editing file

Lactic Acidosis

Color Index:

- Original content
- Important
- Extra info, Dr's notes

Objectives:

Slide No. 3	Define metabolic acid-base disorders including lactic acidosis
Slides (3,5,6)	Understand the causes and clinical effects of metabolic acidosis and alkalosis
Slide No. 7	Recall the lactate metabolism in the body
Slide No. 8	Differentiate between the types of lactic acidosis
Slide No. 4	Understand the clinical significance of measuring anion gap
Slide No. 8	Discuss the causes and diagnosis of lactic acidosis in conditions such as myocardial infarction

Overview:

Introduction to metabolic acid-base disorders:

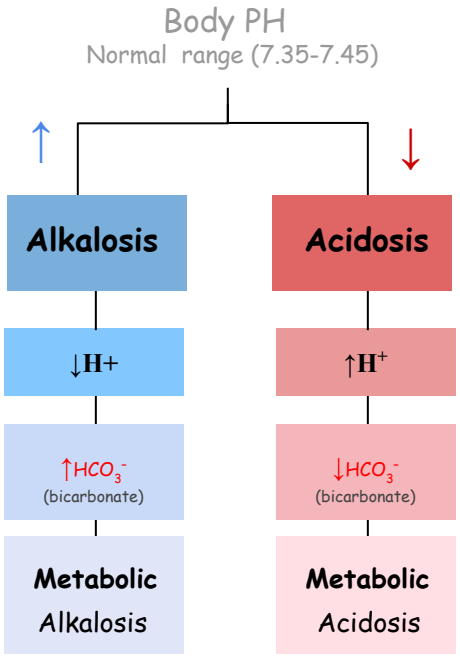
- Metabolic acidosis and alkalosis

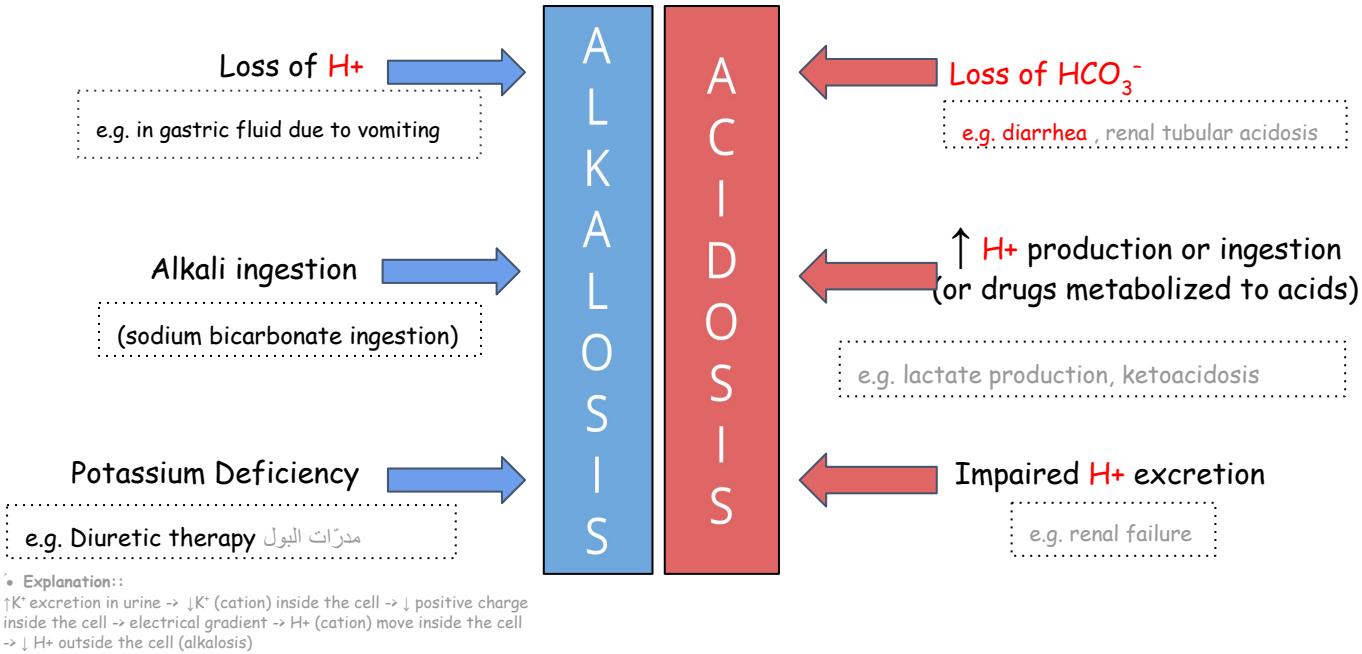
Lactic acidosis:

- Definition
- Lactate metabolism in tissue
- Mechanisms involved in lactic acidosis
- Types and causes of lactic acidosis
- Diagnosis and treatment

Metabolic acid-base disorders

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





- **Explanation::**
↑K^+ excretion in urine -> ↓K^+ (cation) inside the cell -> ↓ positive charge inside the cell -> electrical gradient -> H+ (cation) move inside the cell -> ↓ H+ outside the cell (alkalosis)

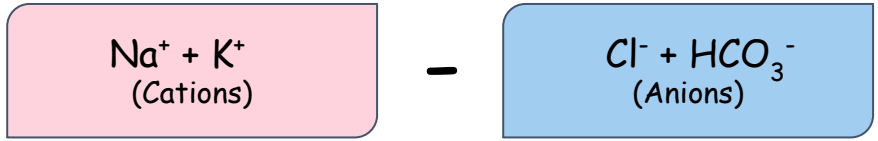
Remember :

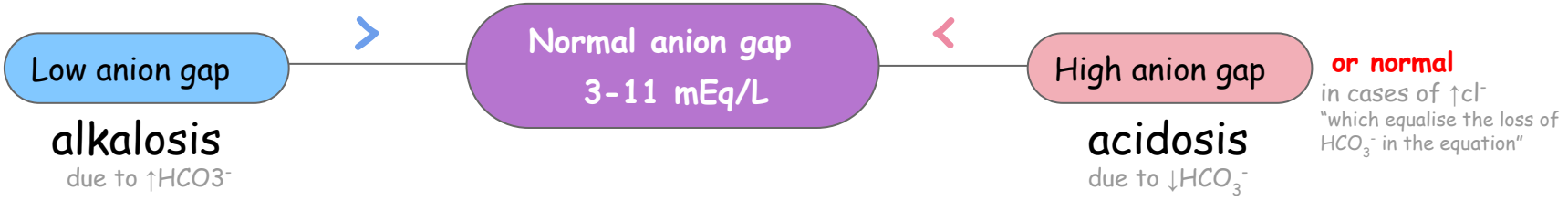
- Respiratory acidosis/ alkalosis : depends on the PCO_2
- Metabolic acidosis/ alkalosis: depends on the conc. Of bicarbonate ions [HCO_3^-]

Anion Gap

★ Helps in assessing acid-base problems

★ it's the difference between the sum of famous cations (+ions) & anions (-ions)





Extra:

Normally in the body to maintain a neutral PH anions=cations (physiologically there's no gap) but since it's hard to calculate each sing electrolyte in the body instead to diagnose acid-base problems famous electrolytes are measured BUT theses famous electrolytes aren't equal in concentrations instead, cations are more than anions and that what creates (anion gap) which was measured.

Metabolic acidosis

Reduction in bicarbonate conc. of ECF

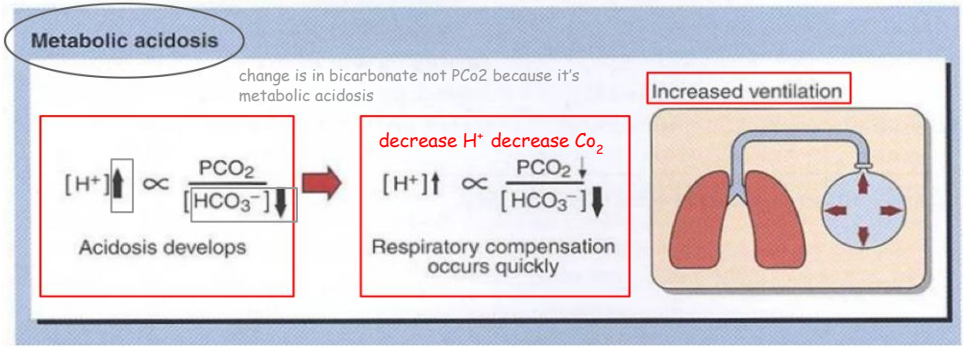
★ High anion gap occurs in:

- **Renal disease**
- **Diabetic ketoacidosis**
  - a condition with very low insulin in the body -> ↑glucagon effect -> glucose release into the blood -> the cells can't use glucose as energy source -> fatty acid metabolism (β-oxidation) -> ketone bodies (acids)
- **Lactic acidosis**
- **Poisoning**

★ Clinical effects:

↑H+ → stimulates → **Hyperventilation**

the compensatory physiological response (respiratory response) to acidosis



- **Respiratory pattern:**
  - deep
  - rapid
  - gasping
- **Risks:**
  - Arrhythmia
  - cardiac arrest
  - Loss of consciousness
  - coma
  - death

Compensation of Acidosis:

- Fast: hyperventilation
- Slow: HCO3- from the kidneys

Chronic diarrhea = normal anion gap

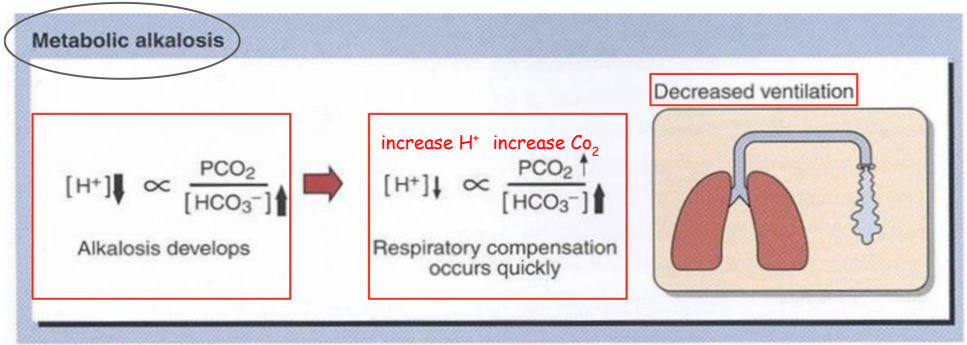
because: loss of bicarbonate (in stool) causes retaining of chloride ions (hyperchloremia) which compensate the loss of bicarbonate

Metabolic alkalosis

Increase in HCO_3^- (bicarbonate) concentration in ECF

★ Clinical effects:

Hypoventilation (depressed breathing) → ↑PCO2 to compensate alkalosis



- **Risks:**
  - Respiratory arrest
  - Confusion
  - Coma
  - Death

Lactic acidosis

Elevated concentration of plasma lactate

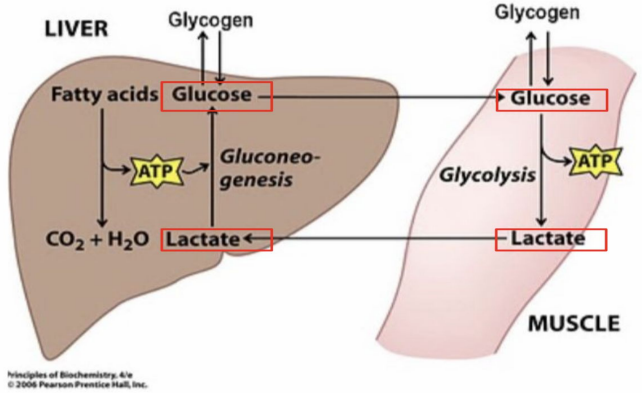
★ Occurs either due to:

- Failure of circulatory system (hypoxia)
- Disorders of carbohydrate metabolism

Lactate metabolism in tissue

- The body tissues produce ~ 1500 mmoles of lactate each day
- The lactate enters bloodstream and metabolized mainly by the liver (Cori cycle) lactic acid cycle (produces glucose)
- All tissues can produce lactate under anaerobic conditions
- Pyruvate is converted to lactate by lactate dehydrogenase enzyme:

$$\text{Pyruvate} + \text{NADH} + \text{H}^+ \xrightarrow{\text{Lactate dehydrogenase}} \text{Lactate} + \text{NAD}^+$$



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)

Recall:
why does cori cycle occurs mainly in liver (not skeletal muscle)?
due to sufficiency of ATP & NAD^+

Extra: why does the body produces lactate?
In anaerobic metabolism there's no oxygen to accept the electrons from NADH and reoxidizing it to NAD+. so, NADH will accumulate in the cell. the reduction of pyruvate into lactate is mediated by the conversion of NADH -> NAD+ and thus it prevent accumulation of NADH which is a serious problem "lactate isn't a problem thanks to cori cycle ;)"

Mechanism involved in lactic acidosis

1. Excessive tissue lactate production >1500 mmoles
2. Impaired hepatic metabolism of lactate with normal lactate production

or could be both

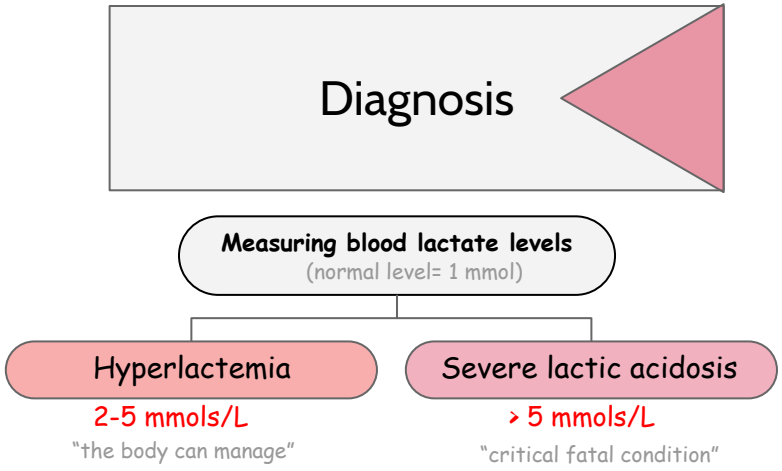
★ Note: There is a difference between the main cause which mentioned and the mechanism

Types and causes of lactic acidosis

Type	Due to	Results in	Causes (Diagnosis)
A	inadequate supply of oxygen to tissues (hypoxia) **"most common"** • treatment: oxygen mask	1. impaired oxidative phosphorylation 2. ↓ ATP synthesis 3. switching to anaerobic glycolysis 4. lactate production "lactate can be used as a marker"	1- Myocardial infarction 2- Pulmonary embolism 3- Uncontrolled hemorrhage 4- Tissue hypoperfusion (shock, cardiac arrest, acute heart failure, etc.) 5- Anaerobic muscular exercise
B	Any other causes not related to oxygen	-	1- disorders in carbohydrate metabolism: congenital deficiency of pyruvate dehydrogenase enzyme (an enzyme that converts pyruvate -> Acetyl coA) So, pyruvate won't be converted to Acetyl coA and the fate of pyruvate will be lactate. 2- Chronic hepatic disease accompanied by shock or bleeding (disturbing cori cycle) 3- Liver failure (disturbing cori cycle) 4- Drug intoxication (produces lactate) "e.g. aspirin poisoning"

★ **oxygen debt**: The amount of oxygen required to recover from oxygen deficiency

Diagnosis & treatment



- Correcting the underlying conditions
- Restoring adequate tissue oxygen
- Avoiding sodium bicarbonate

Recall from foundation block:
Citrate (Acid) inhibits Phosphofructokinase-1 (PFK-1) "an important regulatory enzyme in glycolysis". Consumption of bicarbonate will solve the acidosis and therefore stop this inhibition. So, glycolysis will be active and lactic acid production will be increased.

Take home message

- Lactic acidosis can be caused by hypoxia, excessive production and impaired clearance of lactic acid.
- It carries clinical significance in the diagnosis of myocardial infarction, pulmonary embolism and other metabolic conditions.

Quiz

MCQs

Q1: In a man undergoing surgery, the contents of the upper gastrointestinal tract were aspirated. After surgery, the following values were obtained from an arterial blood sample: pH 7.55, PCO_2=52 mmHg and HCO_3=40 mmol/l. What is the underlying disorder?
a) Metabolic Acidosis **b)** Metabolic Alkalosis **c)** Respiratory Acidosis **d)** Respiratory Alkalosis

Q2: Which of the following laboratory results indicates compensated metabolic alkalosis?
a) ↓pCO2, normal bicarbonate and ↑pH **b)** ↓pCO2, ↓bicarbonate and ↓pH
c) ↑pCO2, normal bicarbonate and ↓pH **d)** ↑pCO2, ↑bicarbonate and ↑pH

Q3: A patient with no history of respiratory diseases developed Hypoventilation, what happened to the PCO2/HCO3 ratio and blood PH to cause him to hypoventilate?
a) Decreased,decreased **b)** Increased,decreased **c)** Decreased,increased **d)** Increased,decreased

Q4: Which of the following will cause metabolic alkalosis?
a) Potassium deficiency **b)** Loss of bicarbonate **c)** Alkali ingestion **d)** Both a,c

Q5: where is lactate mainly metabolized?
a) Skeletal muscle **b)** Liver **c)** Kidney **d)** Small intestine

Q6: Causes of lactic acidosis include all except:
a) Acute Myocardial infarction **b)** Hypoxia **c)** Circulatory failure **d)** Infections

Q7: Causes of metabolic alkalosis include all the following except:
a) Mineralocorticoid deficiency. **b)** Hypokalemia
c) Thiazide diuretic therapy. **d)** Recurrent vomiting.

SAQs

Q1: Omar was doing a vigorous exercise which caused severe hypoxia in most of his skeletal muscle tissues, his lactate level was 7,What can hypoxia cause in this situation?

Q2: Elevated concentration of plasma lactate occurs due to what?

Q3: How does lactate form?

Q4: A patient presented to the ER with a history of impaired carbohydrate metabolism due to a congenital deficiency of an enzyme. his blood lactate was 3, what's the most likely deficient enzyme in this case?

Q5: What's your diagnosis for the patient (from Question 4) ?

★ MCQs Answer key:

1) B 2) D 3) C 4) D 5) B 6) D 7) A

★ SAQs Answer key:

1) Impaired oxidative phosphorylation, decreased ATP synthesis & lactate production.

2) 1-Failure of circulatory system (hypoxia)
2-Disorders of carbohydrate metabolism.

3) all tissues can produce lactate under anaerobic conditions by converting pyruvate to lactate which is done by lactate dehydrogenase enzyme.

4) Pyruvate dehydrogenase enzyme.

5) Lactic acidosis Type B, the blood lactate is 3 so the patient has hyperlactemia.

Team members

Girls team :

- Ajeed Al-rashoud
- Alwateen Albalawi
- Elaf Almusahel
- Haifa Alessa
- Lama Alassiri
- Lina Alosaimi
- Nouf Alhumaidhi
- Noura Alturki
- Nouran Arnous
- Reem Algarni
- Shahd Alsalamh
- Taif Alotaibi

Boys team :

- Abdullah Altuwaijri
- ★ Alkaseem binobaid
- Fares Aldokhayel
- ★ Naif Alsolais
- ★ Sultan Alhammad

Team leaders

Deema Almaziad — **Mohannad Alqarni**

★ This lecture was done by

YOU WILL NEVER HAVE THIS DAY AGAIN, SO MAKE IT COUNT

438 BIOCHEMISTRY TEAM