Biochemstry Team

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.. Lactic Acidosis ..

- Introduction to metabolic acid-base disorders
  - Metabolic acidosis and alkalosis
- Lactic acidosis
  - Definition
  - Lactate metabolism in tissue
  - Mechanisms involved in lactic acidosis
  - Types and causes of lactic acidosis
  - Diagnosis and treatment

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❖Metabolic acid-base disorders

❖Changes in bicarbonate (HCO_3^-) conc. in the extracellular fluid (ECF) causes acid-base disorders.

❖Occur due to high conc. or loss of H^+ ions.

PH:
7.35- 7.45 Normal
< 7.35 acid
>7.45 alkaline

Metabolic acid-base disorders can lead to:

- Metabolic acidosis (H elevated and HCO3↓)
  - Impaired H^+ excretion or Loss of HCO_3
  - Increased H^+ production or ingestion
- Metabolic alkalosis (H decreased and HCO3↑)
  - Loss of H^+ in vomit or alkali ingestion like NaHCO3
  - Potassium deficiency*as a result of diuretic therapy
  - Increase in bicarbonate conc. in ECF

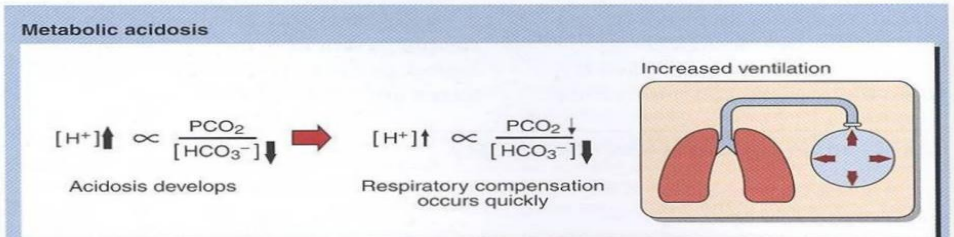
* Potassium has very small amount in ECF. So, if there is K deficiency, K will start coming out of the cell. Then, In exchange for it, H ion goes inside the cell. That lead to loss of H ions in the ECF.

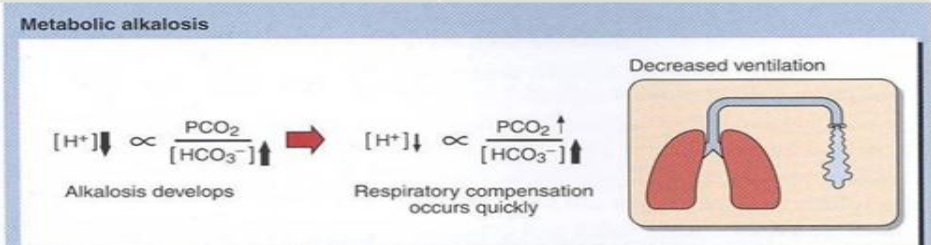
Anion Gap

Definition	It is a biochemical tool that we use to see the person's metabolic status (acidosis or alkalosis)"	
How we measure it ?	• It is the difference between the sum of: ➢Na+ and K+ (cations) and ➢the sum of Cl – and HCO3– (anions)	(Na)-(Cl+Hco3) * We omit K when we doing calculation because it present in so low amount.
Why we do it	• Helps in assessing acid-base problems and the high anion gap occures in: Renal disease,Diabetic ketoacidosis,Lactic acidosis, Poisoning.	• **Normal anion gap: 3-11 mEq/L** • **>11 mEq/L (acidosis)** • **<3 mEq/L (alkalosis)**

Clinical effects of acidosis & alkalosis

Acidosis	↑H^+ conc. → **Hyperventilation** → deep, rapid, and gasping respiratory pattern.	**Lead to** Arrhythmia, cardiac arrest, Loss of consciousness, coma, death.
Alklosis	↓H → **Hypoventilation** - Respiratory arrest	**Lead to** Confusion, coma, death.

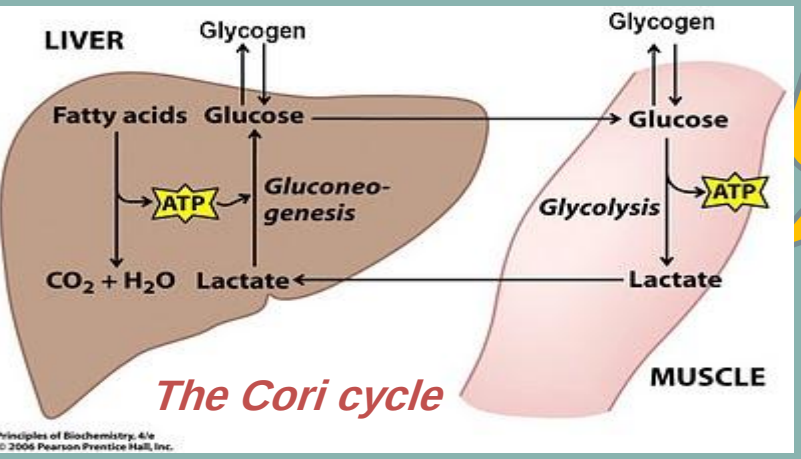




Lactate metabolism in tissue

Lactate is metabolized in kidney(30%) Liver (60%) (Krebs cycle) to CO_2 and water

The body tissues produce ~ 1500 mmoles of lactate each day
Pyruvate is converted to lactate by lactate dehydrogenase enzyme



The lactate enters blood stream and metabolized mainly by the liver

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$$\text{Pyruvate} + NADH + H^+$$

↓ *Lactate dehydrogenase*

$$\text{Lactate} + NAD^+$$

Lactic acidosis

Elevated conc. of plasma lactate is called lactic acidosis

Failure of circulatory system (hypoxia)

Disorders of carbohydrate metabolism

And this lead to **Excessive tissue lactate production or Impaired hepatic metabolism of lactate**

Types and causes of lactic acidosis

	Type A	Type B
Causes	**Hypoxia** in tissues (most common) Due to : - Myocardial infarction - Pulmonary embolism - Uncontrolled hemorrhage - Tissue hypoperfusion (shock, cardiac arrest, acute heart failure, etc.) - Anaerobic muscular exercise **How does it occur?** - Hypoxia causes impaired oxidative phosphorylation ➔ ↓ATP synthesis ➔cells switch to anaerobic glycolysis for ATP synthesis ➔produces lactate as a final product. **- The amount of oxygen required to recover from oxygen deficiency is called <u>oxygen debt</u>**	-**Disorders in carbohydrate metabolism ?** ➔ Congenital lactic acidosis is due to deficiency of pyruvate dehydrogenase enzyme. **- Chronic hepatic disease accompanied by shock or bleeding** **- Liver failure** **- Drug intoxication.**

Diagnosis and treatment

Dignosis/by measuring blood lactate levels

- Normal level: < 2 mmols/L
- Hyperlactemia: 2 – 5 mmols/L
- Severe lactic acidosis: > 5 mmols/

Treatment/ -Correcting the underlying conditions

- Restoring adequate tissue oxygen
- <u>Avoiding</u> sodium bicarbonate

Q1: Increase production of H^+ ions lead to:

A- acidosis

B- alkalosis

C- both

D- none of the above

Q2: Normal anion gap is:

A- 5-6 mEq/L

B- 8 mEq/L

C- < 3 mEq/L

D- 3-11 mEq/L

Q3: Diabetic ketoacidosis will lead to:

A- High anion gap

B- low anion gap

C- Normal anion gap

D- alkalosis

Q4: the physiological response to metabolic alkalosis:

A- Hyperventilation

B- Hypoventilation

C- both

D- none of the above

Q5: the range of hyperlactemia:

A- 6 mmols/L

B- 10 mmols/L

C- 9-11 mmols/L

D- 2-5 mmols/L

Answers:

A

D

A

B

D