Biochemistry – Lactic Acidosis

CVS block

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Metabolic Acid-Base disorders:
Changes in the bicarbonate's concentration in the ECF causes acid-base disorders.

These changes occur due to High concentrations or loss of H+ ions.

It can lead to:
- Metabolic Acidosis
- Metabolic Alkalosis.

To clarify:

- **Bicarbonate:** HCO_3^-
- **Carbonic acid** H_2CO_3
- **pH = 7.4 (normally) << if pH high = alkalosis, if pH is low = acidosis**

H+ refers to acidity

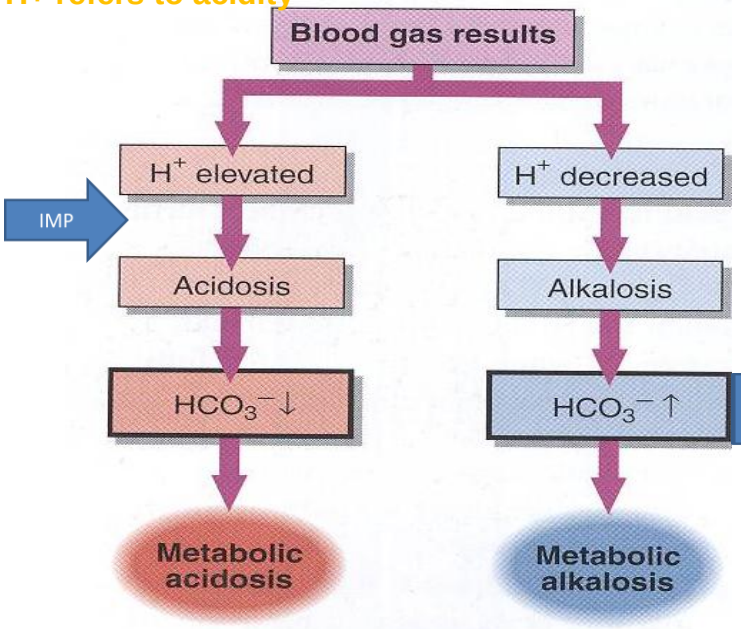


Fig. 1 **Recognizing primary metabolic acid–base disorders by inspecting the HCO_3^- concentration.**

Most important indicator

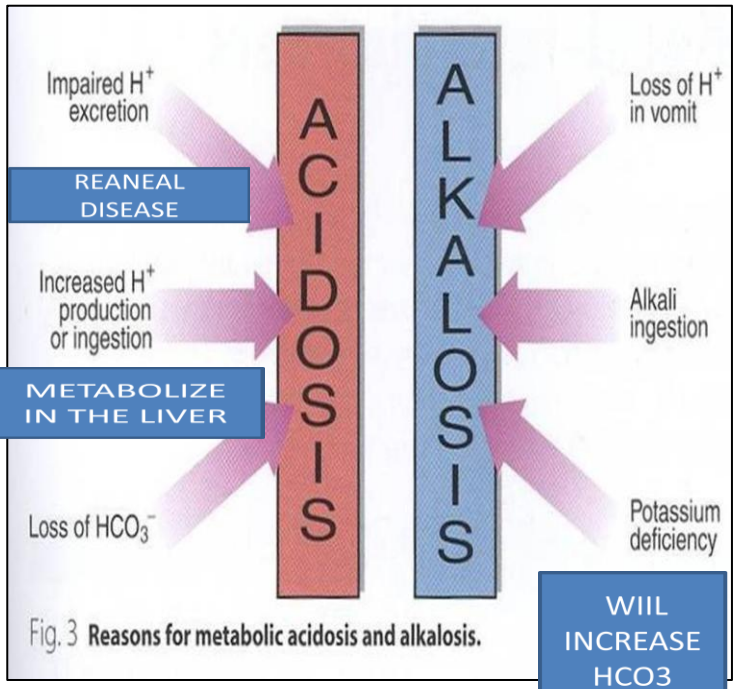


Fig. 3 **Reasons for metabolic acidosis and alkalosis.**

Metabolic acidosis:

Reduction in bicarbonate concentration of ECF.

Causes of Metabolic acidosis:

- Increased production of H+ ions
- Ingestion of H+ or drugs metabolized to acids
- Impaired excretion of H+
- **Loss of Bicarbonate from the GIT or in the urine.**

Anion gap:

- It is the difference between the sum of:
  -Na+ and K+ (cations) and
  -the sum of Cl – and HCO3– (anions)
  Anion gap = $(Na^+ + K^+) – (Cl^- + HCO_3^-)$
  *(Remember that these are the major electrolytes in the body, knowing that there are other electrolytes that help in balancing the acid-base concentration in the blood such as albumin and other proteins)
- Helps in assessing acid-base problems
- Normal anion gap: 3-11 mEq/L
- High anion gap: >11 mEq/L (acidosis)
- Low anion gap: <3 mEq/L (alkalosis)

طرح من مجموع الاول ثم مجموع الثاني

Remember that:

Anion gap is a biochemical tool that can help in assessing acid-base problems. It is not a physiological reality.

***High anion gap occurs in**: "these are also the conditions that induce metabolic acidosis"

- Renal disease: H+ ions with other anion will be trapped in our bodies elevating acidity.
- Diabetic ketoacidosis: in diabetics, there is insulin deficiency, as a result there will be altered metabolism and the body will shift from glucose to fatty acids. This will lead to the presence of high amounts of ketone bodies in the blood.
- Lactic acidosis
- Poisoning: such as, methanol poisoning, ethylene glycol poisoning.

Metabolic acidosis with normal anion gap is referred to as **hyperchloraemic acidosis**, it is seen in :

- Chronic diarrhea: occurs when fluid bicarbonates are lost from the body.
- Renal tubular acidosis: similar to renal disease, except that bicarbonate is lost here.

Clinical effects of acidosis:

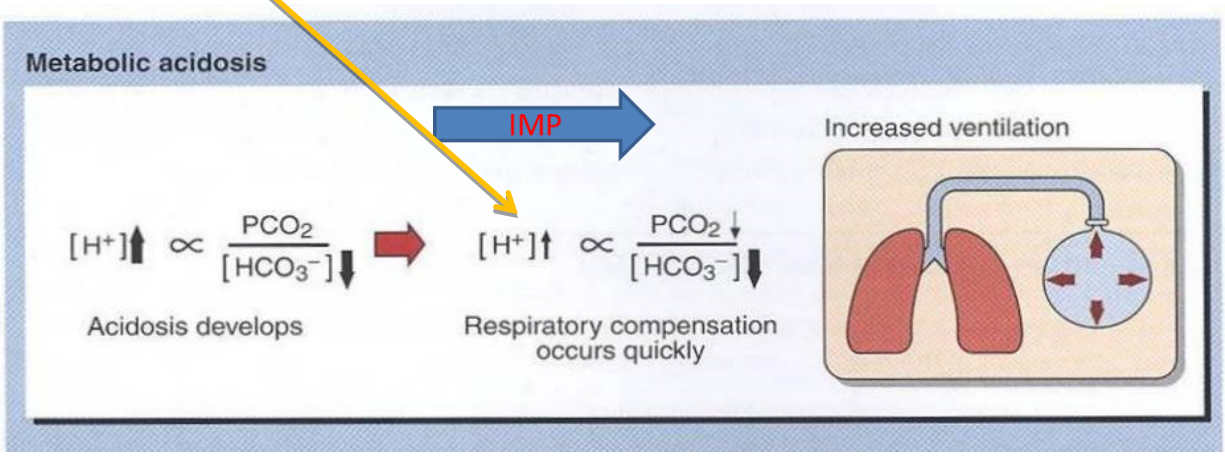
يحاول الجسم للرجوع للحالة الطبيعة بتحفيز الاستجابة التنفسية

- Hyperventilation is the compensatory physiological response to acidosis.
- Increased H+ concentration stimulates respiratory response.
- Hyperventilation: deep, rapid, and gasping respiratory pattern (Also Known As: Kussmaul breathing).
- Arrhythmia, cardiac arrest, hyperkalemia (that sometimes might lead to death).
- Loss of consciousness, coma, and death.

زيادة في البوتاسيوم

Notice H+ conc. is reduced, however, it's still elevated

Remember: carbon dioxide is acidic.



The effect of the compensatory mechanism in Metabolic Acidosis (which is hyperventilation) is that less carbon dioxides stays in the circulation, and that will decrease the acidity.

Metabolic Alkalosis:

Increase in bicarbonate concentration in ECF.

Causes:

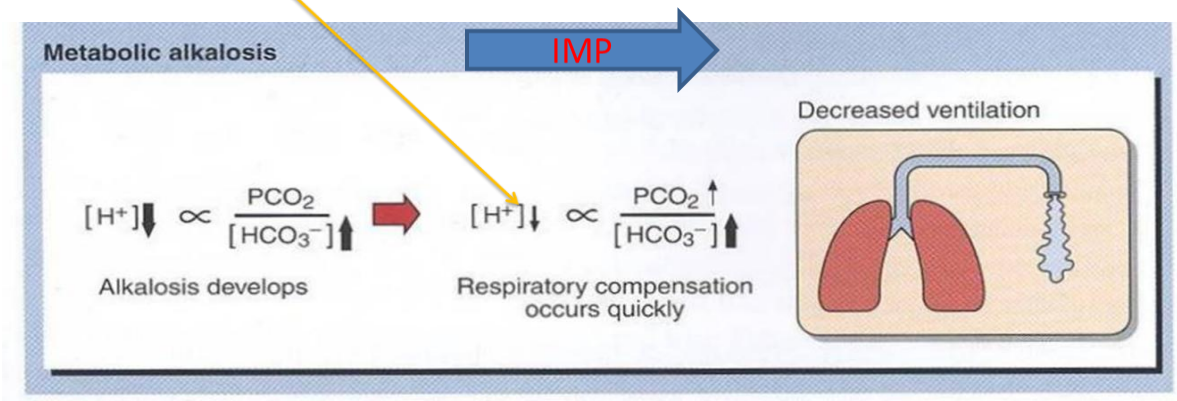
- Loss of H+ ions in gastric fluid due to vomiting. يقلHCL
- Ingestion of Sodium bicarbonate.
- Potassium deficiency "It's a complex mechanism that will probably be discussed in the renal block. "

Clinical effects of alkalosis:

- Hypoventilation (depressed breathing)
- Increased PCO_2 (acidic) to compensate alkalosis.
- Respiratory arrest.
- Confusion, Coma, and death.

Notice H+ conc. is elevated, however, it's still low

لانه فقط محاوله تعويض



The effect of the compensatory mechanism in **Metabolic Alkalosis** (which is **hypo**ventilation) is that **more** carbon dioxides stays in the circulation, and that will **increase** the acidity.

Lactic acidosis: (one of the causes of high anion gap)

Elevated concentration of plasma lactate is called lactic acidosis

Lactic acidosis occurs due to:

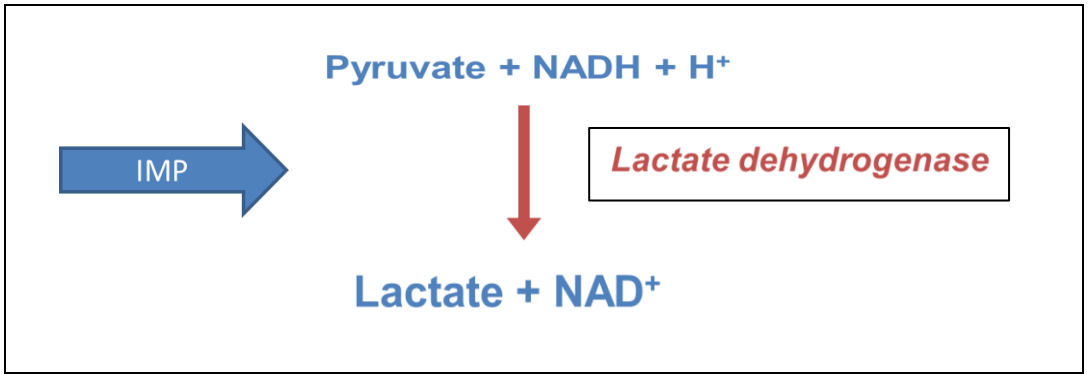
- Failure of circulatory system (e.g. if the arteries (coronary) supplying the heart were clogged, due to oxygen deficiency the heart tissues will switch to anaerobic pathways of energy production. This will result in the formation of lactate as end product ----------> lactate levels will be elevated)
- Disorders of carbohydrate metabolism

Lactate metabolism in tissue:

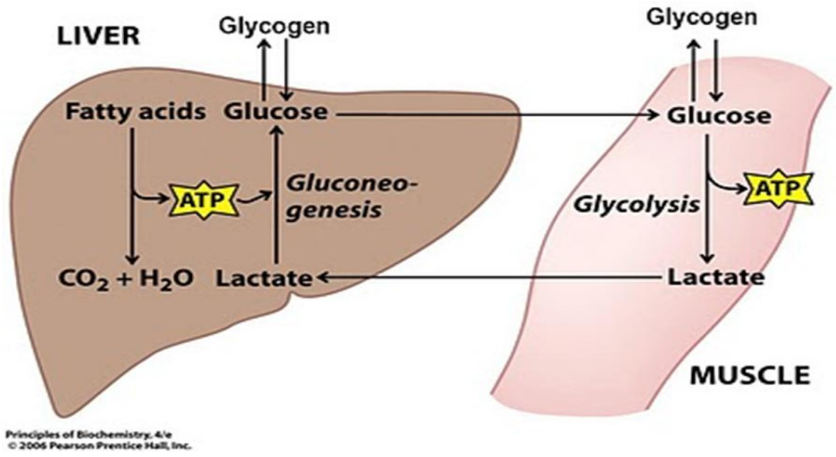
- The body tissues produce ~ 1500 mmoles of lactate each day
- The lactate enters blood stream and metabolized mainly by the liver (Cori cycle)
- All tissues can produce lactate under anaerobic conditions
- Pyruvate is converted to lactate by lactate dehydrogenase enzyme
- The skeletal muscles produce 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)

في حالات التمارين القوية

للتوضيح :
الغالبيه تتحول في الكبـــد بنسبه 60 % وفي الكليه بنسبه 30%
اما 10 % المتبقيه فتكون عمليه تحويل LACTATEمن
الى ماء وثاني اكسيد الكربون في دوره كربس



يوضح فقط تحويل
LACTATE
الى جلوكوز في الكبد من
خلالCORI CYCLE



The Cori cycle

Mechanisms involved in lactic acidosis

Lactic acidosis occurs due to:

- Excessive tissue lactate production
- Impaired hepatic metabolism of lactate

للتوضيح فقط
قاعده عامــه : زياده الشئ عادة اما زياده
انتـــــاج او قله اخراج !!!

Types of Lactic Acidosis

- Type A
- Type B

Clarification of lactic acidosis types:

The *Cohen-Woods classification* categorizes causes of lactic acidosis as follows:

- Type A: Decreased perfusion or oxygenation
- Type B:
  - B1: Underlying diseases (sometimes causing type A)
  - B2: Medication or intoxication
  - B3: Inborn error of metabolism

Type A:

- Due to Hypoxia in tissues (Most Common)<<which is mostly caused by the reduced perfusion.
- Hypoxia is causes impaired oxidative phosphorylation (in the ETC) and decreased ATP synthesis.
- To survive these 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. This caused by:

Ischemia= localized Hypoxia to certain tissues

- **Myocardial infarction**
- **Pulmonary embolism**
- **Uncontrolled hemorrhage**
- **Tissue hypoperfusion (shock, cardiac arrest, acute heart failure, etc.)**
- Anaerobic muscular exercise

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 **(e.g. Phenformin: hypoglycemic agent)**

NOT LACTTATE dehydrogenase enzyme
المشكله في الكبـــــد

تسمم ناتج عن الدواء

Important to remember: patients presenting with one of the factors causing lactic acidosis (hepatic disease for example) do not usually develop the condition. In most cases a no. of factors (from both types, A and B) lead to the development of the condition. Therefore in addition to the hepatic disease, other factors such as sepsis, shock, bleeding

Diagnosis and treatment:

Diagnosis: is 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 **(oxygen debt)**
- Avoiding sodium bicarbonate. Why??>>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.

  Extra:" recent studies show that sodium bicarbonate could be used in some cases, however, it's still controversial"
  http://www.pneumonologia.gr/articlefiles/Acid_base_bicarbonate.pdf