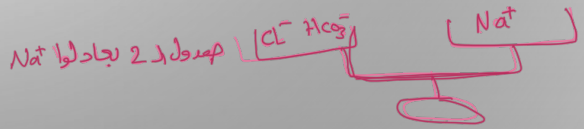
SERUM ELECTROLYTE ANIONS

عنا الصوديوم ١٣٥ ل ١٤٥ الكلورايد +
البايكاربونيت واشياء ثانيه زي الفوسفيت
ولاكتيت عشان تعادل الصوديوم لحاله

Chloride

ال Function for blood
بحافظ على ال blood لانه ماشي مع Na+
بحافظ عليه Blood volume
وال Electric بحافظ عليها لانه وين مافي صوديوم بروح بلحق وراه كلورايد واحد + والثاني -
حكينا ال Function + مش بس l كمان H2O
اذا مرتفع الصوديوم رح تلاقي الكلورايد. مرتفع وانخفضت الصوديوم رح تلاقي الكلوريد منخفض لكن مرات رح تلاقي الكلورايد مرتفع والصوديوم مامعه خبر شو بكون قباله نازل الباي كاربونيت

- The major extracellular anion
- Function in body:
  - Maintaining osmolality
  - Blood volume and
  - Electric neutrality



- Cl is usually shifted according to Na and bicarbonate
- Excess chloride in the body is excreted in urine and sweat, excessive sweating will induce the release of aldosterone which will conserve Na and Cl

Chloride

- Chloride maintains electrical neutrality in two ways:
- Na is reabsorbed along with Cl in the proximal tubules. Na reabsorption is limited by the amount of Cl- available
- Electroneutrality is also maintained by chloride through the chloride shift.
  - Carbon dioxide generated by cellular metabolism within the tissue diffuses out into both the plasma and the red cells
  - In the red cell, CO2, forms carbonic acid (H2CO3), which splits into H+ and HCO3- (bicarbonate).
  - Deoxyhemoglobin buffers H+, whereas the HCO3- diffuses out into the plasma and Cl diffuses into the red cell to maintain the electric balance of the cell.

Electronentrality is also maintained by bicarbonate HCO3
الي بتنتج اصلاً من RBC'S بالدم

$$CO_2 + H_2O \underset{}{\overset{CA}{\rightleftharpoons}} H_2CO_3 \overset{CA}{\rightleftharpoons} HCO_3^- + H^+$$

HCO_3^- → diffusion to the plasma
الي بتبادل مع Cl^- وتدخل جوا RBC's
عشان تحل Electric Balance

H^+ ح تنسحب مع Hb وترتبط مع ال Hb مع ال histidine وتكون deoxy عشان يفرغ الحمولة تبعته من O_2

وهاي العملية كلها بتصير بين ال RBC's وال plasma

- أي شي disorder of Cl^- بكون من Na^+ ارتفع Na^+ برتفع معه واذا انخفض بنخفض معه في عنا حالات exciption

- بكون علاقته مع مين؟! مع Bicarbonate

- حكينا ال hyperchloremia ممكن يكون due to H^+ of HCO_3^- حكينا انهم عكس بعض اذا انخفض ال HCO_3^- ح يرتفع Cl^- مثلاً diarrhea بطلع ال soln من GI في عنا بال duodenum بصير secretion of HCO_3^- فال HCO_3^- ح يطلع من intestant نتيجة ال diarrhea بس ال HCl الي بال stomach لو صار عليه اشي فال H^+ ↑↑ وال HCO_3^- صاره release فال Cl^- ↑↑

metabolic acidosis والـ و RTA والـ acidosis والـ

كيف رح اتخلص منها عن طريق الـ resbairation

H^+ رح ترجع ترتبط مع HCO_3^-

$HCO_3^- + H^+ \longrightarrow H_2CO_3 \longrightarrow CO_2 + H_2O$ (بالتنفس CO_2 ↑)

فشو رح يصير للـ HCO_3^- ← رح تقل ↓↓ وهما يقل شو بصير الـ Cl^- ؟! برتفع ↑↑

Hypochloremia

↓↓ Cl

1. vomiting → HCl قاعد بطلع
   فالواحد بخسرا
2. Keto acidosis → عشان الـ keton bodies بدها Na^+ رح يزيدوا
   والـ Cl^- والـ HCO_3^- بروح كلشيا
   ↓ CL ↓ HCO_3^-
3. aldosterone deficancy → retension for K^+ and excrection for Na^+ →
   وشو بروح مع Na^+ أكيد الـ Cl^- فشو رح يقل ↓↓ Cl^- + ↓↓ Na^+
4. Salt losing → nephrone لما تكون الـ absorption احنا منفلتر كلشي ومفروض نعمل
   خربانه الـ Tubule رح تروح كل المحتويات بالـ urine
5. ↑↑ HCO_3 → alkalosis فالـ Cl^- رح يكون ↓↓

Compansation of respairatory alkalosis → ↑↑ CO_2 زي بلع شلن اختنق من الصوبة الـ CO_2 ما رح يطلع بالتنفس لأنه مخنوق

$\uparrow\uparrow CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$

Chloride applications

- Chloride disorders are often the result of the same causes that disturb Na levels because chloride passively follows Na
- There are a few exceptions.
  - Hyperchloremia may also occur when there is an excess loss of bicarbonate as a result of GI losses, RTA or metabolic acidosis
  - Hypochloremia may occur with excessive loss of chloride from prolonged vomiting, diabetic ketoacidosis, aldosterone deficiency or salt-losing renal diseases.
  - A low serum level of chloride may be encountered in conditions associated with high serum bicarbonate concentrations such as compensated respiratory acidosis or metabolic alkalosis.

Determination of the chloride

- Specimen: serum or plasma, whole blood samples, urine (24-hr) or sweat may be used
- Lithium heparin is the anticoagulant of choice.
- Hemolysis does not cause significant change in serum or plasma values as a result of decreased levels of intracellular chloride (marked hemolysis, decrease due to dilutional effect).
- Methods: there are several methodologies includes:
  - ISE (most commonly used where an ion-exchange membrane is used to selectively bind Cl ions)
  - Amperometric coulometric titration
  - Mercurimetric titration
  - Colorimetry
- Amperometric coulometric titration method using coulometric generation of silver ions (Ag which combine Cl to quantitate the Cl ion concentration
- $Ag^+ + Cl^- \longrightarrow AgCl$

Reference range

TABLE 15-10 REFERENCE RANGES FOR CHLORIDE

Plasma, serum	98–107 mmol/L
Urine (24-h)	110–250 mmol/day, varies with diet

بعتمد على الكمية اللي أكلها

لما بدي احلل HCO3 لازم اخليهم بشكل واحد لأنه عنده ٣ أشكال
لا بحوله CO z وبقيس PCO أو بحولهم كلهم; HCO3 وبقيس
concentration ال

Bicarbonate

ECF بس هو مش أكثر واحد الأكثر صوّاك هو

- Is the second most abundant anion in the ECF
- The total CO2 comprises the bicarbonate (90%), carbonic acid and dissolved CO2 so total CO2 measurement is indicative of HCO3- measurement
- Bicarbonate is the major buffering system in the blood where carbonic anhydrase in RBCs converts CO2 and H2O to carbonic acid

و حكينا اذا صار acidosis بعمل تفاعل ← وبحوله co2
وبطلعه بالتنفس

$$CO_2 + H_2O \xleftrightarrow{CA} H_2CO_3 \xleftrightarrow{CA} H^+ + HCO_3^-$$

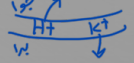
90%

- Bicarbonate diffuses out of the cells in exchange for chloride to maintain ionic charge neutrality within the cell

Bicarbonate regulation

- Most of the filtered bicarbonate ion is reabsorbed in the kidneys (85% in proximal tubules and 15% in the distal) in the form of CO2 (due to low permeability of tubules to bicarbonate)
- Normally nearly all the bicarbonate ions are reabsorbed from the tubules, with little lost in the urine
- When bicarbonate ions are filtered in excess of hydrogen ions available, almost all excess HCO3- flows into the urine.
- In alkalosis, with relative increase in bicarbonate ion compared to CO2, the kidneys increase excretion of HCO3- into the urine, carrying along a cation such as sodium. This loss of HC3O- from the body helps correct pH
- In acidosis, the excretion of H into the urine is increased and HCO3- reabsorption is virtually complete

Clinical applications

- Acid-base imbalances cause changes in bicarbonate and CO2 levels. A decreased bicarbonate/ CO2 occurs in metabolic acidosis leads to exhalation of CO2 by the lungs (hyperventilation), which lowers pCO2.
- Elevated total CO2 concentrations occur in metabolic alkalosis as bicarbonate is retained, often with increased pCO2, as a result of compensation by hypoventilation.
- Typical causes of metabolic alkalosis include:
  - Severe vomiting → HCL بطلع
  - Hypokalemia → 
  - Excessive alkali intake

Hesterical attack / Panic attack → بتنفسوا كتير سريع بطلع كمان كمية CO2 كبيرة من الجسم وبصير عندهم alkalosis

اللي بيشرب بيشرب antiacid وكتير باكلها → بصير alkalosis

Hypoventelation بصير عندي alkalosis وهيكون بحالة CO2 عشان يزيد CO2 وبحبس CO2 بالدم ↑H+

Method

- Specimen: venous serum or plasma.
- Serum or lithium heparin plasma is suitable for analysis.
- The sample is capped until the serum or plasma is separated and the sample is analyzed immediately
- If the sample is left uncapped before analysis, CO2 escapes. Levels can decrease by 6 mmol/L per hour
- Two common methods are ISE and an enzymatic method.
  - ISE for measuring total CO2, uses an acidic reagent to convert all the forms CO2 to CO2 gas and measured by a pCO2 electrode
  - The enzyme method alkalinizes the sample to convert all forms of CO2 to HCO3-.

method of determine HCO_3

ISE

بتحول كل HCO_3^- لـ CO_2 باستخدام

acidic reagent

$HCO_3^- \longrightarrow CO_2(g)$

وبقيس عن طريق pressure of co2 Electrode

Enzyme method

عن طريق phosphoEnol pyruvate Enzyme ← [PEP]

وبعمل alkalinizes عشان احول كل

$CO_2 \longrightarrow HCO_3^-$

$$HCO_3^- + PEP \xrightarrow[\text{carpoxalate}]{PEP} H_2PO_4^- + \text{Oxaloacetate}$$

بوجود

$$\text{oxaloacetate} + NADH + H^+ \longrightarrow \text{Malate} + NAD^+$$

طيب شو الفرق أنه NADH الـ absorpance = 340nm

بينما الـ NAD^+ مالوش فأنا بقيس NADH بس فيه منه تفاعل وصار NAD^+ ز تنقص

الـ abs مقدار النقصان " diffrance " الي صار = كمية الـ HCO_3 الي بالعينة

بتناسب تناسب طردي اذا نقص كثير معناها قيمة HCO_3 موجودة كتير بالعينة واذا شوي معناها HCO_3 شوي

يعني بقيس الـ NADH قبل اضافة العينة وبعد وبطرح والناتج الي بطلع

بتناسب تناسب طردي مع HCO_3

Okey

Method

- HCO3 is used to carboxylate phosphoenolpyruvate (PEP) of phosphoenolpyruvate (PEP) carboxylase, which catalyzes the formation of oxaloacetate.

$$\text{Phosphoenolpyruvate} + HCO_3^- \xrightarrow{\text{PEP carboxylate}} \text{Oxaloacetate} + H_2PO_4^- \qquad \text{(Eq. 15-4)}$$

- This is coupled to the following reaction, in which NADH is consumed as a result of the action of malate dehydrogenase (MDH)

$$\text{Oxaloacetate} + \text{NADH} + H^+ \xrightarrow{\text{MDH}} \text{Malate} + NAD^+ \qquad \text{(Eq. 15-5)}$$

- The rate of change in the absorbance of NADH is proportional to the concentration of HCO3-

Reference ranges

- Carbon dioxide, venous 23-29 mmol/L (plasma, serum).

Lactate

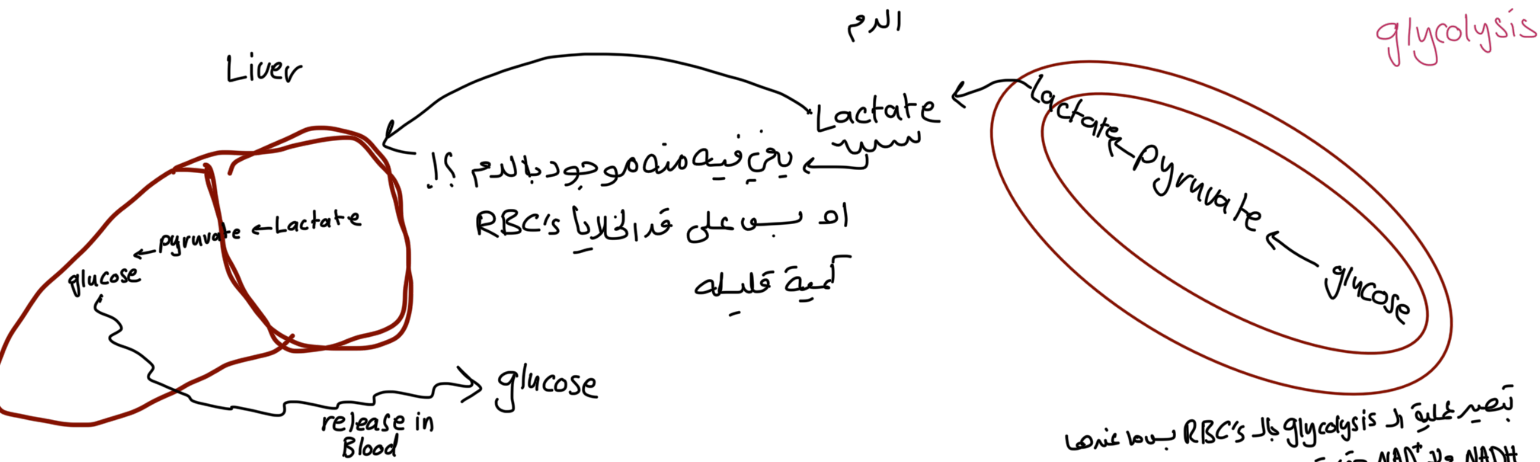
- Lactate is a by-product of an emergency mechanism that produces a small amount of ATP (2 moles)

- Under hypoxic conditions, acetyl CoA formation does not occur and NADH accumulates, favoring the conversion of pyruvate to lactate through anaerobic metabolism.

- The accumulation of excess lactate in blood is an early sensitive and quantitative indicator of the severity of oxygen deprivation (more than pH)

هو by product لعمليات الـ Metabolism العادية للـ RBC's

لأنه ما عندها لا ميتوكندريا ولا oxiditive phosphorilation فشو بتعمل كل كمية لما يصير عندي



تصير عملية الـ glycolysis بالـ RBC's بس ما عندها NADH ولا NAD^+ حتى تحول لـ ATP فبتظر تحوله لـ Lactate والـ Lactate بنفرز بالدم وبروح للـ liver والكبد بحوله لـ glucose والـ glucose بنفرز بالدم

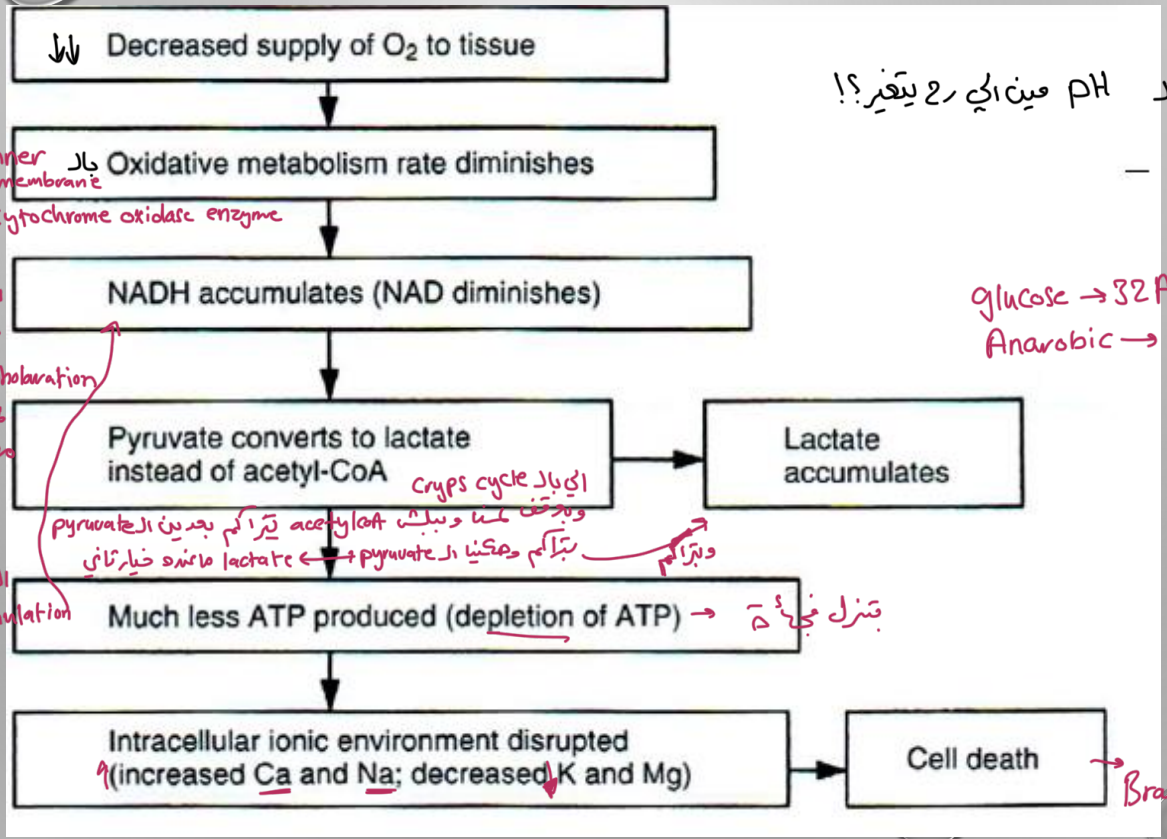
فالـ Lactate ماله regulation لأنه قلال الي بالدم بكونوا وبروحوا على الكبد حتى يرجعوا glucose

بس لما يصير عندي hypoxia لا ناقص دمه كثير أو مشاكل بالقلب أو أي مشكلة صحية بروح على الطوارىء وبعطوه oxygen

بعطيه لا إما نفس الموجود بالهوا 21% أو بزيدها لـ 30% or 40%
وممكن يوصل لـ 100%
وبكون مخنوق عالاخر طالع من حريق

وبتابع الـ lactate عنده أي نقص O_2 رح يرتفع الـ Lactate فهو early indicate for acidosis

يعني أول ما يحول للـ aneorobic معناها رح يصير عندي accumulation lactate بالتالي رح يصير acidosis


Decreased supply of O_2 to tissue
Oxidative metabolism rate diminishes
NADH accumulates (NAD diminishes)
Pyruvate converts to lactate instead of acetyl-CoA
Lactate accumulates
Much less ATP produced (depletion of ATP)
Intracellular ionic environment disrupted (increased Ca and Na; decreased K and Mg)
Cell death
أي تغير بال pH مين اللي رح يتغير؟!
ال Brain
glucose → 32 ATP
Anarobic → 2 ATP
أول حدا بنضر ال Brain

Regulation

- It is not regulated as with potassium and calcium
- As oxygen delivery decreases below a critical level, blood lactate concentration rise rapidly and indicate tissue hypoxia earlier than pH
- The liver is the major organ for removing lactate by converting lactate back to glucose by a process called gluconeogenesis

Clinical application

- Measurement of blood lactate are useful for metabolic monitoring in critically ill patients, for indicating the severity of the illness, and patient prognosis

There are two types of lactic acidosis:

- Type A is associated with hypoxic conditions, such as shock, myocardial infarction, severe congestive heart failure, pulmonary edema, or severe blood loss
- Type B is of metabolic origin, such as with diabetes mellitus, severe infection, leukemia, liver or renal disease, and toxins (ethanol, methanol, or salicylate poisoning).

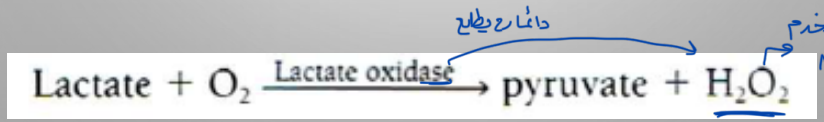
Determination of lactate

- Special care should be practiced when collecting and handling specimens for lactate levels
- A tourniquet should not be used because venous stasis will increase lactate levels
- If a tourniquet is used, blood should be collected immediately and the patient should not exercise the hand before and during collection
- After sample collection, glucose is converted to lactate by a way of anaerobic glycolysis and should be prevented:
  - Heparinized blood may be used but must be delivered on ice and the plasma must be quickly separated
  - Iodoacetate or fluoride will inhibit glycolysis without affecting coagulation

Method

Lactate → pyruvate اي لجول lactate Oxidase enzyme بستخدم ال

- Current enzymatic methods make lactate determination readily available.
- The most commonly used enzymatic method uses lactate oxidase to produce pyruvate and H2O2.

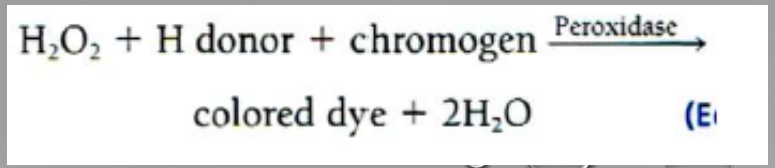


دائما بطلع

إذا ما بدي بطلع بالتفاعل بستخدم NADH و NAD+ وقتها بدي dehydrogenase وبروح على الطريقة تاعت 340nm

- One of two couple reactions may then be used. Peroxidase may be used to produce a colored chromogen from H2O2

الله يصبرني :-



Reference range

ENZYMATIC METHOD, PLASMA	
Venous	0.5–2.2 mmol/L (4.5–19.8 mg/dL)
Arterial	0.5–1.6 mmol/L (4.5–14.4 mg/dL)
CSF	1.1–2.4 mmol/L (10–22 mg/dL)

بنقدر نربطه بكل الelectrolyte اللي احنا ناقل

K^+, Na^+, Cl^-, HCO_3^- ← megerment اللي عملتله

Calculation عامل اذا بدي اشوف اشيء ثاني مرتفع بدرج

Anion gap (AG)

$(K^+ + Na^+) - (Cl^- + HCO_3^-) = \text{Anion gap}$

بالوضع العادي هو 10 - 20 بالوضع الطبيعي انت هاعندك gap فيه (+) بجادل (-)

- Routine measurement of electrolytes usually involves only Na+, K+, Cl-, and HCO3-
- These values may be used to approximate the anion gap (AG), which is the difference between unmeasured anions and unmeasured cations.
- There is never a “Gap” between total cationic charges and anionic charges
- AG is useful in indicating an increase in one or more of the unmeasured anions in the serum and also in the form of quality control for the analyzer used to measure these electrolytes.

Anion gap (AG)

مثلاً عندي

$Na^+ = 145$
$K^+ = 5$
$Cl^- = 106$
$HCO_3^- = 8$

$(145 + 5) - (106 - 8)$
$150 - 114 = 36$

Anion gap محاها عندي Cl^- or HCO_3^- مرتفع مش من المحسوبات anion محاها عندي 20 لـ 10 حكينا لأنه عالي له

لما اشوف HCO_3^- نازل محاها عنده acidosis
بس ممكن يكون HCO_3^- عادي بس Na^+ مرتفع
عنده hypernatremia ممكن يكون كلشي ملخبط
والشخص ماعنده أعراض
وممكن يكون خلل بالجهاز

❑There are two commonly used methods for calculating the anion gap

إذا ماحكى K^+ →

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

❑With a reference range of 7-16 mmol/L

الRange 2/ بختلف

❑The second method:

إذا حكى K^+ →

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

❑It has a reference range of 10-20 mmol/L

Anion gap (AG)

الحالات اللي بصير فيها AG ؟!

- An elevated anion gap may be caused by:
  - Uremia/renal failure, which leads to PO_4^{-3} and SO_4^{-2} retention
  - Ketoacidosis, as seen in cases of starvation or diabetes
  - Methanol, ethanol, ethylene glycol poisoning, or salicylate
  - Lactic acidosis
  - Hypernatremia
  - Instrument error

بالوضع العادي ماعندي لا سلفيت ولا فوسفيت هين رح يعادلهم الـ Na^+ فـ $\uparrow\uparrow Na^+$

لـ Cl^- و HCO_3^- رح يكونوا ما معهم خبر

$\uparrow\uparrow AG = \uparrow\uparrow Na^+ - [Cl^- + HCO_3^-]$

رح يكونوا Negative charge ويعادلهم Na^+

برضه شحنة سالبة

lactate برضه شحنة سالبة

$\uparrow\uparrow Na^+$ نفسه مدفع

آلة خربانة

CASE STUDY 15-2

A 60-year-old man entered the emergency department after 2 days of "not feeling so well." History revealed a myocardial infarction 5 years ago, when he was prescribed digoxin. Two years ago, he was prescribed a diuretic after periodic bouts of edema. An electrocardiogram at time of admission indicated a cardiac arrhythmia. Admitting lab results are shown in Case Study Table 15-2.1.

Questions

1. Because the digoxin level is within the therapeutic range, what may be the cause for the arrhythmia?
2. What is the most likely cause for the hypomagnesemia?
3. What is the most likely cause for the decreased potassium and ionized calcium levels?
4. What type of treatment would be helpful?

CASE STUDY TABLE 15-2.1 LABORATORY RESULTS

VENOUS BLOOD
Digoxin: 1.4 ng/mL, therapeutic 0.5–2.2 (1.8 nmol/L, therapeutic 0.6–2.8)
Na^+: 137 mmol/L
K^+: 2.5 mmol/L
Cl^-: 100 mmol/L
HCO_3^-: 25 mmol/L
Mg^{2+}: 0.4 mmol/L
Ion/free Ca^{2+}: 1.0 mmol/L

Na	135-145
K	3.4-5.0
Cl	98-107
HCO3	23-29
Mg	0.63-1.0
Ca/ionized	1.16-1.32