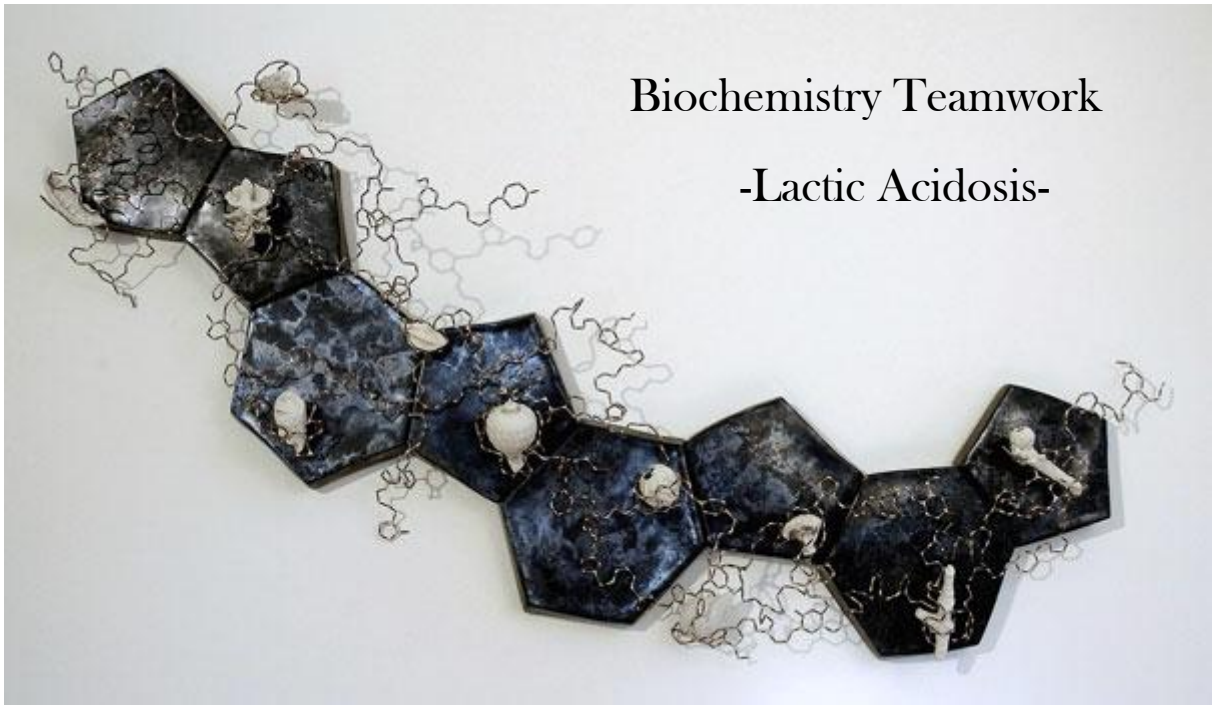

Team Leaders	
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Team Members	
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Metabolic acid-base disorders

- Changes in bicarbonate conc. in the extracellular fluid (ECF) causes acid-base disorders
- Occur due to high conc. or loss of H+ ions
- Can lead to:
  - Metabolic acidosis
  - Metabolic alkalosis

You have to know followings:-
H ions and co2 are acidic
Hco3 are alkali or basic

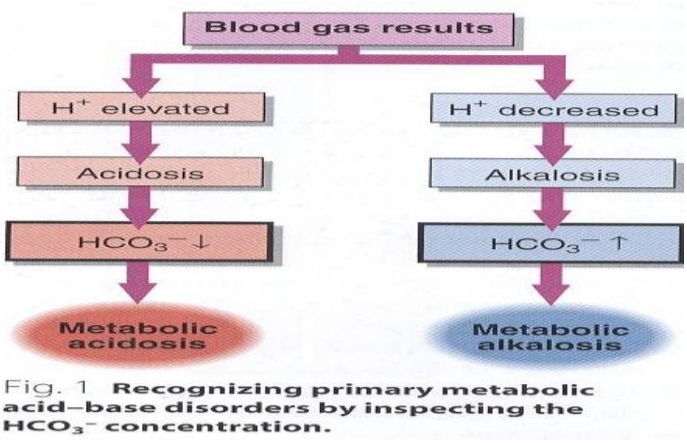


Fig. 1 Recognizing primary metabolic acid–base disorders by inspecting the HCO_3^- concentration.

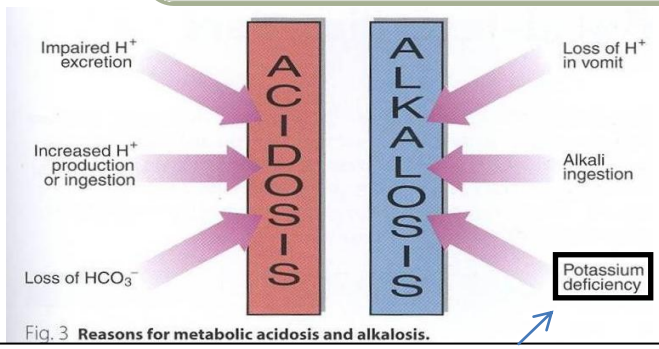


Fig. 3 Reasons for metabolic acidosis and alkalosis.

Ex: If we take diuretic drugs, the K^+ ions are decreased in ECF so H^+ ions are used by cells instead of K^+ to balance the electric gradient. ∴ H+ in ECF is ↓

In human body Acid-base balance system is the major system in the body that maintains the PH in the normal range.
Bicarbonate conc. or function has the most important role.

Metabolic acidosis

- Reduction in bicarbonate conc. of ECF Causes:
- Increased production of H^+ ions
- Ingestion of H^+ or drugs metabolized to acids
- Impaired excretion of H^+

Anion gap

- It is the difference between the sum of:
- Na+ and K+ (cations) and
- the sum of Cl – and HCO3– (anions)
- Helps in assessing acid-base problems

Anion gap is measured biochemically not physiologically, which means that in case of decreased anions, plasma proteins which are negatively charged increases to compensate. So decreased anions >> there is no change in physiological functions, but the change is biochemical.

Low anion gap: <3 mEq/L alkalosis	Normal anion gap: 3-11 mEq/L	High anion gap: >11 mEq/L (acidosis)

Anions are more which leads to alkalosis

Cations are more which leads to acidosis

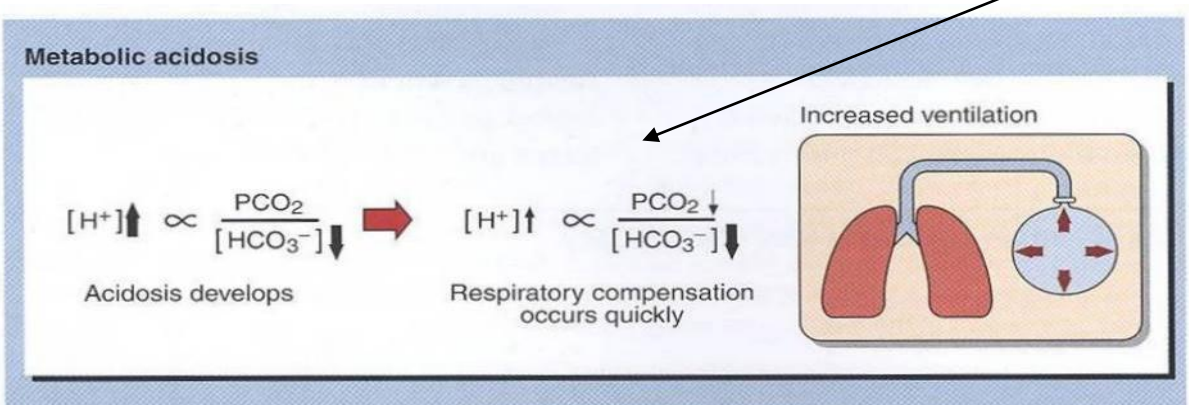
High anion gap occurs in:

- Renal disease — imapaired H^+ secretion
- Diabetic ketoacidosis — diabetics produce many ketone bodies that are acidic when metabolized
- Lactic acidosis
- Chronic diarrhea — loss of ions with fluids
- Poisoning
- Renal tubular acidosis

Clinical effects of acidosis

- Hyperventilation is the compensatory physiological response to acidosis
- Increased H^+ conc. stimulates respiratory response
- Hyperventilation: deep, rapid, and gasping respiratory pattern
- Arrhythmia, cardiac arrest, hyperkalemia
- Loss of consciousness, coma, death

Hyperventilation to remove acidic CO_2



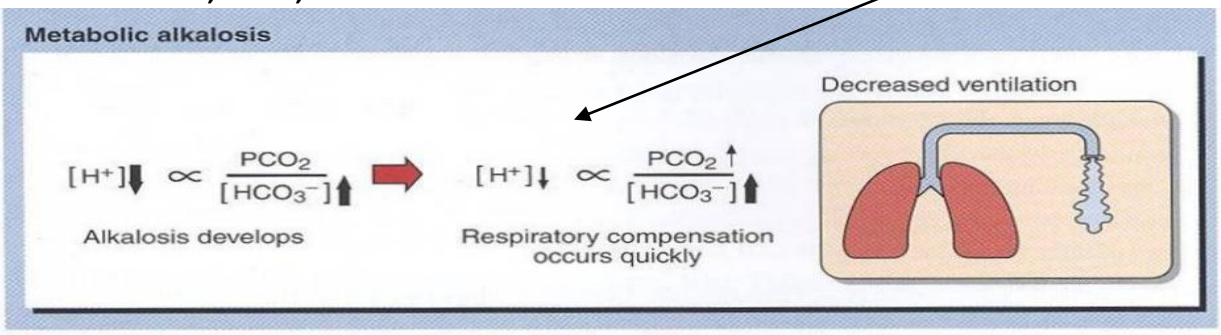
Metabolic alkalosis

- Increase in bicarbonate conc. in ECF
- The causes are:
  - Loss of H^+ ions in gastric fluid due to vomiting
  - Ingestion of sodium bicarbonate
  - Potassium deficiency (as a result of diuretic therapy).

Clinical effects of alkalosis

- Hypoventilation (depressed breathing)
  - Increases PCO_2 to compensate alkalosis
  - Respiratory arrest
- Confusion, coma, death

Hypoventilation to maintain more acidic CO_2

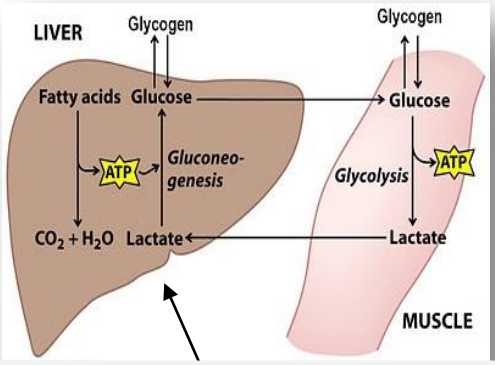


Lactic acidosis

- Elevated conc. of plasma lactate is called lactic acidosis
- Occurs either due to:
  - Failure of circulatory system
  - Disorders of carbohydrate metabolism
- The body tissues produce ~ 1500 mmoles of lactate each day
- The lactate enters blood stream and metabolized mainly by the liver (Cori cycle)
- All tissues can produce lactate under anaerobic conditions
- Pyruvate is converted to lactate by lactate dehydrogenase Enzyme.

A problem in glycolysis leads to accumulation of lactate acid

Cells which are highly active (in glycolysis) produce more lactate because the amount of pyruvate produced is more than the amount used in oxidative phosphorylation (spill over). But all cells (active or not) produce lactate in anaerobic state



pyruvate dehydrogenase plays an important role in conversion of lactate back into pyruvate " not mentioned by The DR , but plays role in lactic acidosis Type B

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

Lactate dehydrogenase

$$Lactate + NAD^{+}$$

The Cori cycle

- The skeletal muscles produce high amounts of lactate during vigorous exercise.
- Lactate is metabolized in liver (60%) and kidney (30%) to glucose
- Some lactate is metabolized to CO2 and water (Krebs cycle) (10%)

We get rid of lactate by Cori's cycle in the liver to produce glucose, so if there's a problem in the liver we might develop lactic acidosis

Mechanisms involved in lactic acidosis

Lactic acidosis can occur due to:

- Excessive tissue lactate production
- Impaired hepatic metabolism of lactate

Types and causes of lactic acidosis

Type A

- Due to hypoxia in tissues (most common)
- Hypoxia causes impaired oxidative phosphorylation "and" respiratory chain "leads to decreased ATP synthesis "DR says it's very important "
- To survive, the cells switch to anaerobic glycolysis for ATP synthesis
- This Produces lactate as a final product
- The amount of oxygen required to recover from oxygen deficiency is called oxygen debt

- **Type A is due to inadequate supply of oxygen to tissues in:**
- Myocardial infarction
- Pulmonary embolism
- Uncontrolled hemorrhage
- Tissue hypoperfusion (shock, cardiac arrest, acute heart failure, etc.)
- Anaerobic muscular exercise

remember pyruvate dehydrogenase complex? http://tiny.cc/5oc7aw

If disorder affects that complex, pyruvate is forced to go back and form lactate.

Type B

- Due to 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 done by measuring blood lactate levels**
  - Hyperlactemia: 2 – 5 mmols/L
  - Severe lactic acidosis: > 5 mmols/L
- **Treatment:**
  - Correcting the underlying conditions
  - Restoring adequate tissue oxygen
  - Avoiding sodium bicarbonate DR says that it's so important to know the cause

Lactate levels less than 2 are normal. Levels between 2 and 5 "hyperlactemia" are not lactate acidosis because the cells have a buffering capacity and they take care of extra lactate

Why do we avoid giving Sodium Bicarbonate incase of Lactic Acidosis ?

because: When we inject the patient of lactic acidosis with sodium bicarbonate (basic), it will lead to transient alkalosis. The body will compensate and increase the acidity. Once the transient alkalosis is diminished, the compensatory mechanism will worsen the acidosis.

Review Questions

1- Which one of the following statements is true about lactic acidosis?
   A- Increased in Hydrogen ions .
   B- Decreased in Hydrogen ions.
   C- Increased in concentration of Bicarbonate.
   D- A & C
2- A 20 year male administered to KKUH suffering from some annoying symptoms. We measured the anion gap and we found that it was = 16 mEq\L . which of the following is most likely to be noticed in this patient ?
   A- Depressed Breathing.
   B- Confusion.
   C- Hyperventilation.
   D- Decreased in Hydrogen ions.
3- Which one of the following is the most important cause of lactic acidosis?
   A- Impaired liver
   B- Muscle fatigue.
   C- Hypokalemia.
   D- Decreased in H+.
4- Which one of the following is the cause of Type A lactic acidosis?
   A- Hypoxia.
   B- Dysfunction of the Liver.
   C- Deficiency in Pyruvate Dehydrogenase Enzyme.
   D- A & C
5- Pyruvate is converted to lactate by :
   A- Lactate dehydrogenase.
   B- Pyruvate dehydrogenase.
   C- PFK1
   D- All are true.

Answers : A,C,A,A,A