmol/L** decrease in HCO_3^- for every **10 mmHg decrease** in $PaCO_2$.
- **Chronic:**
- **4–5 mmol/L** decrease in HCO_3^- for every **10 mmHg decrease** in $PaCO_2$ (because kidneys have more time to adjust).

🧠 **Simple Summary:**

Type	What Happens	HCO_3^- change
Acute	Fast drop in CO_2 → fast pH rise	↓ 1–2 mmol/L
Chronic	Slow adaptation → kidneys lower HCO_3^- more	↓ 4–5 mmol/L

Important Overlapping Disorders:
- **Sighing Syndrome** (excessive deep breaths without a real need)
- **Panic Disorder** (anxiety attacks cause hyperventilation)
- **Cardiopulmonary Disease** (lung/heart diseases lead to breathing problems)

These overlap around **Hyperventilation Syndrome**, where people breathe too much and lose too much CO_2 → leading to **respiratory alkalosis**.

🧠 **Simple Venn Diagram Idea:**
css
CopyEdit
[Sighing Syndrome]
**/ **
[Panic Disorder] - [Cardiopulmonary Disease]
\ /
[Hyperventilation Syndrome]

⚡ **Metabolic Acidosis**
Definition:
- **Primary disorder** where **pH decreases** because of:
- **Loss of bicarbonate (HCO_3^-)**
- OR **Fixed addition of H^+** (acid).

Anion Gap Concept:

- When there's **extra acid** added → **High Anion Gap** (AG).
- If bicarbonate is lost but no extra acid → **Normal Anion Gap**.

Anion Gap formula:

$AG = [Na^+] - ([Cl^-] + [HCO_3^-])$
Normal range: around **8–12 mEq/L**.

Low Albumin Note:
- Albumin is negatively charged.
- If albumin is low, it **lowers AG** → you must **adjust** AG: Add 2.5 mEq/L to AG for every 1 g/dL ↓ albumin
  Add 2.5 mEq/L to AG for every 1 g/dL ↓ albumin

Metabolic Acidosis = ↓ pH

If extra acids (e.g., lactate, ketones) → High AG
If bicarbonate lost (e.g., diarrhea) → Normal AG

If extra acids (e.g., lactate, ketones) → High AG
If bicarbonate lost (e.g., diarrhea) → Normal AG

Causes of Metabolic Acidosis
Types:
- **High Anion Gap Metabolic Acidosis (HAGMA):**
- Loss of bicarbonate AND addition of acids.
- **Normal Anion Gap Metabolic Acidosis (NAGMA):**
- Loss of bicarbonate only, chloride increases to compensate.

Quick Bar Chart (visualized on your slide):

Type	Changes	Causes
High AG	HCO_3^- ↓, AG ↑	Lactate, Ketones, Toxins
Normal AG	HCO_3^- ↓, Cl^- ↑	Diarrhea, Renal issues

Causes: High vs Normal Anion Gap
- **High AG Acidosis** (addition of unmeasured acids):
- **Lactate**
- **Ketones** (e.g., DKA, starvation)
- **Toxins** (methanol, ethylene glycol, salicylates)
- **Normal AG Acidosis** (loss of bicarbonate, no acid accumulation):
- **Diarrhea**
- **Renal Tubular Acidosis (RTA)**
- **Ureteral diversions**

Simple Table:

High AG	Normal AG
Lactic acidosis	Diarrhea
Ketoacidosis	RTA
Toxins (methanol, aspirin)	Ureteral issues

⚡ **Table of Mechanisms**

This slide summarizes causes:

- **High AG Causes:** Lactic acidosis, ketoacidosis, methanol, ethylene glycol, aspirin.
- **Normal AG Causes:** Diarrhea, RTA (Type 2, Type 4), ureterosigmoidostomy.

🧠 **Tiny Table Summary:**

Increased AG	Normal AG
Methanol	Diarrhea
Lactic acidosis	RTA Type 2/4
DKA	Ureteral diversions

⚡ **CAT MUDPILES Mnemonic**

Mnemonic for causes of High Anion Gap Acidosis:

Letter	Cause
C	Carbon monoxide, Cyanide, Congenital heart disease
A	Aminoglycosides
T	Theophylline, Toluene
M	Methanol
U	Uremia
D	Diabetic ketoacidosis
P	Paracetamol, Phenformin, Paraldehyde
I	Iron, Isoniazid, Inborn errors of metabolism
L	Lactic acidosis
E	Ethanol, Ethylene glycol
S	Salicylates

⚡ **Non-Anion Gap Metabolic Acidosis**

Causes:

GI Loss of HCO_3^-	Renal Acidosis
Diarrhea	Hypokalemia (RTA 2/1)
Ureterosigmoidostomy	Hyperkalemia (RTA 4)
GI Fistula, Villous Adenoma	Tubulointerstitial Disease

NAGMA = Loss of bicarbonate
- From GI → Diarrhea, fistulas
- From kidneys → RTA types

📍 **Non-Anion Gap Metabolic Acidosis**

🔶 **Definition**:

- Normal anion gap (AG).
- Hyperchloremic acidosis.

🔶 **Causes**:

- **GI bicarbonate loss**:
- **Diarrhea** → losing HCO_3^- → chloride (Cl^-) replaces bicarbonate (HCO_3^-).
- **External fistula** → leaking fluids rich in bicarbonate.
- **Ureterosigmoidostomy / ileal loop conduit** → urine redirected to intestine, bicarbonate loss.
- **Renal bicarbonate loss** (Renal Tubular Acidosis - RTA):
- **Type I RTA (Distal, Classical)** → Proton secretion defect → Urine pH >5.5 → hypokalemia, kidney stones.
- **Type II RTA (Proximal, Fanconi)** → Bicarbonate reabsorption defect → Urine pH <5.5 → hypokalemia.

- **Type IV RTA (Hyperkalemic)** → Hyporeninemic hypoaldosteronism → high K^+.

📋 (Small table shown: summarizing defects + key features for each RTA)

📍 **Diagnosis Flowchart (Hyperchloremic Metabolic Acidosis)**

🔶 Step 1: Check **Urine Anion or Osmolal Gap**:

- **High NH_4^+ (anion gap negative)** → Check bicarbonate excretion:
- If **increased** → proximal RTA (or acetazolamide use).
- If **decreased** → GI bicarbonate loss.
- **Low NH_4^+ (anion gap positive)** → Look at **urine pH and serum K^+**:
- pH <5.5 + high K^+ → Type IV RTA
- pH >5.5 + high K^+ → Voltage-dependent RTA
- pH >5.5 + normal or low K^+ → Classic distal RTA.

📍 **Compensation for Metabolic Acidosis**

🔶 General Rule:

- Primary problem = ↓ pH < 7.35
- Primary defect = ↓ HCO_3^-
- Compensation = ↓ PCO_2

🔶 Formulas:

- Expected **PCO_2** = (1.5 × HCO_3^-) + 8 (±2) (OR)
- PCO_2 = HCO_3^- + 15 (OR)
- PCO_2 = last 2 digits of pH × 100

(These help assess if compensation is **appropriate**.)

📍 **Decreased Anion Gap**

🔶 **Causes**:

- **Hypoalbuminemia** (most common).
- **Hypercalcemia** (high calcium).
- **Hypermagnesemia** (high magnesium).
- **Lithium intoxication** (replaces sodium).
- **Hypergammaglobulinemia** (excess IgG).
- **Bromide or iodide intoxication** (interferes with lab tests).

💡 **Summary Key**:

- Low AG → think hypoalbumin, high cations, or unmeasured anions.

📍 **Metabolic Acidosis - Metabolic Effects**

🔶 **Respiratory System**:

- **Hyperventilation** to blow off CO_2.
- **Shift of hemoglobin curve** to the right initially (release more O_2), then shifts back left with prolonged acidosis (worsens O_2 delivery).
- **Decreased 2,3 DPG** → poor O_2 delivery.

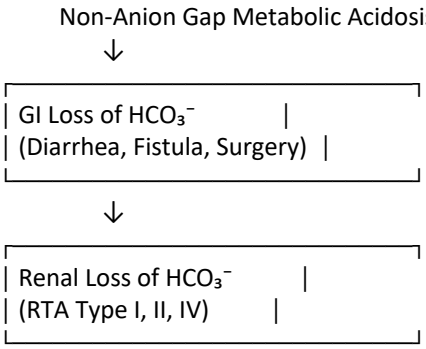
🔶 **Cardiovascular System**:

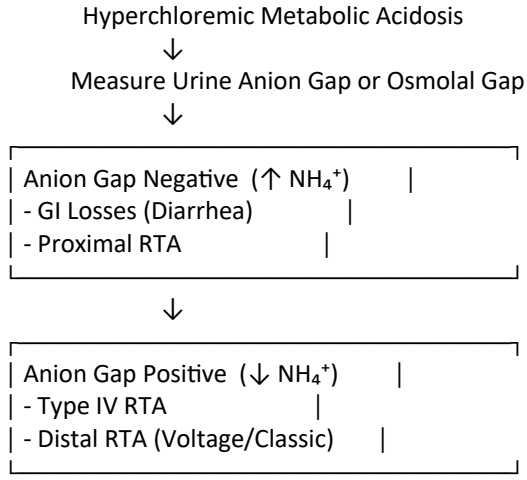
- ↓ Heart contractility.
- Arrhythmias (especially if hyperkalemia).

🔶 **Other Effects**:

- **Increased bone resorption** → osteoporosis (only with chronic acidosis).
- **K^+ shifts out of cells** → **hyperkalemia** → dangerous arrhythmias.

📋 (Diagram shows brain, heart, lungs, kidneys — highlighting effects like tachycardia, hyperventilation, vasodilation.)





Cardiovascular Effects: Acidosis vs. Alkalosis

Acidosis	Alkalosis
- Impaired cardiac contractility (heart can't pump strongly)	- Arteriolar constriction (narrowing of small arteries)
- Arteriolar dilation (small arteries widen)	- Reduced coronary blood flow (less blood to the heart)
- Venoconstriction (veins tighten)	- Reduced anginal threshold (easier to get chest pain)
- Centralization of blood volume (blood moves to important organs)	- Decreased threshold for cardiac arrhythmias (irregular beats happen easier)
- Increased pulmonary vascular resistance (lungs' vessels tighten)	
- Decreased cardiac output (heart pumps less blood)	
- Decreased systemic BP (lowers overall blood pressure)	
- Decreased hepatorenal blood flow (liver and kidneys get less blood)	

- Decreased threshold for cardiac arrhythmias (easy for irregular beats)	
- Less responsiveness to catecholamines (body hormones like adrenaline don't work well)	

🧪 **Metabolic, Neurologic, and Respiratory Effects: Acidosis vs. Alkalosis**

Acidosis	Alkalosis
Metabolic	**Metabolic**
- Insulin resistance (harder to control blood sugar)	- Stimulation of anaerobic glycolysis (makes more lactic acid)
- Inhibition of anaerobic glycolysis	- Formation of organic acids
- Reduction in ATP synthesis (less energy made)	- Decreased oxyhemoglobin dissociation (oxygen sticks to hemoglobin too much)
- Hyperkalemia (↑ potassium)	- ↓ Ionized calcium
- Protein degradation (muscles break down)	- Hypokalemia (↓ potassium)
- Bone demineralization (weak bones if chronic)	- Hypomagnesemia (↓ magnesium)
	- Hypophosphatemia (↓ phosphate)
Neurologic	**Neurologic**
- Inhibition of metabolism and cell-volume control	- Tetany (muscle spasms)
- Obtundation and coma	- Seizures
	- Lethargy
	- Delirium
	- Stupor
Respiratory	**Respiratory**
- Compensatory hyperventilation (breathing faster) but risk of muscle fatigue	- Compensatory hypoventilation (breathing slows) → hypercapnia (↑ CO_2) and hypoxemia (↓ oxygen)

⚡ **Mixed Acid-Base Disorders**

- **Metabolic and Respiratory Acidosis** — serious! (both cause acidosis → very bad)
- **Metabolic and Respiratory Alkalosis** — serious! (both cause alkalosis → risky)
- **Metabolic Acidosis & Respiratory Alkalosis** — mixed but can sometimes compensate
- **Metabolic Alkalosis & Respiratory Acidosis** — mixed disorder
- **Metabolic Acidosis & Alkalosis + Respiratory Disorder** — very mixed picture

🔴 *Note*: When **both are in same direction** (both acidic or both alkaline), it's worse because body can't compensate.

Δ Delta Gap (Mixed Disorders Detection)

- **Delta gap** = patient's anion gap - normal anion gap.
- It's like an HCO_3^- equivalent: ➔ *Every 1 unit increase* in **anion gap** should match *1 unit decrease* in **HCO_3^-**.
- **If delta gap is higher than expected:** ➔ *Extra metabolic alkalosis* also present.
- **If delta gap is lower than expected:** ➔ *Extra metabolic acidosis* also present.

✅ **Delta gap helps you spot hidden disorders!**