Biochemistry Team 435

جامعة الملك سعود
King Saud University 1957

LACTIC ACIDOSIS

"IF IT DOESN'T CHALLENGE YOU, IT WON'T CHANGE YOU"

Color index:
- Important
- Extra explanation

* Please check out this link to know if there are any changes or additions.

PHYSIOLOGY TEAM 435

Acidosis Vs Alkalosis

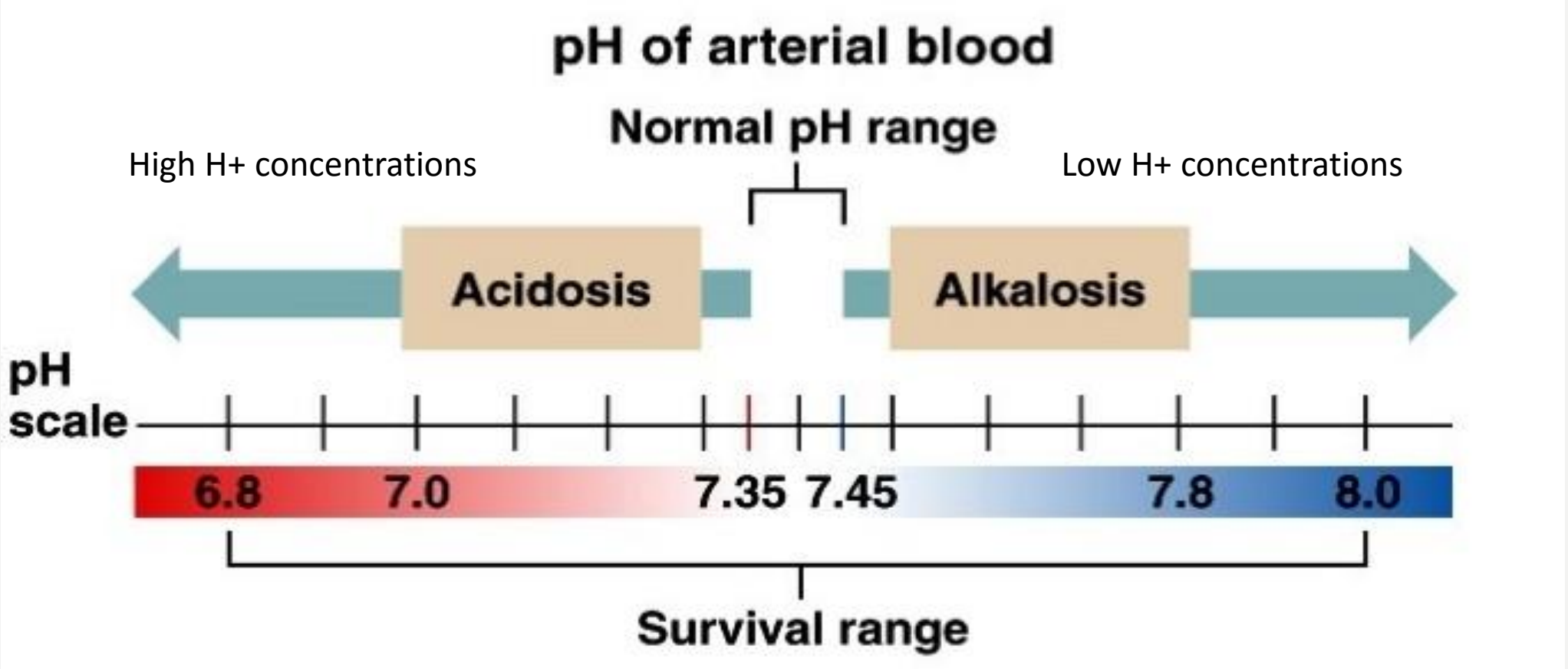
Respiratory acidosis.	Respiratory alkalosis.
Hypoventilation. Accumulation of CO2 in the tissues. PCO2 increases – H+ Increase pH decreases.	Hyperventilation. Excessive loss of CO2 . PCO2 decreases (↓ 35 mmHg). – H+ decrease pH increases.

Metabolic acidosis.	Metabolic alkalosis.
- Ingestion, infusion, or production of a fixed acid. - Decreased renal excretion of hydrogen ions. - Loss of bicarbonate or other bases from the extracellular compartment. - pH decreases.	- Excessive loss of fixed acids from the body - Ingestion, infusion, or excessive renal reabsorption of bases such as bicarbonate. - pH increases.

- **The respiratory system can compensate for (يُعوض) metabolic acidosis or alkalosis by altering alveolar ventilation.**
- **Metabolic acidosis > Hyperventilation.**
- **Metabolic alkalosis > Hypoventilation.**

This slide might help you to understand some of the important concepts in the lecture ☺

RECALL:


pH of arterial blood
Normal pH range
High H+ concentrations
Low H+ concentrations
Acidosis
Alkalosis
pH scale
6.8
7.0
7.35
7.45
7.8
8.0
Survival range

OBJECTIVES:

- Know the condition s associated with excessive blood lactate production.
- Recognize the importance and consequence of lactate production.
- Identify fates of lactate.
- Evaluate lactic acidosis as a medical emergency.

METABOLIC ACID-BASE DISORDERS

- What are they?

Disorders that are caused by changes in bicarbonate concentration in the extracellular fluid (ECF), occur due to high concentration or loss of hydrogen ions.

They can lead to: -

	1- Metabolic acidosis.	2-Metabolic alkalosis.
Hydrogen ions concentration	Elevated	Decreased
Bicarbonate level (HCO_3^-)	Decreased	Elevated
Causes:	- Impaired H+ excretion. - Increased H+ production or ingestion. - Loss of HCO3–	- Loss of H+ in vomit. - Alkali ingestion. - Potassium deficiency.

METABOLIC ACID-BASE DISORDERS

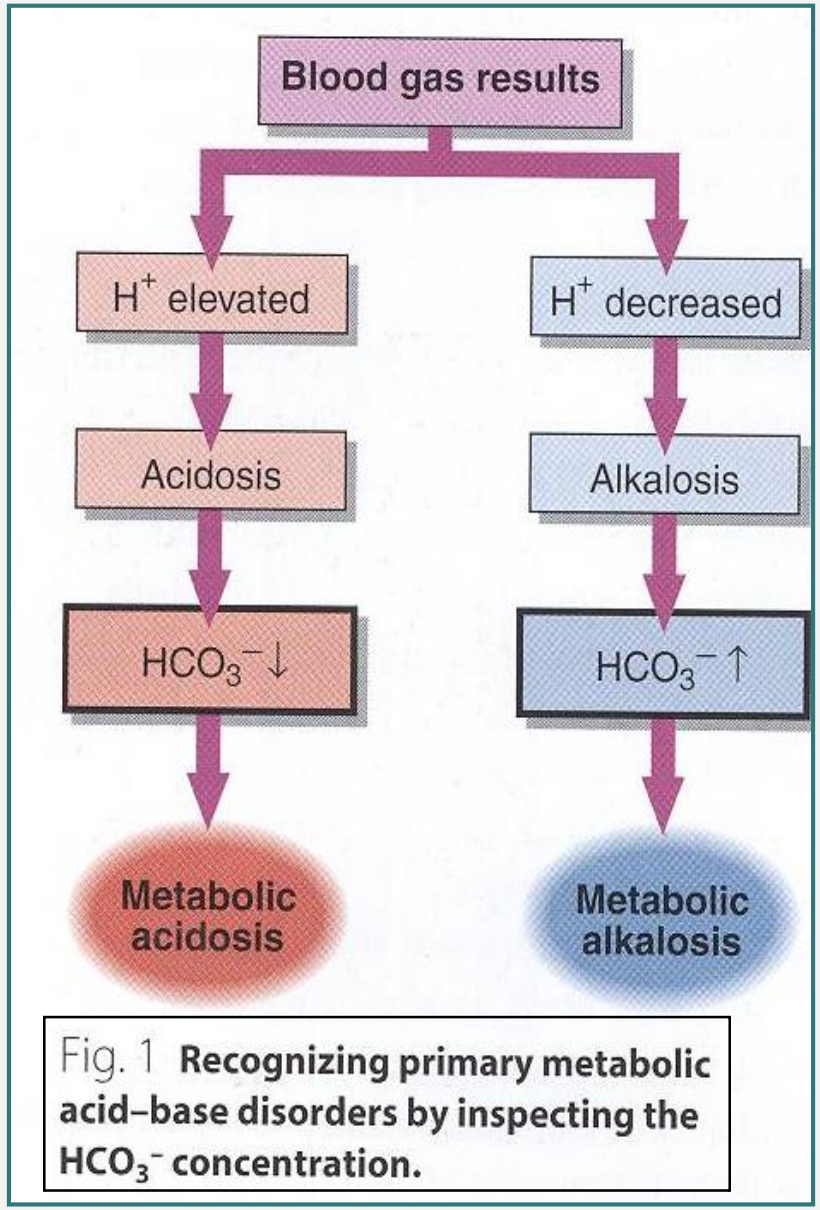


Fig. 1 **Recognizing primary metabolic acid–base disorders by inspecting the HCO_3^- concentration.**

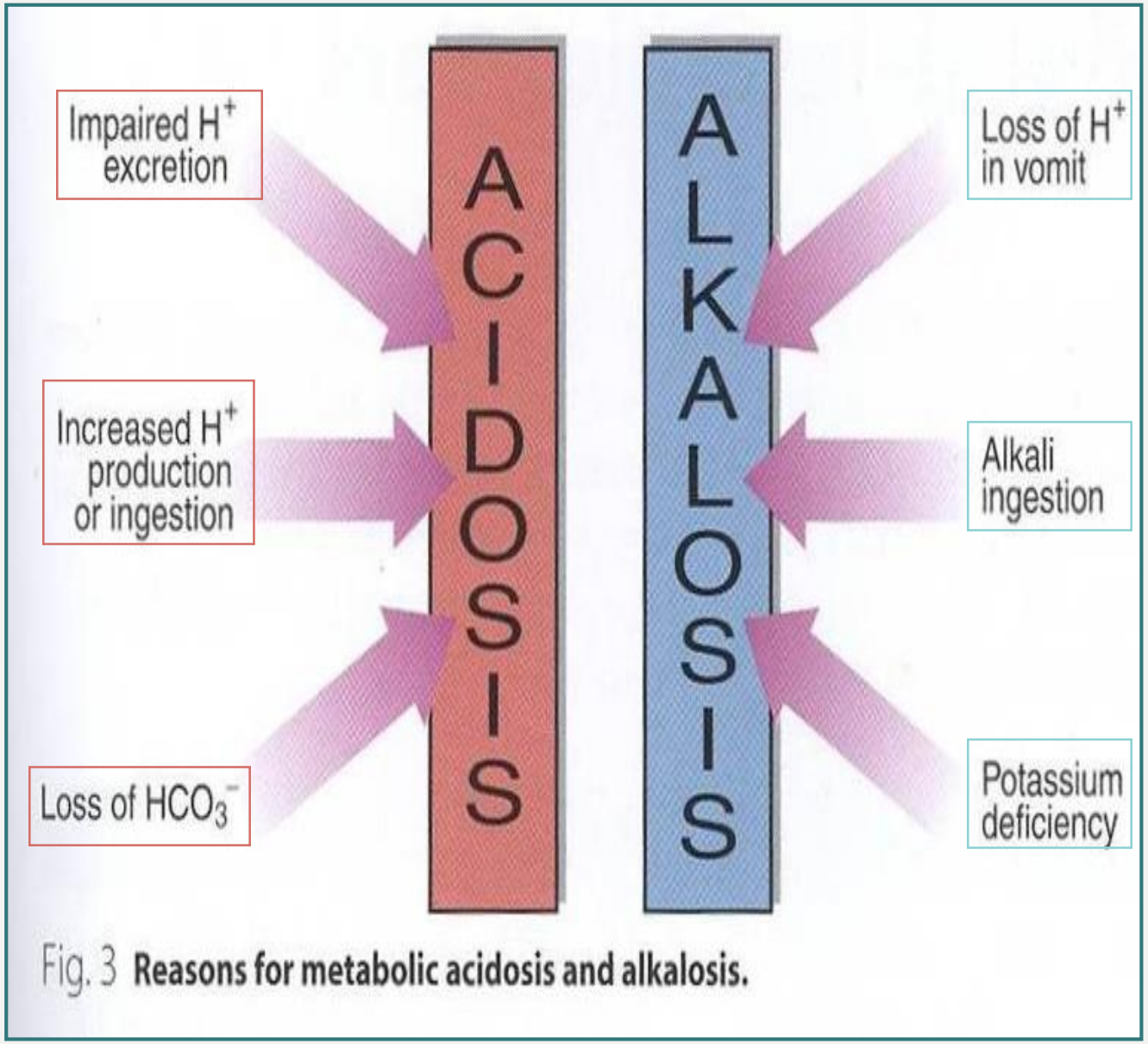


Fig. 3 **Reasons for metabolic acidosis and alkalosis.**

ANION GAP

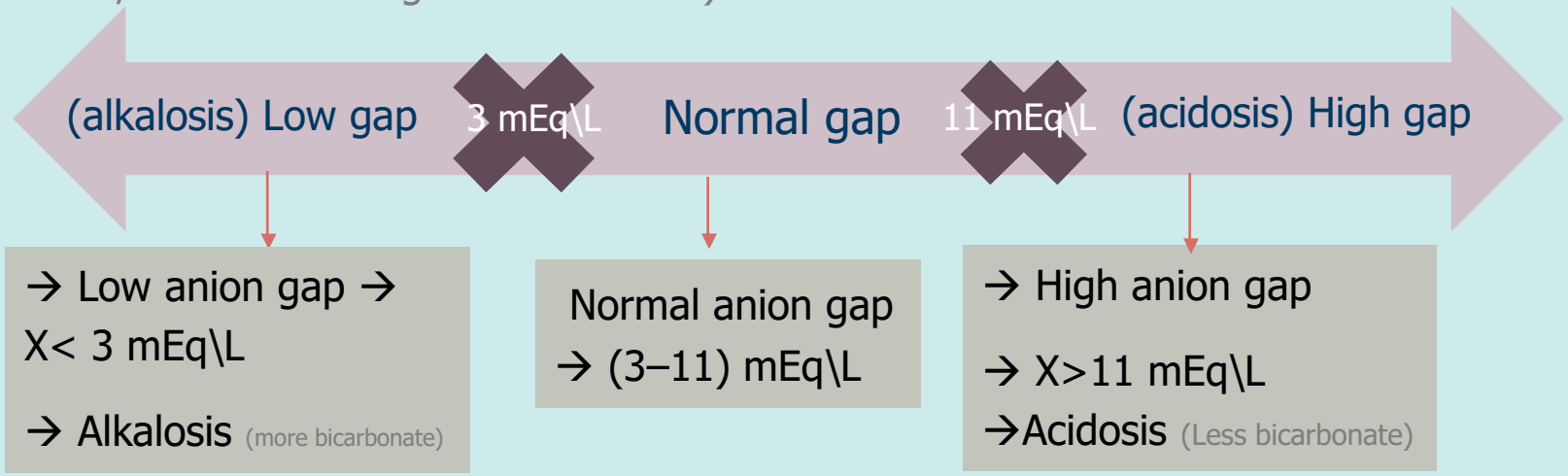
- What is it?

It is **the difference** between the sum of: cations (Na+ and K+) and anions (Cl^- and HCO_3^-).

- Its importance: It helps in assessing acid-base problems.

- How?

After calculation the anion gap (By measuring all the cations, then measuring all anions, and subtracting the two values) we look at the value:



Understand it, don't only memorize!

* The formula of AG is:

$AG = (Na^+ + K^+) - (Cl^- + HCO_3^-)$

Because of that we consider the value of:

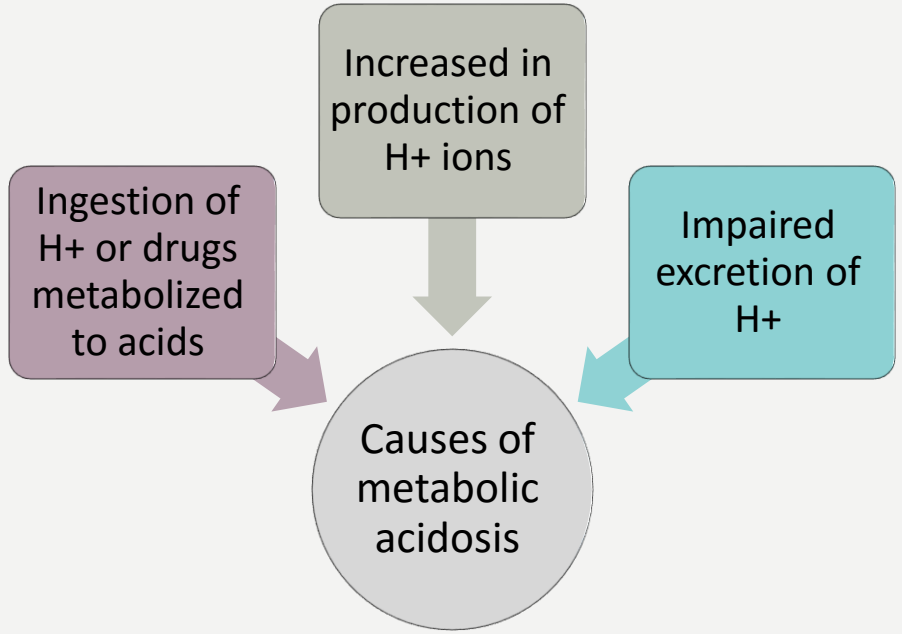
- **Alkalosis < 3** (Bc anion in the formula have –ve charge)
- **Acidosis > 11** (Bc cations in the formula have +ve charge)

Useful Video

METABOLIC ACIDOSIS

What is it?

A **reduction** in bicarbonate concentration of extracellular fluid (ECF). When alkaline molecule (HCO_3^-) decreased = Acidic molecules will have the upper hand.

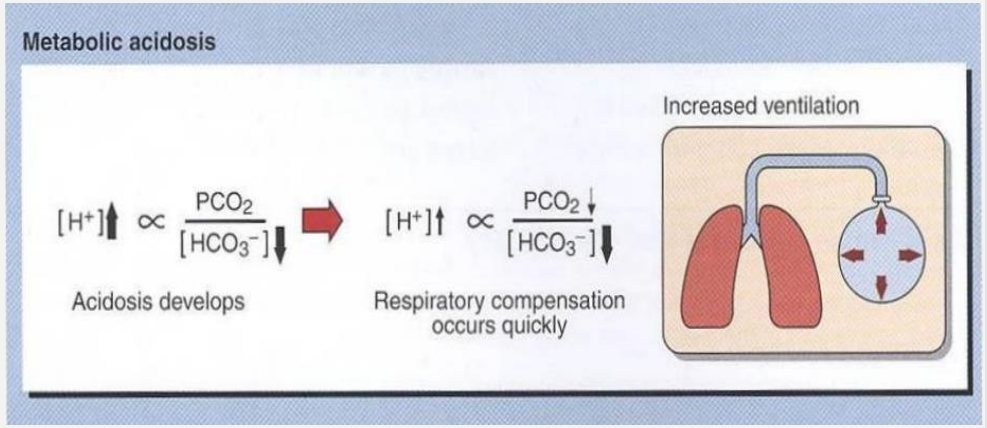


$$\uparrow[H^+] \propto \frac{PCO_2}{\downarrow[HCO_3^-]} \Rightarrow \uparrow[H^+] \propto \frac{\downarrow PCO_2}{\downarrow[HCO_3^-]}$$

Acidosis develops

Hyperventilation
Respiratory compensation occurs quickly

كما درسنا في البلوك السابق أننا نستطيع أن نتحكم ب Metabolic acidosis or alkalosis by respiration (hyperventilation or hypoventilation
في الmetabolic acidosis نرى أن: ارتفاع تركيز أيونات الهيدروجين يتناسب طرديًا مع PCO_2 وعكسيًا مع تركيز HCO_3^- .. عندما يبدأ الجسم بالتحكم بهذه الحالة تبدأ عملية الHyperventilation كي نتخلص من حمض الكربونيك (H_2CO_3) الناتج من غاز ثاني أكسيد الكربون وبذلك نستطيع أن نخفف من تركيزأيونات الهيدروجين.. نرى أن PCO_2 بدأ بالانخفاض، واستجابة لذلك خفّت حدة ازدياد عدد أيونات الهيدروجين (السهم بعد الهايبر فنتليشن صار أنحف وهذا دليل على إن حدته قلت)



METABOLIC ACIDOSIS

Causes of metabolic acidosis

Renal disease	Renal failure affects the **functioning nephrons** therefore there is **no** adequate **excretion** of various acids (they will accumulate and cause the acidosis)
Lactic acidosis	When your body generate ATP by anaerobic pathway, lactic acid levels in your blood will get elevated.
Diabetic ketoacidosis	when can't produce enough insulin (plays a key role in helping sugar (glucose) enter your cells.) Without enough insulin, your body begins to break down fat as fuel. This process produces a buildup of acids in the bloodstream called ketones, eventually leading to diabetic ketoacidosis if untreated.
Chronic diarrhea	Loss of bicarbonate (HCO_3^-) stores through diarrhea.
Poisoning	e.g. Aspirin poisoning leads to lactate accumulation.
Renal tubular acidosis	

Understand it, don't only memorize!

Clinical effects of acidosis

Hyperventilation

Compensatory physiological response

↑[H^+ conc]

Stimulates **respiratory response**

Loss of consciousness, coma, death

Arrhythmia, cardiac arrest

- It is deep, rapid and gasping respiratory pattern.
- **Your body is trying to get more O_2 and to remove CO_2**
- **How to remember that hyperventilation happens when there is metabolic acidosis?**

ببساطة لما نسوي تمرين رياضي سريع استهلك منا طاقة راح نتنفس بسرعة (Hyperventilation) عشان شيئين:

١- نعوض الoxygen debt.

٢- **نقلل من حدة الmetabolism acidosis الصادر من كثرة تركيز Lactic acid.**

HOW?

It affects the heart by reducing its contractility, one of the methods is by an action potential effect.
It causes an elongation owing to inhibition of K+ exchange as a consequence of reduced Ca^{2+} current.

Metabolic Alkalosis

Increase in **bicarbonate HCO_3^-** concentration in ECF.

Causes

- Loss of H^+ ions in gastric fluid due to vomiting.
  - Remember: our stomach Is filled with acidic molecules.
  - chronic vomiting. Normal vomiting does not cause it.
- Ingestion of sodium bicarbonate
  - $NaHCO_3$ is alkaline
- Potassium K^+ deficiency as a result of diuretic therapy
  - loss of K through Kidneys That will cause reabsorption of bicarbonate.

Clinical effects

Hypoventilation

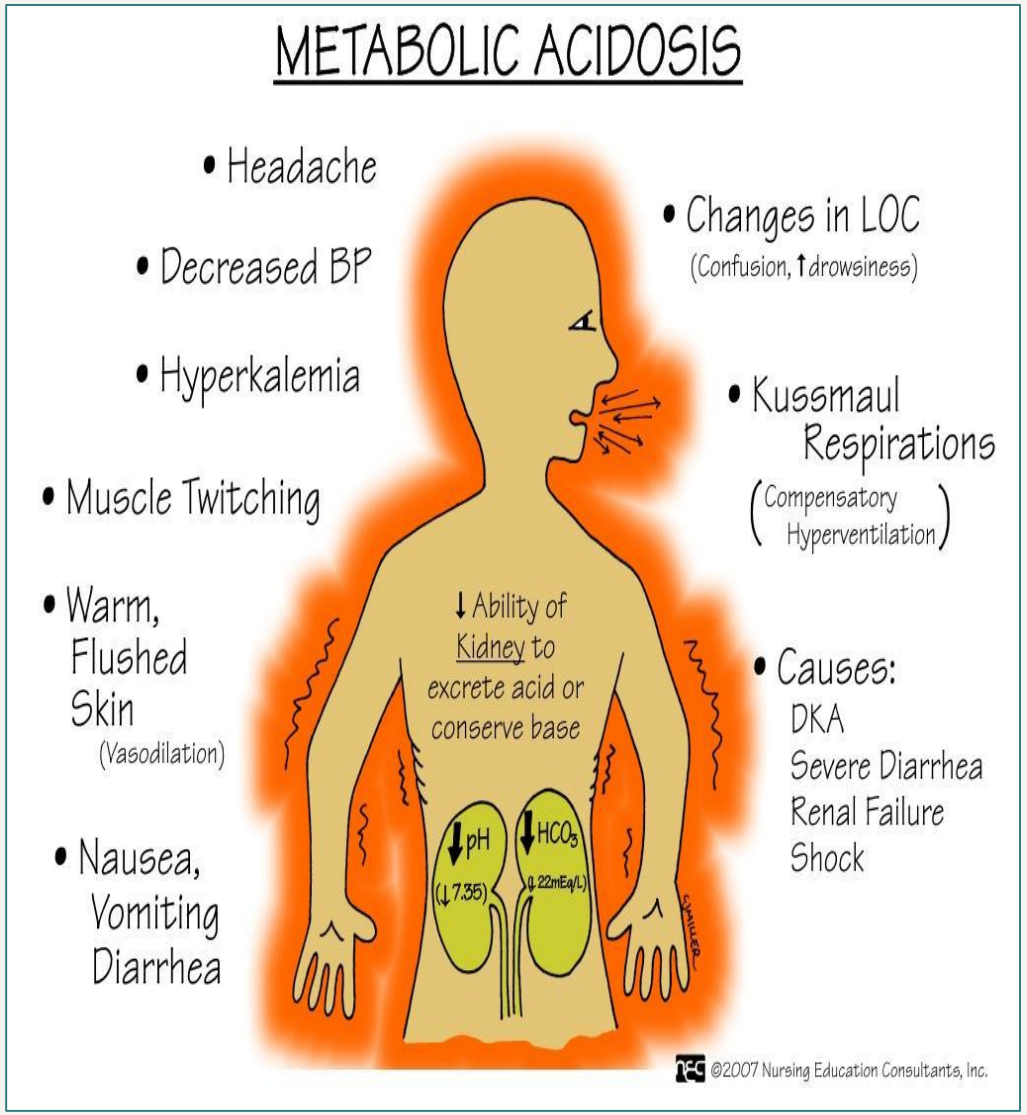
(Depressed breathing)

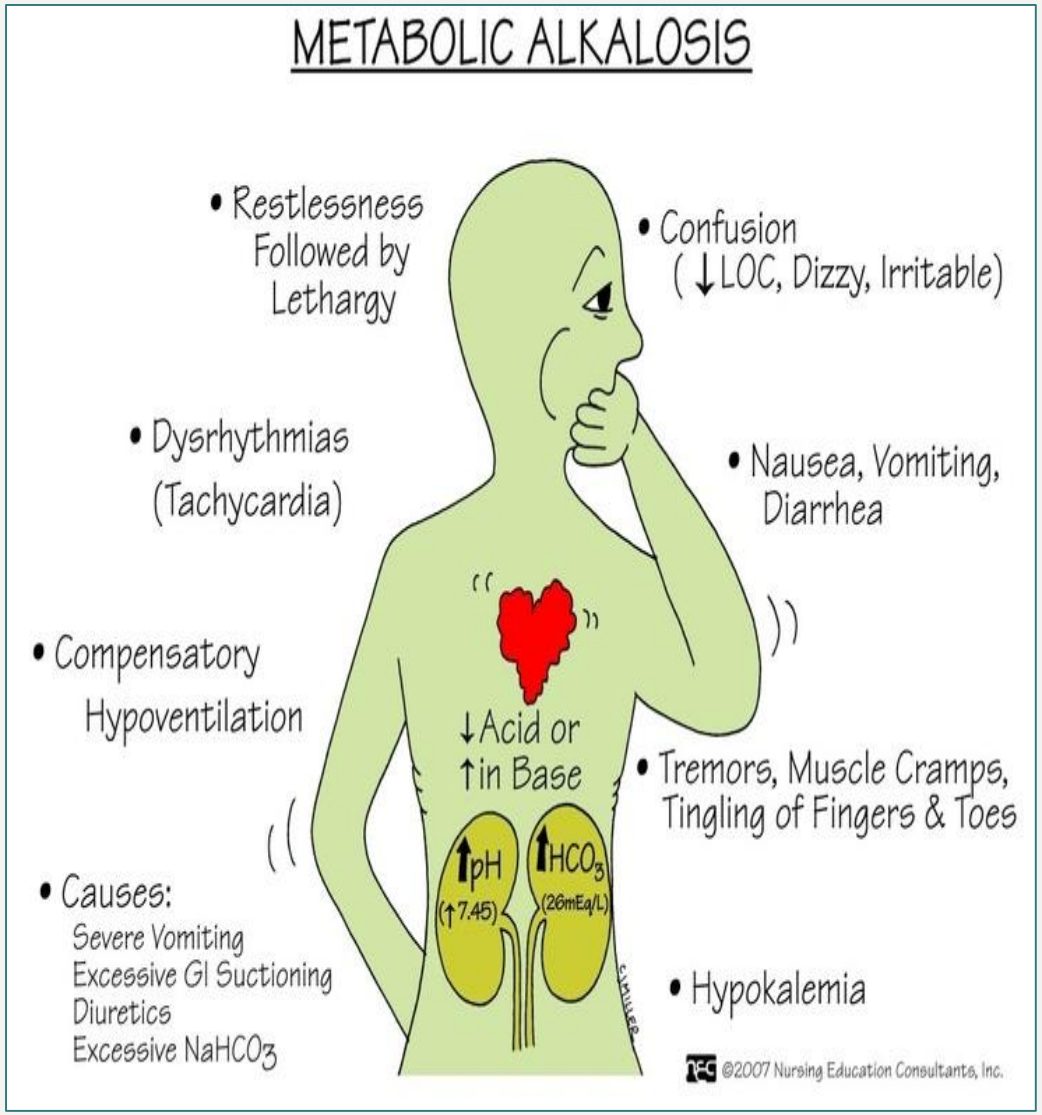
Compensatory physiological response

- Increase PCO_2 to compensate alkalosis.
- Respiratory arrest

Confusion, coma, death

METABOLIC ACIDOSIS VS METABOLIC ALKALOSIS





Metabolic Acidosis VS Alkalosis

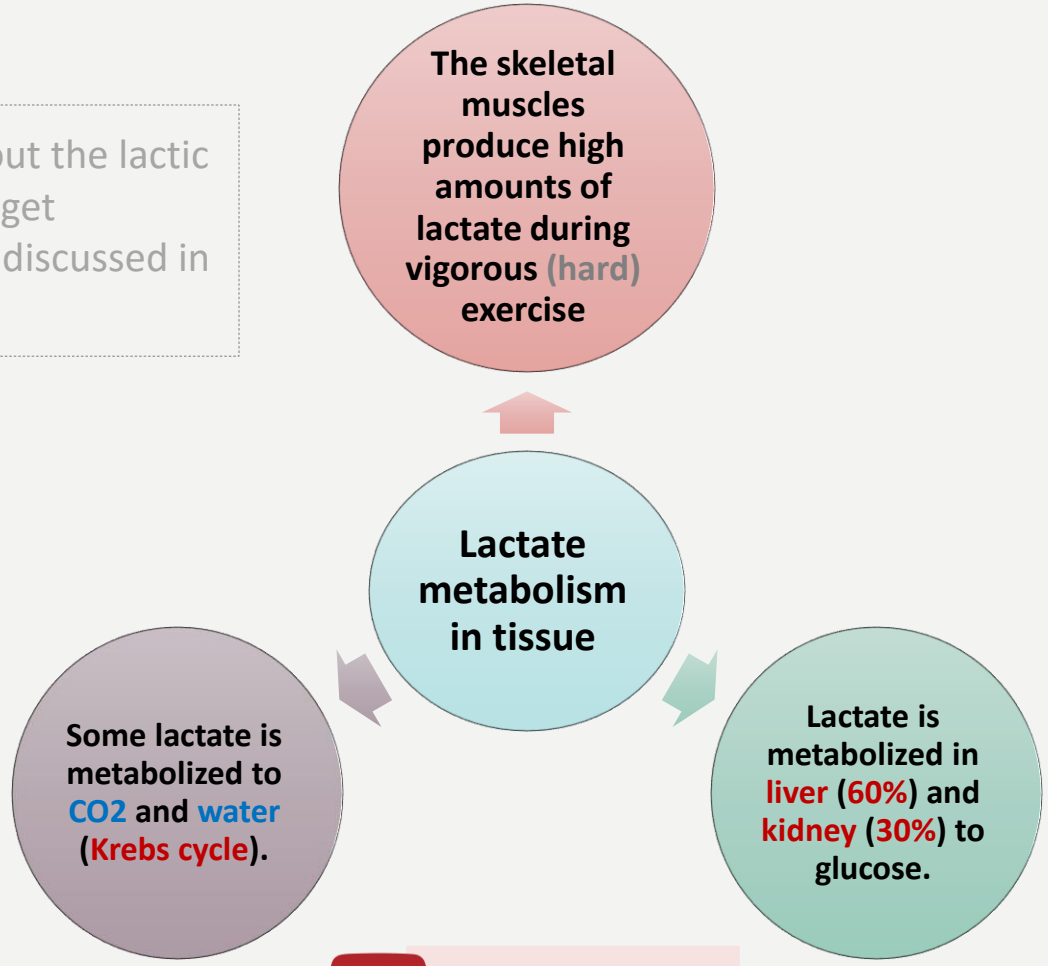
LACTIC ACIDOSIS

What is it?

An elevation in concentration of plasma lactate.

Occurs either due to:

- Failure of circulatory system (hypoxia)
  - It happens when the circulatory system doesn't deliver enough of O2 (e.g. in ischemia or arrhythmia) , therefore the muscles will switch to anaerobic metabolism to produce energy.
- Disorders of carbohydrate metabolism
  - The body can't clear out the lactic acid , therefore it will get accumulated. (will be discussed in details later)



Lactic acidosis

Biochemistry Team 435

Lactate Metabolism in Tissues

The body tissues produce ~ 1500 millimoles of lactate each day.

The lactate enters blood stream and metabolized mainly by the liver (60%) (Cori cycle)

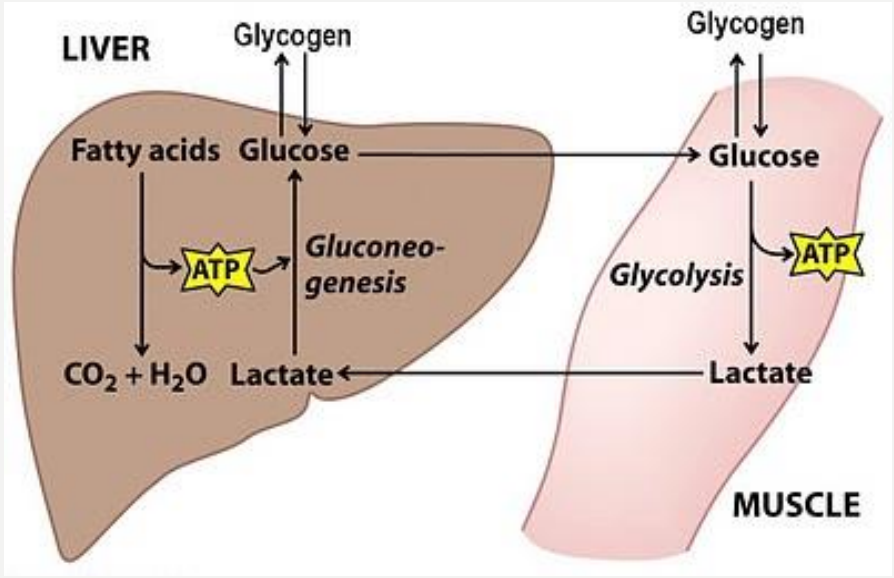
All tissues can produce lactate under anaerobic conditions.

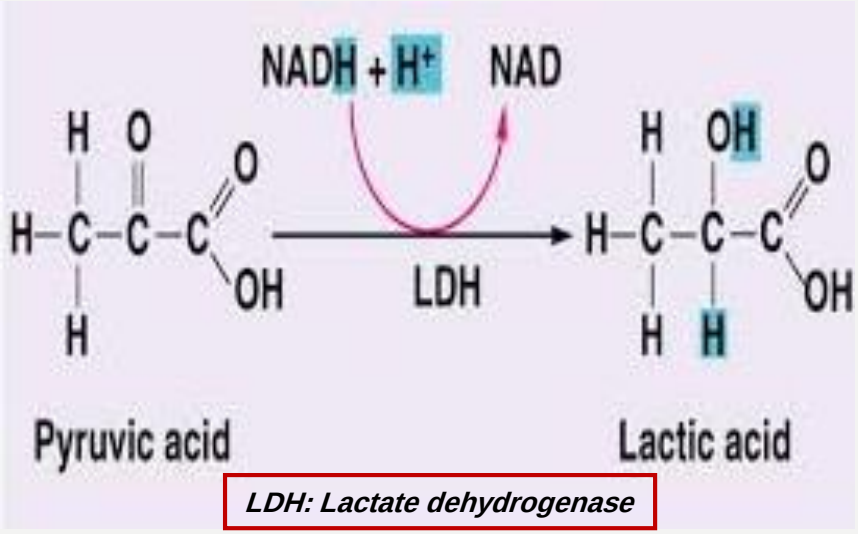
Pyruvate is converted to lactate by **lactate dehydrogenase enzyme.**

Weight lifting is anaerobic process.

Cori cycle :
Because of exercising the muscles will produce lactate, which will enter the blood stream and go to the liver, the liver then will convert the lactate into glucose via gluconeogenesis, and ultimately the newly formed glucose is transported to the muscles to be used for energy again.

REMEMBER:
the liver has the major role in removing lactic acid from the body (the kidneys also can do gluconeogenesis (30%), but the liver has the major role).





cori cycle

LACTATE METABOLISM IN TISSUE

Lactic acidosis can occur due to:

- Excessive tissue lactate production
- Impaired hepatic metabolism of lactate

Types and Causes of lactic acidosis

Type A

- **Happens due to:**

hypoxia in tissues (most common).

- **How?**

1- hypoxia causes → **impaired oxidative phosphorylation** + **decreased** ATP synthesis.
2- In order to survive, the cell switches to anaerobic glycolysis for ATP synthesis.
3- this produces lactate as a final product.

- **Oxygen debt:**

The amount of oxygen required to recover from oxygen deficiency.

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

Type B

سبب تايب ون هو الهايبوكسيا ، الهايبوكسيا ستسبب نقص في الأكسجين ، وعليه ستقل كمية الاي تي بي المنتجة (لأن معظم الأي تي يأتي من الايروبيك) ، فحتى تنجو الخلية من هذه الظروف ستستخدم تحلل الجلوكوز اللاهوائي ، وجميعنا نعرف من الفاونديشين بلوك والمسكلو بلوك أن اللاهوائي ينتج حمض اللاكتيت ، مماسيزيد من الحمضية ، وستدخل بالاسيدوزز

Types and Causes of lactic acidosis

Type A

Type B

- الإنزيم مسؤول عن تحويل البيروفيت إلى أستيل كو أي حتى يستخدم في الكريبس سايكل.
- هنا الشخص عنده دفشنسي ، فبالتالي البيروفيت ما راح يتحول إلى أستيل كو أي ، وعليه ستصبح كميته في الجسم عالية.
- ياترى ماذا سيحدث في هذا البيروفيت؟
راح يتحول إلى اللاكتيك أسيد ، مما سيتسبب بحدوث الاسيدوزز.

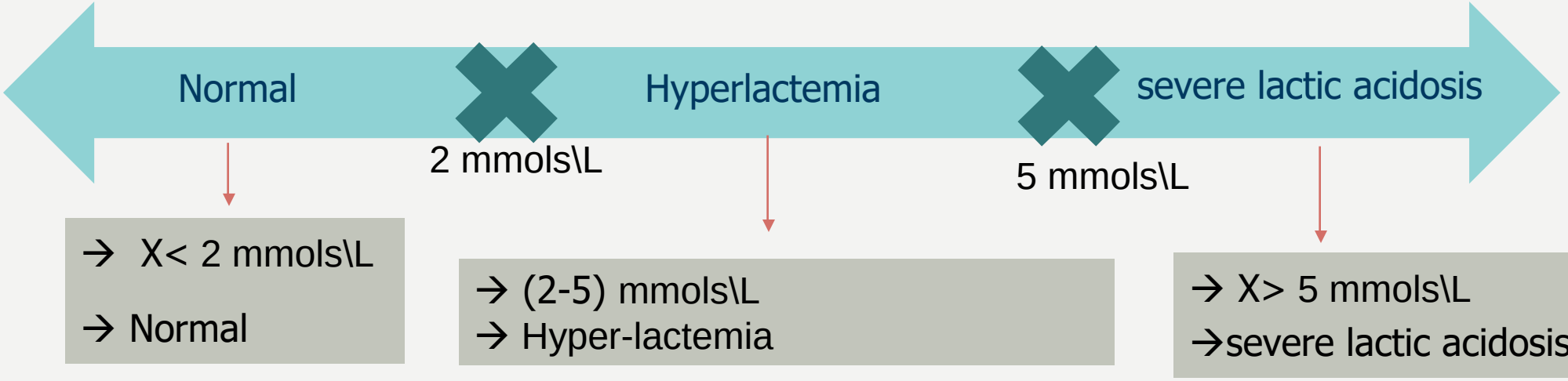
- **Happens due to:**

disorders in carbohydrate metabolism.

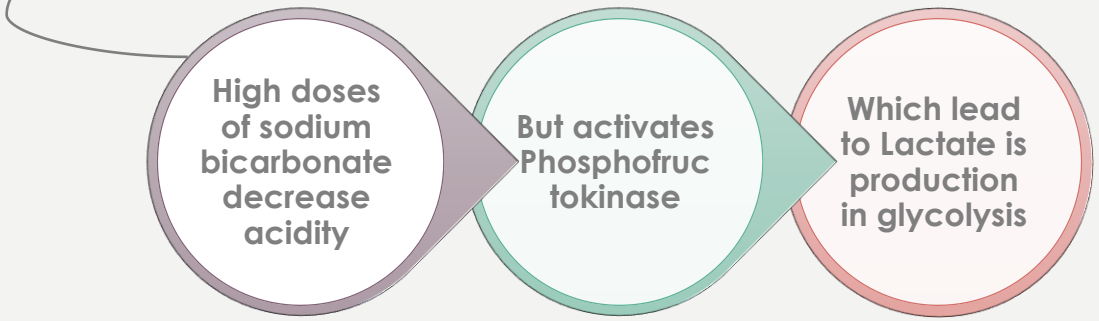
- **Congenital lactic acidosis is due to** deficiency of pyruvate dehydrogenase enzyme. (it is responsible of the conversion of the pyruvate into acetyl-coA, so if it's deficient pyruvate won't get converted into acetyl-coA, therefore high levels of pyruvate will accumulate which will ultimately lead to the overproduction of lactic acid *the cell wants to utilize it*)
- **Chronic hepatic disease accompanied by shock or bleeding.**
- **Liver failure.**
- **Drug intoxication** (mainly the hypoglycemic drugs, they affect the mitochondrial function).

DIAGNOSIS AND TREATMENT

- **Diagnosis done by:** measuring **blood lactate levels**.
- **Levels:**



- **Treatment:**
  - Correcting the underlying conditions.
  - Restoring adequate tissue oxygen.
  - **Avoiding sodium bicarbonate**.



Summary

Metabolic acid-base disorders	
What are they	Disorders that are caused by changes in bicarbonate concentration in the extracellular fluid (ECF).
occur due to	high concentration **or** loss of **H+ ions.**
Metabolic Acidosis	A reduction in bicarbonate concentration in ECF. - **Leads to:** ↑ H+ ions conc. & ↓ HCO3- level. - **causes:** Impaired H+ excretion, Increased H+ production or ingestion, Loss of HCO3−.
Metabolic alkalosis	Increase in bicarbonate concentration in ECF. - **Leads to:** ↓ H+ ions conc. & ↑ HCO3- level. - **causes:** Loss of H+ in vomit, Alkali ingestion (NaHCO3) , K+ deficiency due to diuretic therapy.
Metabolic Acidosis & Alkalosis	
Acidosis	-**Causes**: Renal disease , renal tubular acidosis , lactic acidosis ,diabetic ketoacidosis, poisoning , chronic Diarrhea. -**Clinical effects** : hyperventilation (stimulated by elevated H+ ions), loss of consciousness, coma, death.
Alkalosis	-**Clinical effects** : Hypovrntilation → increase in PCO2 → respiratory arrest. Confusion , coma ,death.
Anion gap	
What is it?	It is the difference between the sum of: cations and anions.
How?	• After calculation the anion gap we check the value: If the value < 3 mEq\L → alkalosis . If the value > 11 mEq\L → Acidosis.

Summary

Lactic acidosis	
It is an **elevation** in concentration of plasma lactate.	
Occurs due to	• Failure of the circulatory system (hypoxia). • Disorders of carbohydrate metabolism.
Lactate metabolism	• The tissues produce 1500 millimole of lactate each day. • 60% of lactate is metabolized by liver (cori cycle). • **Pyrovate** is converted to **lactate** by lactate dehydrogenase enzyme.
Type A lactic acidosis	• **Happens due to**: hypoxia in tissues (most common). • hypoxia causes: impaired oxidative phosphorylation + decreased ATP synthesis. • **Oxygen debt:** The amount of oxygen required to recover from oxygen deficiency. • Type A is due to inadequate supply of oxygen to tissues in: - Myocardial infarction. - Pulmonary embolism. - Uncontrolled hemorrhage. - Tissue hypo-perfusion (shock, cardiac arrest, acute heart failure, etc.). • It leads to chocolate cyanosis "brownish-blue color of the skin and blood"
Type B lactic acidosis	• **Happens due to:** disorders in carbohydrate metabolism: • 1-Congenital lactic acidosis is due to deficiency of pyruvate dehydrogenase enzyme (which is responisble for conversion of the pyruvate into acetyl-coA) • 2-Chronic hepatic disease accompanied by shock or bleeding. • 3-Liver failure. • 4- Drug intoxication.
Diagnosis and treatment	• Diagnosis by: measuring blood lactate levels. • Normal level is below 2 mmols/L , **Hyperlactemia** is between 2 & 5 , and **severe lactic acidosis** is above 5. • **Treatment:** Correcting the underlying conditions, Restoring adequate O2 to tissues , and Avoiding sodium bicarbonate.

MCQs

1.Ketone body formation is most likely to cause:

A. infection
B. acidosis
C. bleeding
D. protein deficiency

2. What is the type of lactic acidosis associated with hypoxia:

A. Hypoxic lactic acidosis
B. type A lactic acidosis
C. type B lactic acidosis
D. chronic lactic acidosis

3. to diagnose a patient with lactic acidosis ..... Analysis must be used:

A. glucose level in blood
B. lever enzyme activity
C. blood lactate levels
D. lactate levels in urine

4. a patient with high pH levels and increased HCO3- in blood. He will most likely be presenting with:

A. hyperventilation
B. decreased ventilation
C. severe abdominal pain
D. excessive sweating

5. what is the percentage of lactate metabolism in the lever during strenuous exercise:

A. 90%
B. 50%
C. 30%
D. 60%

6. Which of the following is (are) produced by the rapid and incomplete breakdown of fatty acids?

A. Acetone and ketoacids
B. Lactic acid
C. Amino acid
D. Urea

1. B
2. B
3. C
4. B
5. D
6. A

MCQs

7. A diabetic patient came to the ER – emergency room- complaining of abdominal pain, nausea and vomiting. Also he shows shortness of breath. What is his underlying condition:

A. Hyper-lactemia
B. lactic acidosis
C. ketoacidosis
D. none of the above.

Explanation: the diabetic patient metabolizes fatty acids in low insulin stages and ketone bodies are formed causing the depletion in blood pH.

8.Lactic Acidosis:

A. Is caused only by rapid and incomplete catabolism of fatty acids
B. is accompanied by the formation of large amounts of ATP.
C. develops in response to prolonged anaerobic catabolism
D. is caused only by extreme exercise characterized by muscle soreness

9.All are true for renal handling of acids in metabolic acidosis except :

A. Hydrogen secretion is increased.
B. Bicarbonate reabsorption is decreased.
C. urinary acidity is increased.
D. urinary ammonia is increased.

7. C
8. C
9. B

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- دلال الحزيمي.
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- خوله العريني.
- رهف بن عباد.
- غاده القصيمي.
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Special thanks to Samar AlOtaibi and the Physiology team ☺

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