Acid Base balance

Content

- Buffer systems and its efficiency
- Requirement of maintenance of acid base balance
- Causes of acid base imbalances
- Regulation of acid base balance
  - Renal
  - Respiratory

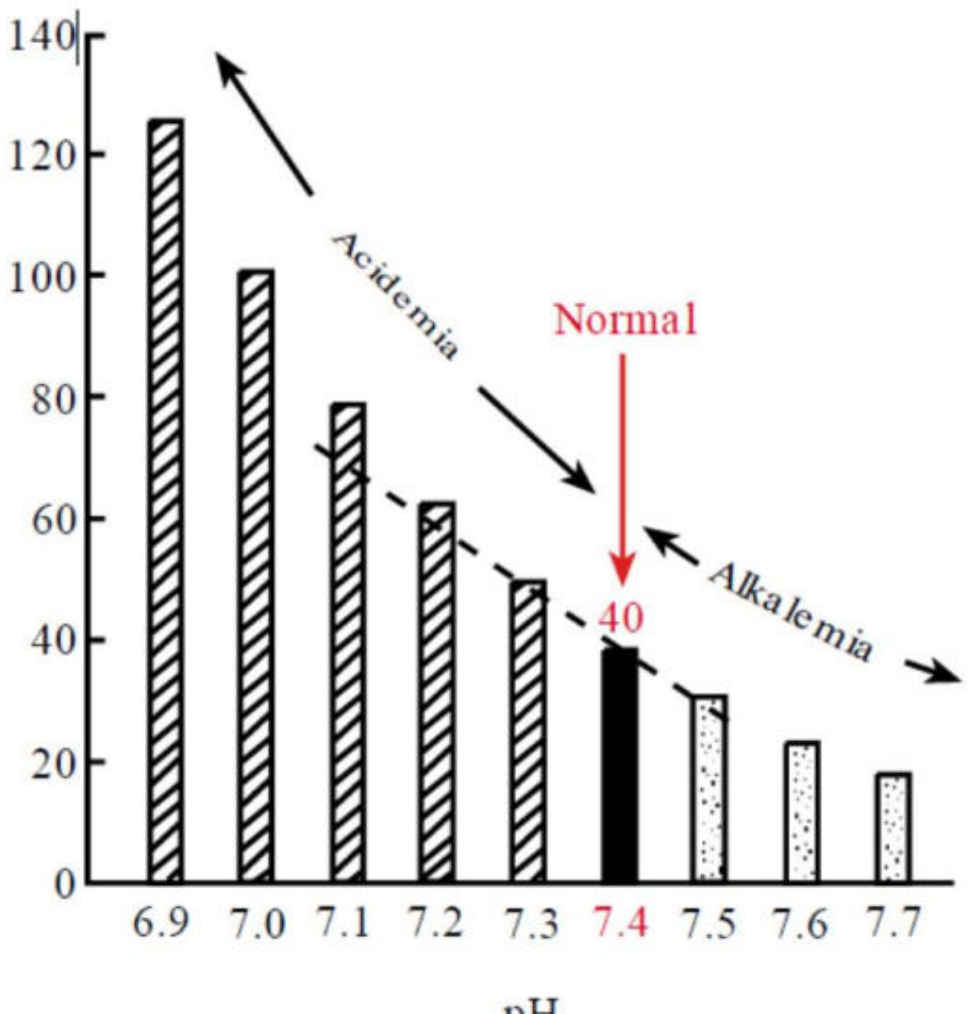
Case report 1

- A patient with a history of chronic lung disease has suffered from emphysema which has grown progressively worse over a period of years. The patient experiences chronic shortness of breath. Analysis of patient's blood reveals the following PCO2=60 mmHg: [HCO3] =34mM pH=7.38
- What could be the diagnosis?

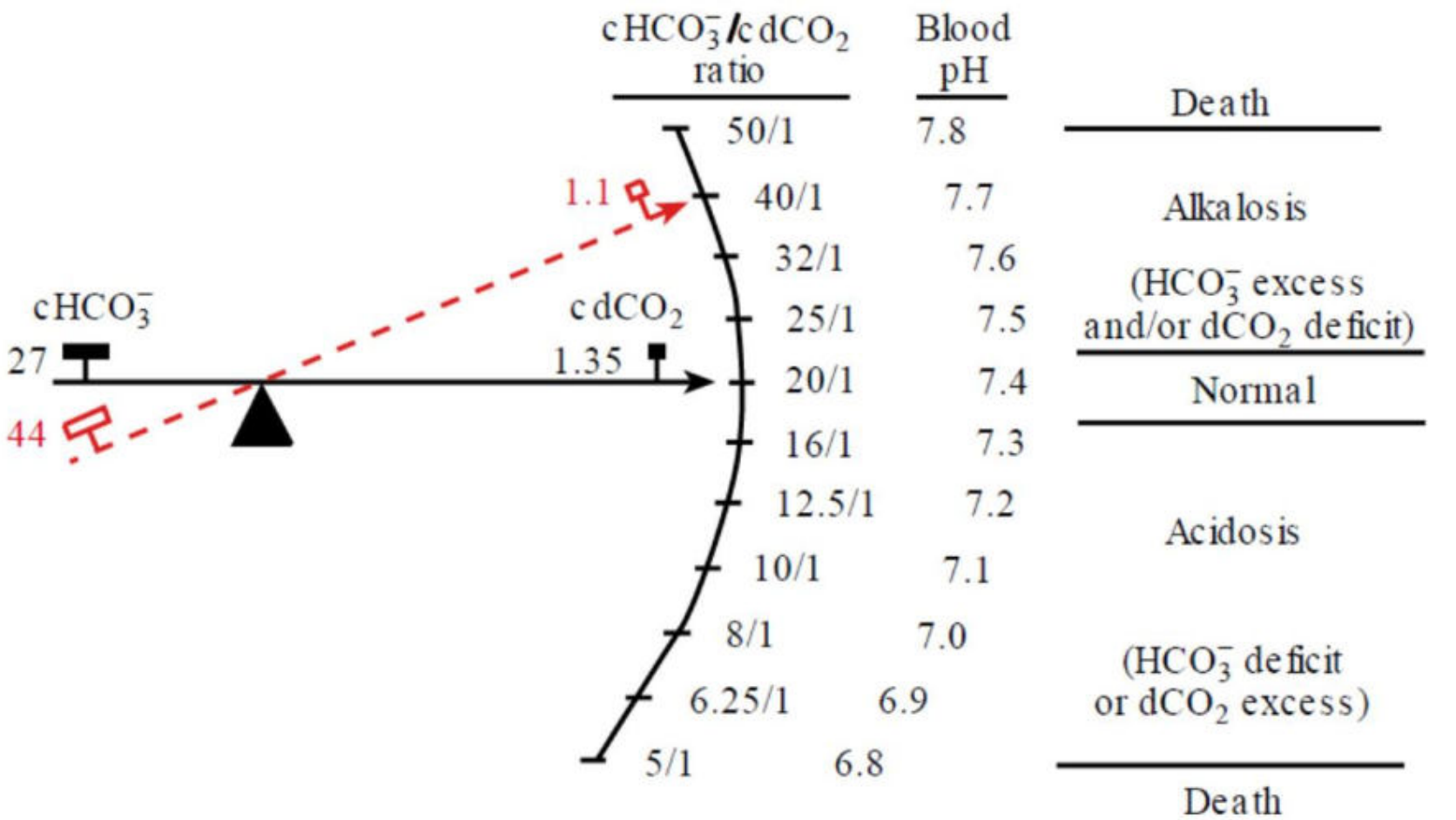
Case report 2

- ***A man suffering from untreated diabetes mellitus is admitted to the hospital. Glucose and acetoacetate are present in his urine and he exhibits shallow breathing. Analysis of his blood indicates [HCO3-] =16 mM and PCO2=30***
- The most likely pH of blood is

Relationship of pH to hydrogen ion concentration



Scheme demonstrating the relation between pH and the ratio of bicarbonate concentration to the concentration of dissolved CO2.



- What is pH?
- Negative logarithm of H+ concentration in a solution

- pH Scale:
- Ranges from 0 to 14
- What is pKa?
- Negative logarithm of dissociation constant
- The pH at which an acid is half dissociated, existing as equal proportions of acid and conjugate base.

What is buffer

- A buffer is a mixture of a weak acid and a salt of its conjugate base that resists changes in pH when a strong acid or base is added to the solution
  .
- Functions of a buffer depends on:
- pH
- pK
- Salt to acid ratio

- Does the dilution change the pH of a buffer?
- pH of a buffer solution is directly proportional to the salt acid ratio. Dilution does not change the ratio
- **Buffer efficiency:**
- Maximum when the ratio of acid/base is within the range of 10:1 to 1:10
- Over a pH range is equal to pKa±1

- For optimum function of biomolecules : Enzymes, transport molecules, nucleic acid
- To avoid disruption of structure and function of cells
- Several serious health consequences: Acidosis, alkalosis

Buffer systems

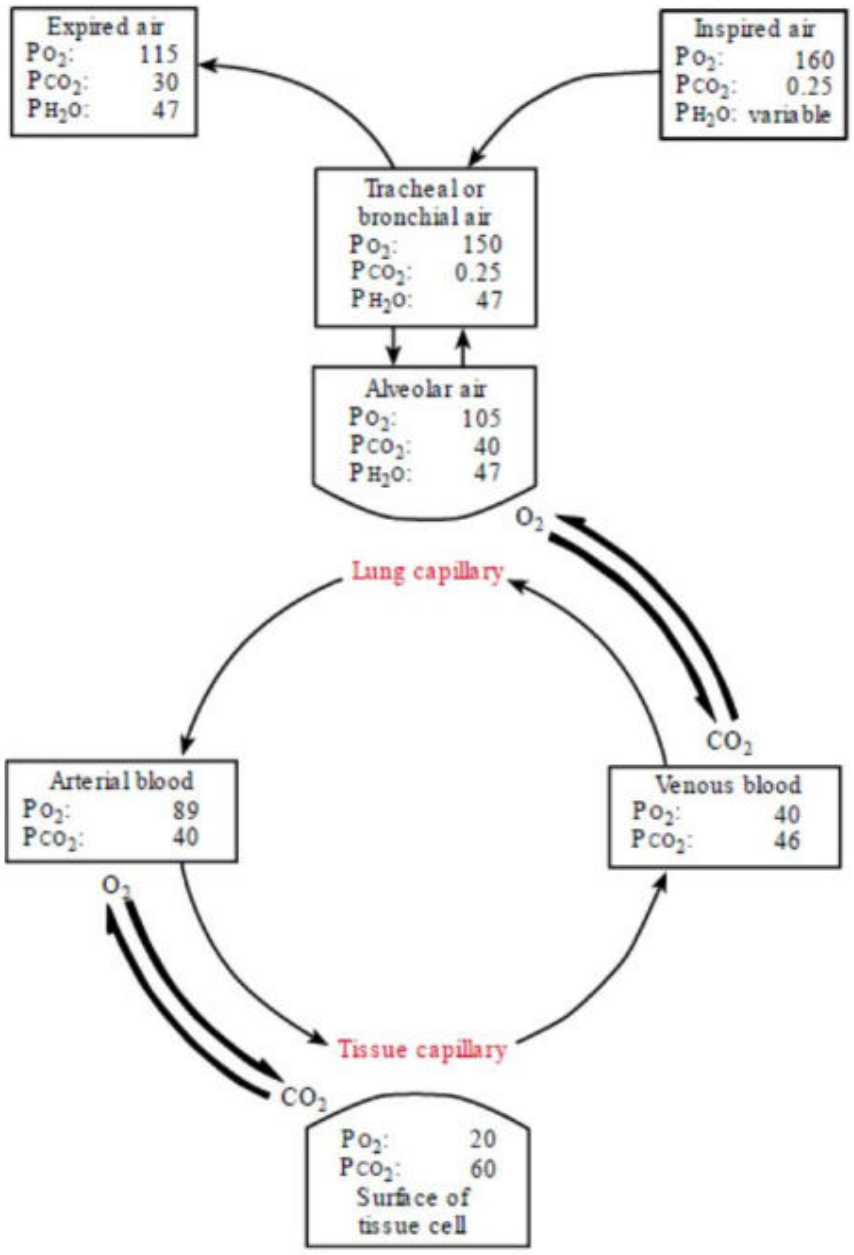
- 1. Bicarbonate/Carbonic acid buffer systems
  - Extra cellular buffer
  - pK=6.1
  - cHCO3-/cdCO2= ?
- 2. Phosphate buffer
  - pK= 6.8
  - cHPO4-/H2PO4-=
  - Intracellular buffer
- 3. Plasma protein and Hemoglobin: Imidazole group of histidine: pK=7.3

Regulation of Acid-Base balance

1. Respiratory mechanism

2. Renal mechanism

Partial pressure of oxygen and carbon di oxide

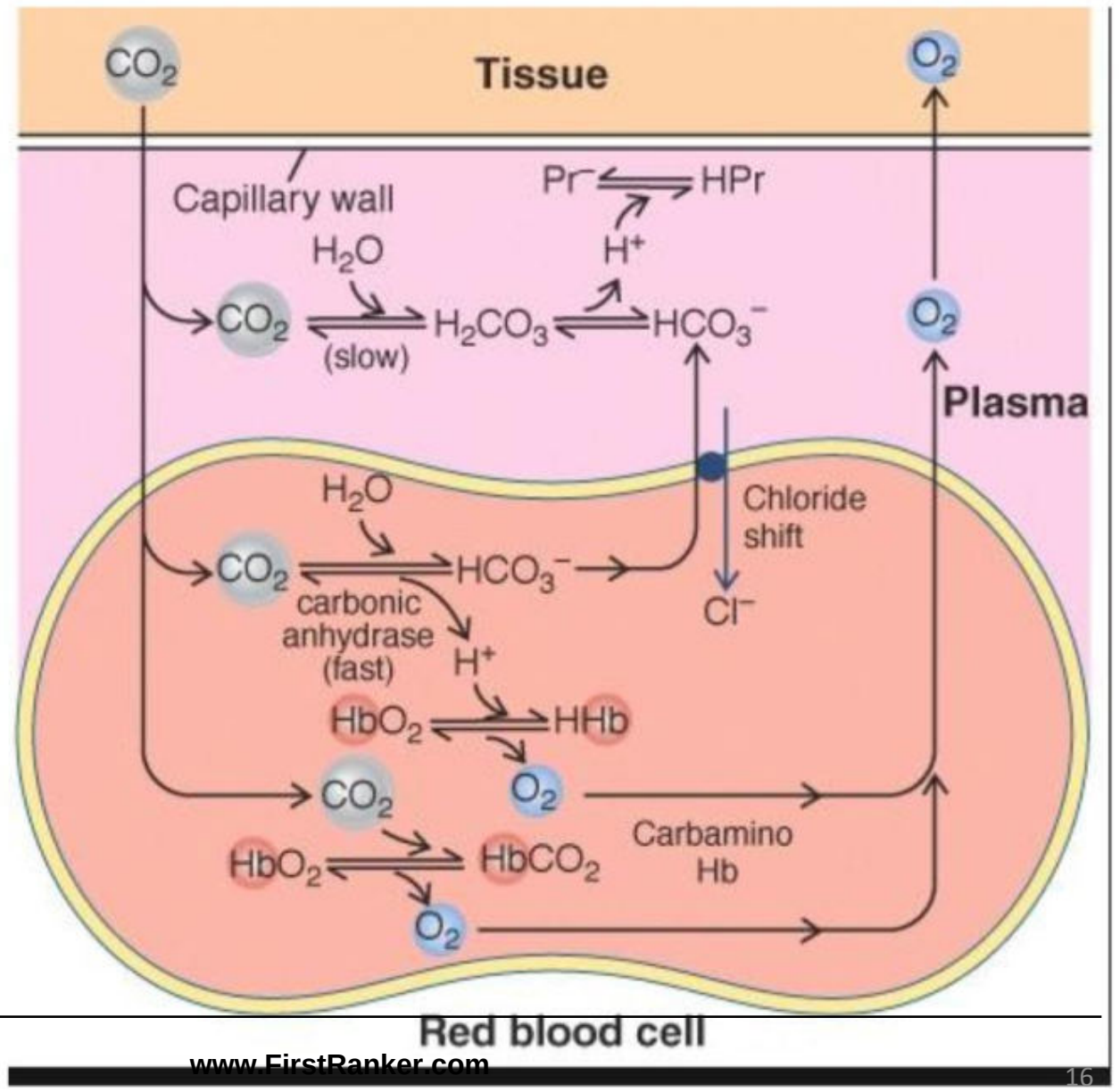


Respiratory Response to Acid-Base Perturbations

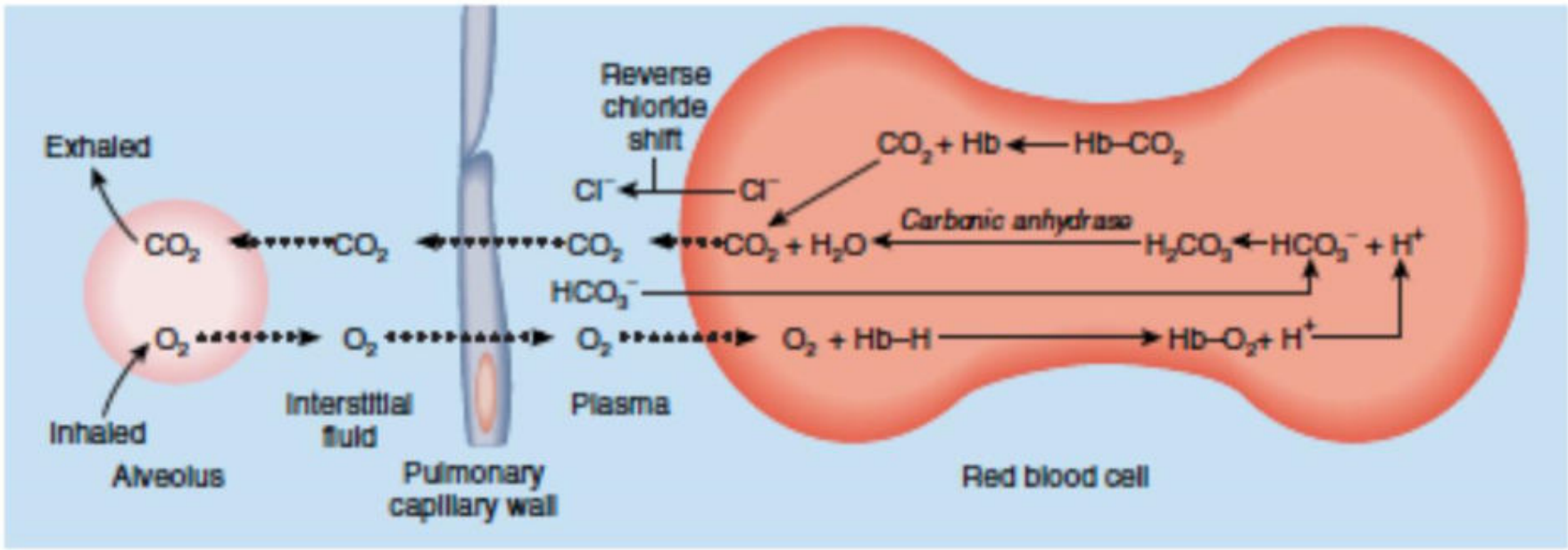
- responds immediately to a change in acid -base status
- several hours may be required for the response to become maximal
- in the early stage plasma pH decreases
- H+ ions equilibrate slowly across the blood -brain barrier, the pH in CSF remains nearly normal
- Stimulated peripheral chemoreceptor induces hyperventilation: Plasma pCO2 decreased
-

- the PCO2 of the CSF decreases immediately because CO2 equilibrates rapidly across the blood –brain barrier, leading to a rise in pH of the CSF that inhibits the central chemoreceptor
- plasma bicarbonate gradually falls because of acidosis, bicarbonate concentration and pH in the CSF will also eventually fall
- stimulation of respiration becomes maximal from both central and peripheral chemoreceptors.

Role of RBC and Hb



Role of RBC and Hb

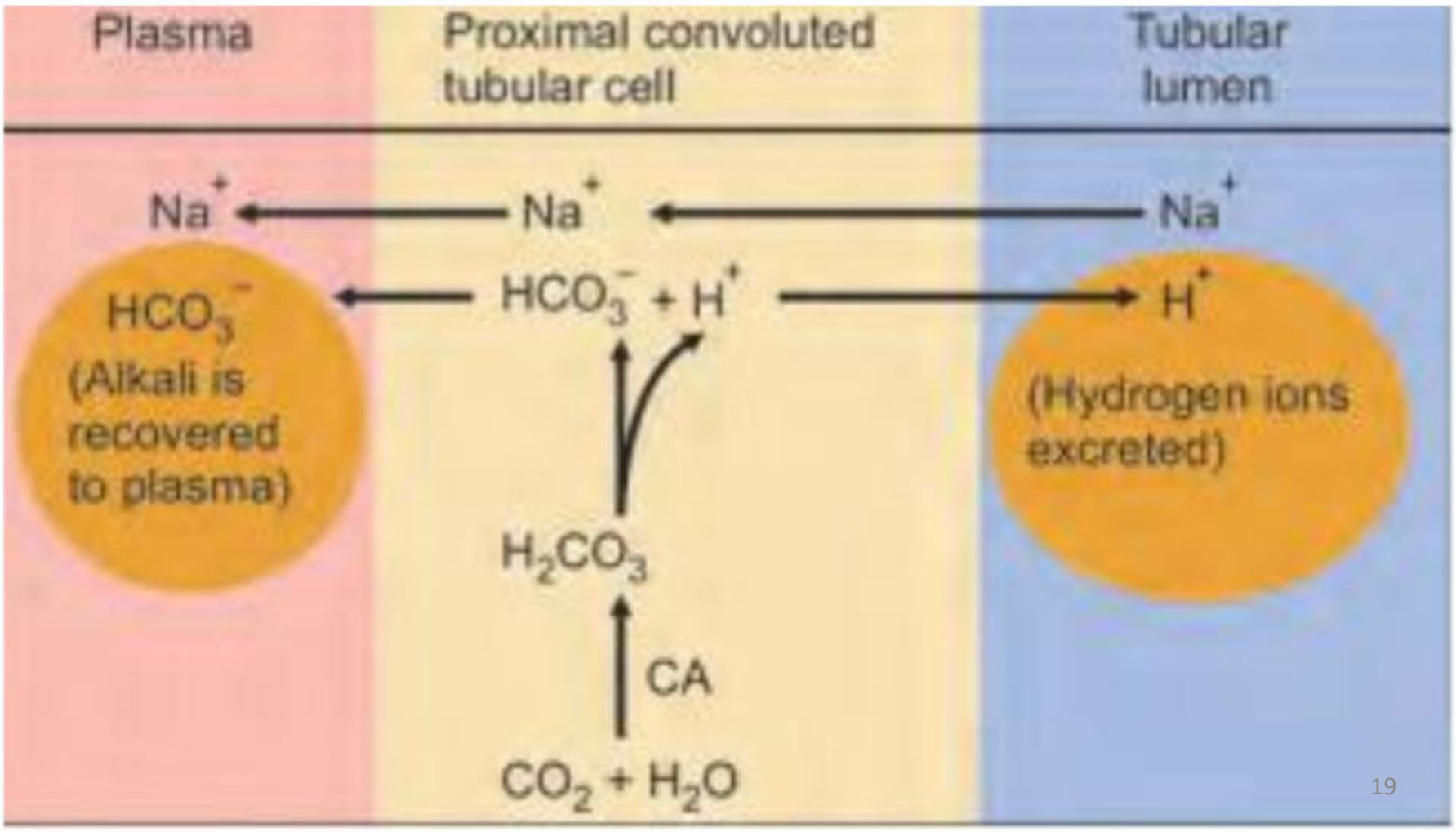


(a) Exchange of O_2 and CO_2 in pulmonary capillaries (external respiration)

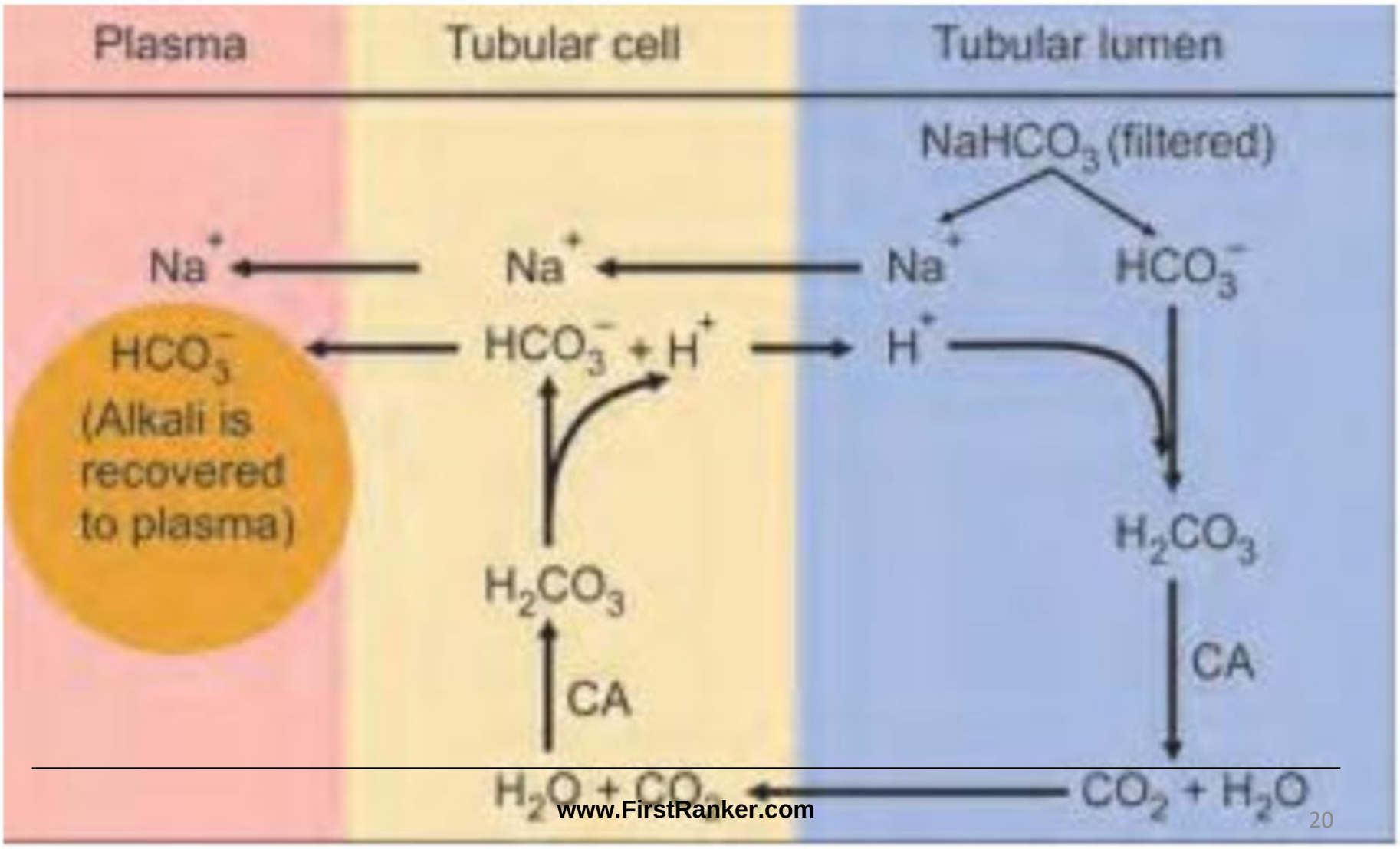
Renal mechanisms in the regulation of Acid-Base Balance

- pH of plasma=
  - 7.4
- PH of urine=
  - 6.0

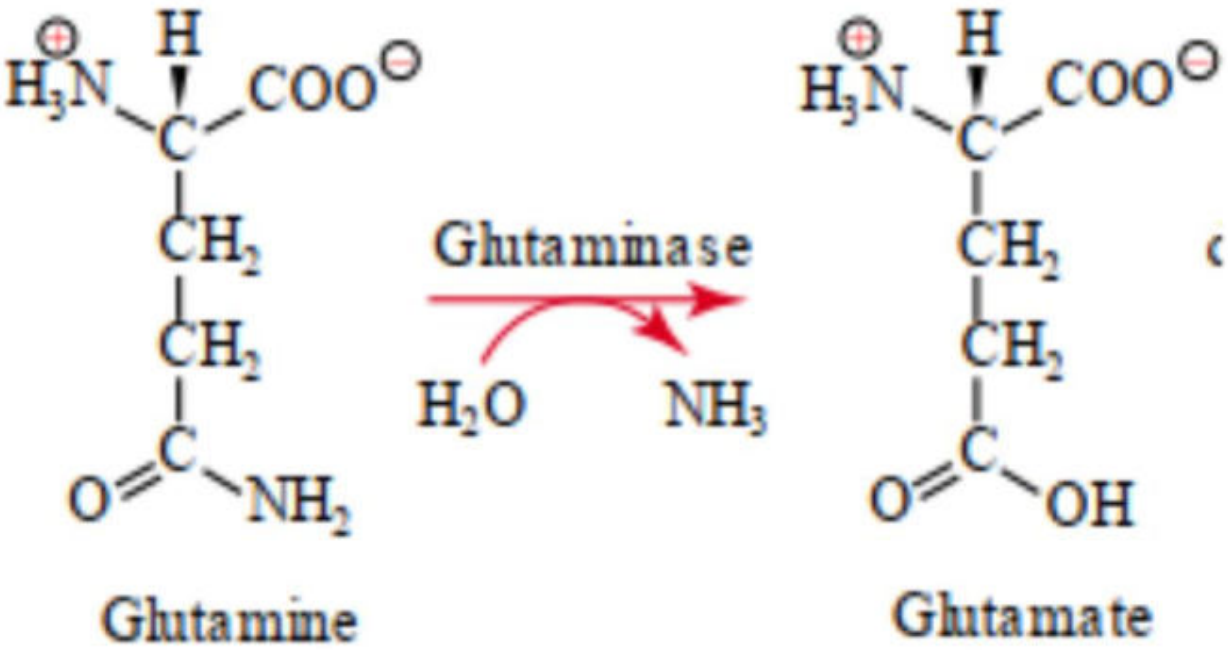
1. Na+-H+ exchange :



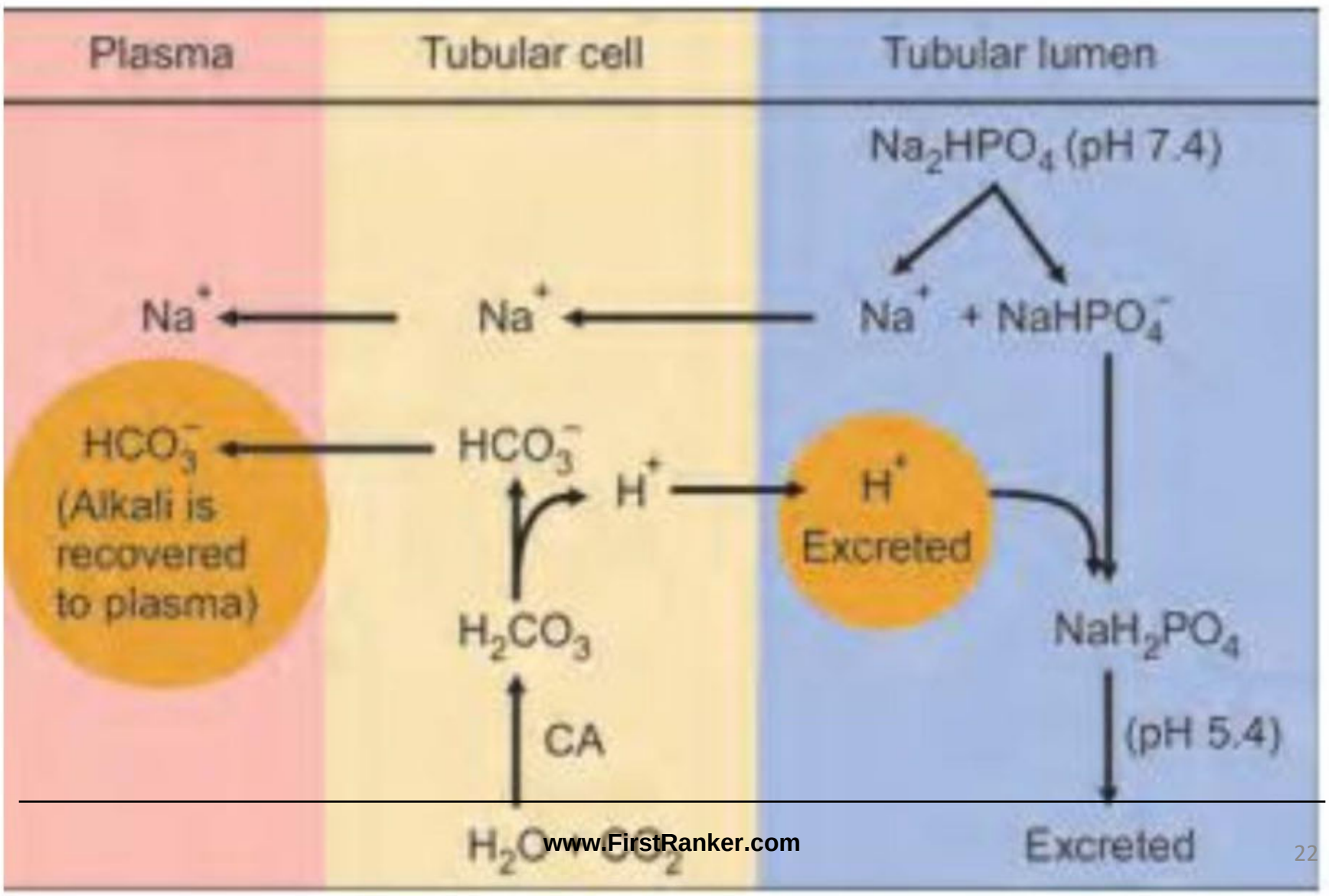
2. Reclamation of HCO3-



3. Renal production of Ammonia and excretion of Ammonium ions



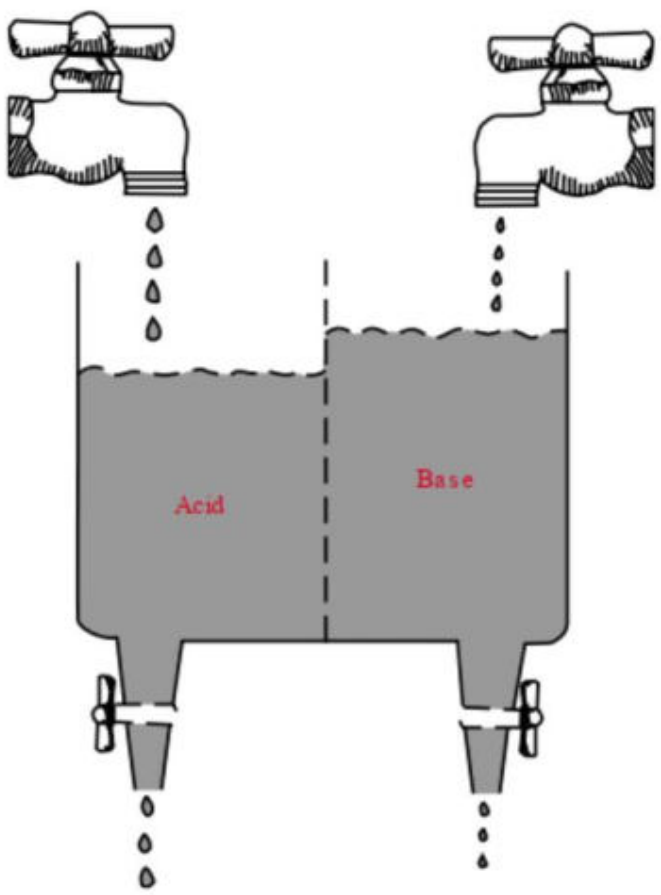
4. Excretion of H+ as H2PO4-



Conditions associated with abnormal acid base status and abnormal electrolyte composition of the blood

- Metabolic acidosis
- Metabolic alkalosis
- Respiratory acidosis
- Respiratory alkalosis

Simple depiction of the body as a two-vat system of acid and base

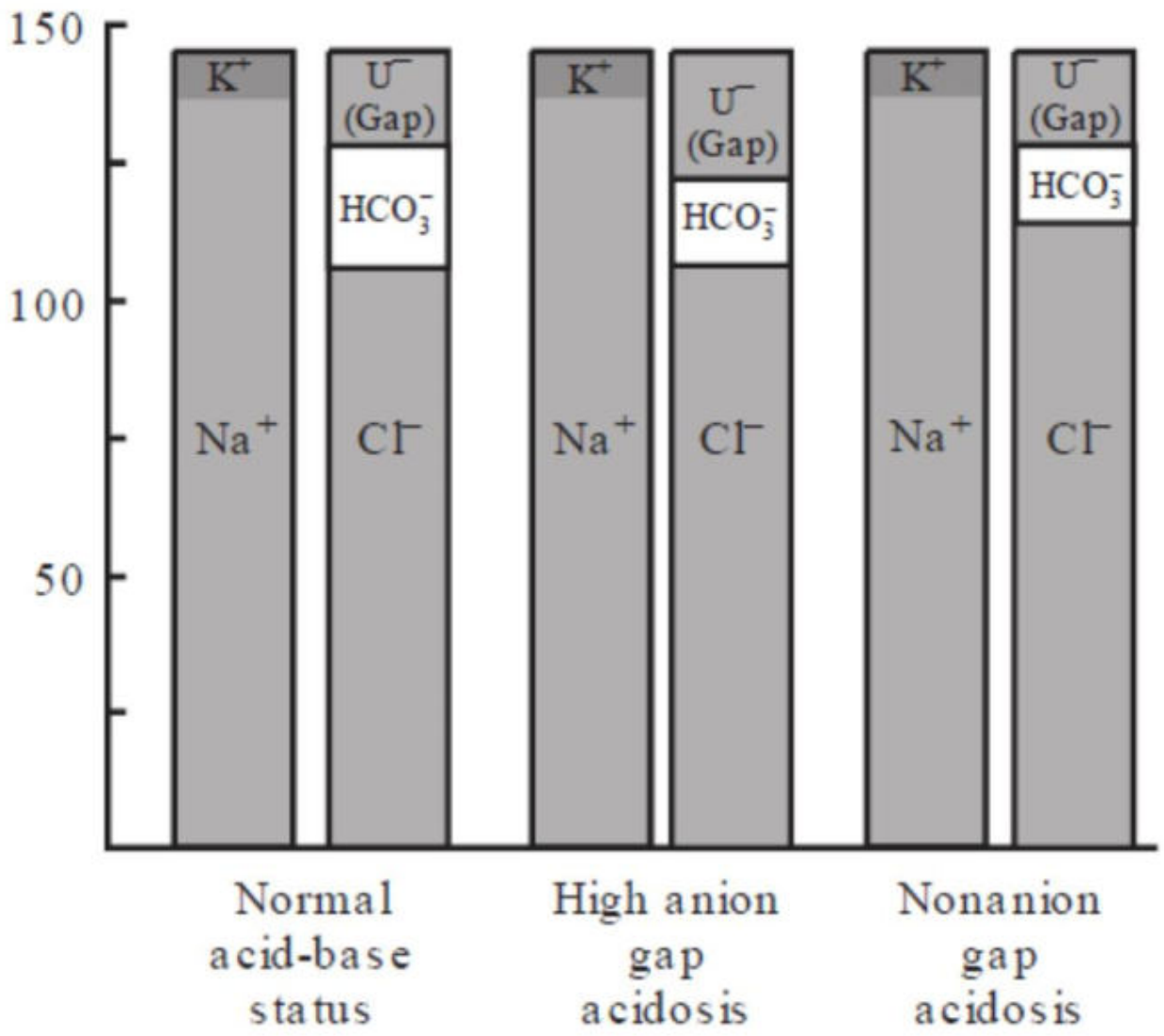


Metabolic acidosis (Primary bicarbonate deficit)

- Decreased plasma HCO3-
- Ratio of cHCO 3- /cdCO 2 is decreased
  Causes
- 1. Production of organic acids that exceeds the elimination: Diabetic ketoacidosis
- 2. Reduced excretion of acids: Renal failure, RTA
- 3. Excessive loss of bicarbonate:
  - Diarrhea (loss of duodenal fluid)

- An alcoholic has come to you with a complaint of severe vomiting. His blood test reveals pH 7.42 and HCO3- 25 mmol/L,

Simple depiction of normal gap, anion gap acidosis, and nonanion gap acidosis.



Increase in anion gap

Methanol
Uremia
Diabetic ketoacidosis
Paraldehyde
Iron, Isoniazid, Ibuprofen
Lactic acidosis
Ethylene glycol, Ethanol
Salicylates, starvation ketoacidosis

- Methanol:
  - Metabolized by the liver to formaldehyde and formic acid

Alcohol	Serum osmol gap	Anion Gap	Serum acetone	Urine oxalate
Ethanol	+	----	-----	-----
Methanol	+	+	-----	-----
Isopropanol	+	---	+	----
Ethylene glycol	+	+	-----	+

Osmol gap

- OSMg = OSMm - OSMc
  The diff erence between the actual osmolality (OSMm), measure by freezing-point depression, and the calculated osmolality (OSMc).
- OSMc (mOsm/kg) = 2 Na (mmol/L)
  + glucose (mg/dL) /18
  + urea (mg/dL) /2.8
- presence of unmeasured osmotically active substances: Volatile alcohols: methanol, isopropanol , ethylene glycol

Uremia or renal failure

- (1) decreased ammonia formation,
- (2) decreased Na+-H+ exchange, and
- (3) decreased GFR.
- All result in decreased acid excretion.
- Acidosis usually develops if GFR falls below 20 mL/min.

Diabetic ketoacidosis

- β-hydroxybutyrate and 2-oxoglutarate accumulate
- decrease in HCO3- and a high anion gap
- Ketoacids also accumulate in states of starvation and alcoholic malnutrition

Paraldehyde toxicity

- after chronic paraldehyde ingestion
- β-hydroxybutyric acid
- Patients with paraldehyde toxicity have a pungent, apple-like odor to their breath

.

Isoniazid, Iron, or Ischemia ("Three I's")

- accumulating organic acids with a predominance of lactic acid
- production of toxic peroxides that act as mitochondrial poisons and interfere with normal cellular respiration
- Ischemia results in anaerobic metabolism with accumulation of organic (mainly lactic) acids.

Lactic acidosis

- Derived mainly from muscle cells and erythrocytes
- end product of anaerobic metabolism and is normally metabolized by the liver
- An increase in the concentration of lactate to >3 mmol/L with the associated increase in H+ is considered lactic acidosis
- caused by severe tissue hypoxia is seen in
  (1) severe anemia, (2) shock, (3) cardiac arrest, and (4) pulmonary insufficiency
- Treatment: origin of lactate (e.g., seizure, hypoxic tissue) is rectified : rapidly metabolized to CO_2, which then is eliminated

Ethylene glycol

- metabolized primarily to glycolic and oxalic acid s
- lead s to an acidosis with high anion and osmolal gaps
- Precipitation of calcium oxalate and hippurate crystals in the urinary tract may lead to acute renal failure
- Patients develop a variety of neurologic symptoms that may lead to coma

Salicylate Intoxication

- blood salicylate concentrations above 30 mg/L

=acidosis develops

- Salicylate, itself an unmeasured anion
- Alters peripheral metabolism, leading to the production of various organic acids
- stimulates the respiratory center to increase the rate and depth of respiration
- mixed respiratory alkalosis and metabolic acidosis.

Normal anion gap acidosis

- Difference between high and normal anion gap acidosis
- high anion gap acidosis= bicarbonate is consumed from buffering excess H+
- normal anion gap acidosis= loss of bicarbonate-rich fluid from the kidney or the gastrointestinal tract : more Cl- ions are reabsorbed with Na+ or K+ to maintain electrical neutrality so that hyperchloremia ensues

- Normal anion gap acidosis is divided into (1) hypokalemic, (2) normokalemic, and (3) hyperkalemic acidosis

- **Normal anion gap acidosis with Hypokalemia:**
- Gastrointestinal loss
- RTA

Gastrointestinal loss

- Diarrhea may cause acidosis as a result of loss of (1) Na+, (2) K+, and (3)HCO_3^-
- water, K+, an HCO_3^- in the intestine are not reabsorbed ,
- The resulting hyperchloremia is due to replacement of lost bicarbonate with Cl^-
- a hypokalemic, normal anion gap metabolic acidosis develops

Renal tubular acidosis, Type I and II

- Loss of bicarbonate due to decreased tubular secretion of H+ = distal or type I RTA
- Decreased reabsorption of HCO3-= Proximal or type II RTA
- proximal and distal RTAs may be differentiated by measurement of urine pH after administration of acid :
- proximal R TA, urine pH becomes <5.5, whereas in distal RTA, the distal tubules are compromised and urine pH is >5.5

- **Hyperkalemic normal Anion gap Acidosis: RTA type IV**
- (1) Failure of the kidneys to synthesize renin,
  (2) Failure of the renal cortex to secrete aldosterone, and
  (3) renal tubular resistance to aldosterone.

- inhibits Na+ reabsorption, and both K+ an H+ are thus abnormally retained .
- decreased renal ammonia formation and therefore decreased elimination of H+.

Normal Anion Gap

<u>GI fluid loss</u>	
Severe diarrhoea	Hypokalemia
Pancreatitis	K+ variable
<u>Renal tubular acidosis</u>	
Proximal (type II) RTA	Urine pH <5.5 , K+ normal or low
Distal (typeI) RTA	Urine pH >5.5 with hypokalemia
Type IV RTA	Urine pH < 5.5 with hyperkalemia

Compensation

- Primary compensation: respiratory system
  - Stimulation of RS (Kussmaul respiration)

(1) the elimination of carbonic acid as CO_2,
(2) a decrease in PCO_2 (hypocapnia), and
(3) ultimately a decrease in $cdCO_2$.

- Secondary compensation : by Kidney: takes 2-3 days
- increased excretion of acid and preservation of base by an increase (1) rate of Na+-H+ exchange, (2) ammonia formation, and (3) reabsorption of bicarbonate

Decrease in Anion Gap

Laboratory error

1. Increase in unmeasured cations
2. Lithium intoxication
3. Increased immunoglobulin
4. Monoclonal gammopathies
5. Nephrotic syndrome
6. Hyperlipidemia

Metabolic alkalosis

- (1) excess base is added to the system,
- (2) base elimination is decreased ,
- or (3) acid -rich fluids are lost
- All lead to a primary bicarbonate excess
- alter the cHCO−3 / cdCO2

patient will hypoventilate to raise PCO2

- achieving a PCO2 =55 mm Hg
- Above pH 7.55, tetany may develop:
- cause of the tetany is a decrease concentration of ionized calcium due to increase binding of calcium ions by albumin as H+ ions decrease

- metabolic alkalosis all into
- (1) Cl– responsive,
- (2) Cl– resistant, and
- (3) exogenous base categories

1. *Cl– Responsive Metabolic Alkalosis*

- Occur as a result of hypovolemia
- contraction alkalosis
- Hypovolemia will result in
- (1) increase reabsorption of Na+,
- (2) increase HCO– 3 absorption and
- (3) excretion of K+ and H+.
- Urine Cl– will be less than 10 mmol/L, as both the available Cl– an HCO3 - are reabsorbed with Na+

- **Common causes** of contraction alkalosis include
- prolonged vomiting or
- nasogastric suction and
- the use of certain diuretics
- **Treatment** consists of replacing BW with
- (1) water, (2) NaCl tablets, or
- (3) saline in fusion.

2. *Cl– Resistant Metabolic Alkalosis*

- far less common than Cl– responsive MA
- Associated with:
- (1) primary hyper aldosteronism,
- (2) Cushing syndrome, or
- (3) Bartter syndrome, or with excess addition of exogenous base.
- urine Cl– will be greater than 20 mmol/L.

adrenocortical excess

- K+ an H+ are “wasted ” by the kidneys
- increased Na+ reabsorption stimulated by elevated aldosterone or cortisol
- hypokalemia often further contributes to the alkalosis
  - stimulates NH3 production and thus renal H+ excretion as NH 4+

3. Exogenous Base

- include (1) citrate toxicity following massive blood transfusion,

(2) aggressive intravenous therapy with bicarbonate solutions, and

- (3) ingestion of large quantities of antacids (Milk alkali syndrome)

Chloride responsive (Urine Cl- < 10 mmol/L)

Contraction alkalosis (Hypovolemia)

Prolonged vomiting

Upper duodenal obstruction

Dehydration

Chloride resistant (Urine Cl- > 10 mmol/L)

Mineralocorticoid Excess

Primary hyperaldosteronism

Bilateral adrenal hyperplasia

Secondary hyperaldosteronism

Glucocorticoid excess

Primary adrenal adenoma

Pituitary adenoma secreting ACTH

Exogenous cortisol therapy

Bartter syndrome (defective renal Cl- absorption)

Exogenous base

Bicarbonate containing iv fluid therapy

Massive blood transfusion (Sodium citrate overload)

Milk Alkali syndrome

Compensatory Mechanisms in Metabolic Alkalosis

- **both** respiratory compensation and , if physiologically possible, renal compensation
- **Respiratory compensation:**
- Th e increase in pH depresses the **respiratory center,**
- causing retention of carbon dioxide
- increase in cH2CO3 and cdCO2
- ratio of cHCO− 3 / cdCO2, which was originally increased , approaches its normal value

~~Renal compensation~~

- The **kidneys respond** to the state of alkalosis by
- decrease

(1) Na+-H+ exchange,

(2) formation of ammonia,

and (3) reclamation of bicarbonate

- This response is blunted in conditions of hypokalemia and hypovolemia.

Respiratory acidosis

- occurs **only through decreased elimination** of CO2

- increase in PCO2 (hypercapnia) an dCO2
- decrease in the cHCO3 - / cdCO2 ratio (e.g., the ratio may be 28:1.7 [16:1] or a pH of ≈7.30)

- conditions may be divided into those caused by factors that
  - directly depress the respiratory center
  - mechanical obstruction of the airways
- **Chronic obstructive pulmonary disease (COPD)** is the most common cause

Conditions leading to Respiratory Acidosis

Factors that directly depress the respiratory centre

Drugs such as narcotics
CNS trauma, tumor
Infections of the CNS
Comatose states

Conditions that affect the Respiratory apparatus

COPD (most common)
Severe pulmonary fibrosis
Disease of the upper airway e,g laryngospasm, tumor
Impair lung motion due to pleural effusion
ARDS

Others

Abdominal distension as in peritontitis and ascites
Extreme obesity
Sleep disorder, sleep apnea

Compensatory mechanism

- Immediately via buffers
- Over time via kidneys

- Excess carbonic acid present in blood is bufferd by the **hemoglobin and protein**
- Buffering of CO2 causes a slight rise in cHCO3-
- immediate post hypercapnic state appear as a metabolic alkalosis

Response of Kidney for respiratory acidosis

- similarly to the way that they responds to metabolic acidosis
- Increase in

(1) Na+-H+ exchange,

(2) ammonia formation,
and(3) reclamation of bicarbonate

- Partially compensated= the plasma pH is returned about half way toward normal
  Not effective before 6 to 12 hours and is not optimal until 2 to 3 days.
  COPD= full renal compensation
- COPD with superimposed metabolic alkalosis due to prolonged diuretics

Respiratory response for respiratory acidosis

- stimulates the respiratory center
- Increase pulmonary rate and depth of respiration, provided that the primary defect is not in the respiratory center
- Elimination of carbon dioxide through the lungs results in a decrease in c CO_2;

Respiratory Alkalosis

- decrease in PCO2 (hypocapnia) and the resulting primary defcit in cdCO2
- increased rate and /or depth of respiration
- excess elimination of acid via the respiratory route
- increase in the cHCO3−/ cdCO2 ratio.
- shifts the normal equilibrium of the bicarbonate/carbonic acid buffer system
- reducing the hydrogen ion concentration and increasing the pH
- Also results in a decrease in cHCO3−

- causes of respiratory alkalosis have been

classified as

  - those with a direct stimulatory effect on the respiratory center
  - and those due to effects on the pulmonary system.

Factors causing respiratory Alkalosis

Nonpulmonary stimulation of respiratory center

Anxiety, hysteria
Febrile state
Metabolic encephalopathy
CNS infection
Cerebrovascular accident
Hypoxia
Drugs and agents such salicylates, cathecholamines

Pulmonary disorder

Pnemonia
pulmonary emboli
Interstitial lung disease
CHF
Respiratory compensation after correction of metabolic acidosis

Others

Ventilation induced hyperventilation

Compensatory mechanisms for respiratory alkalosis

- respond in **two stages**
- 1st stage: erythrocyte and tissue buffers provide H+ ions that consume a small amount of HCO3−
- 2nd stage: in prolonged respiratory alkalosis: renal compensation as metabolic alkalosis

ABG parameters in various conditions of acid-base imbalance

Imbalance	Stage	pH	HCO3	pCO2
Metabolic acidosis	Uncompensated	<7.3	Low	Normal
	Compensated	Approx 7.35	Low	Low
Respiratory acidosis	Uncompensated	<7.3	Normal	High
	Compensated	Approx 7.35	High	High
Metabolic alkalosis	Uncompensated	>7.5	High	Normal
	Compensated	Approx 7.45	High	High
Respiratory alkalosis	Uncompensated	>7.5	Normal	Low
	Compensated	Approx 7.45	Low	Low

Summary

- According to Broensted and Lowry: An acid is defined as a substance , ion or molecule that yields H+ in sollution and base is an ion , molecule or substance that can combine with H+ ions.
- Human body produces volatile acids(Carbonic acid) and nonvolatile acid (Sulfuric acid and lactic acid).
- Buffers are the solution that resist the change in pH on addition of acid or base.
- The pH of blood is maintained in a narrow range around 7.35-7.45 by extracellular and intracellular buffering.
- The carbonic-biocarbonate system is the major buffering system.
- The partial pressure of CO2 in blood is 40 mmHg
- The pCO2 is regulated by respiratory system.
- The phosphate buffer system (Na2HPO4/NaH2PO4) operates in the cell and contributes to only about 1% of the plasma buffering capacity.

Summary contd

- Histidine is the most effective amino acid that helps proteins to work as buffer. Albumin has 16 and Hemoglobin has 38 histidine residues.
- Kidneys play a very important role in the regulation of extracellular pH through reabsorption of bicarbonate and secretion of H+, synthesis and excretion of ammonia.
- The clinical disorder associated with accumulation of acids in the tissue and plasma is known as acidosis whereas the build up of alkali in the body is known as alkalosis.
- The respiratory acidosis is seen in cases of pulmonary diseases such as COPD.
- Metabolic alkalosis occurs as a result of net gain of HCO3- or loss of nonvolatile acid
- Assessment of the acid-base imbalance is done by estimation of the arterial blood pH , cHCO3- and pCO2 along with electrolytes

MCQ 1

- A 64 years old man who develops acute renal failure while recovering from myocardial infarction. Blood chemistry reveals Na+140 meq/L , K=4 meq/L , Cl- 115 meq/L , Co2 =5 meq/L , pH 7.12 , paCO2=13 mm Hg , HCo3-=4 meq/L
  - A. His anion gap of 14 indicates metabolic acidosis
  - B. His anion gap of 20 conclusive of respiratory acidosis
  - C. His anion gap of 22 strongly suggestive of metabolic alkalosis
  - D. His anion gap of 21 indicative of high anion gap metabolic acidosis

MCQ2

- A 48 year old man with bronchiectasis presents to the hospital emergency room with 3 days of increasing cough, sputum and dyspnea.About 1 month ago his blood analysis report showed pH 7,38, paO2 55 mmHg, HCO3- 32 meq/L. His current vital signs are BP117/65, pulse 123/min, temp 100oF,. His current ABG in the emergency room pH 7.28, paCO2 70 mmHg, paO2 50 , HCO3- 23 meq/L. Which of the following best characterizes the acid base status of this patient?
  - A. Compensated metabolic acidosis
  - B. Compensated metabolic alkalosis
  - C. Uncompensated metabolic acidosis
  - D. Uncompensated respiratory acidosis

MCQ3

- A 50 year old chronic alcoholics brought to the emergency room in semiconscious state. BP was 100/50 and Heart rate 120/min, Resp rate 35/min, temp 104oFBlood chemistry: Na+= 150 meq/L, K+2.5 meq/L, Cl- 107 meq/L, HCO3- 10 meq/L, pH 7.2,pCO2 =25 mmHg, Alcohol 40 mmol/L (0), Osmolality 370 mOsm/L (280-295), glucose 50 mg/dl, BUN 50 mg/dl (5-22)What is the acid base status?
- A. Metabolic acidosis
- B. Metabolic acidosis with resp compensation
- C. Metabolic alkalosis
- D. Metabolic alkalosis with resp comp

MCQ4

- Which of the following is most appropriate for a 17 year old female suffering from IDDM with the following blood chemistry report:
- pH 7.2, pO2 108 mmHg, pCo2 12 mmHg, HCO3- 5 meq/L
- A. Metabolic acidosis with resp compensation
- B . Metabolic alkalosis with respiratory compensation
- C. Metabolic acidosis
- D. Metabolic alakalosis