

FIZIOLOGIJA ŽIVALI

Laboratorijske vaje

IZLOČANJE 2.del

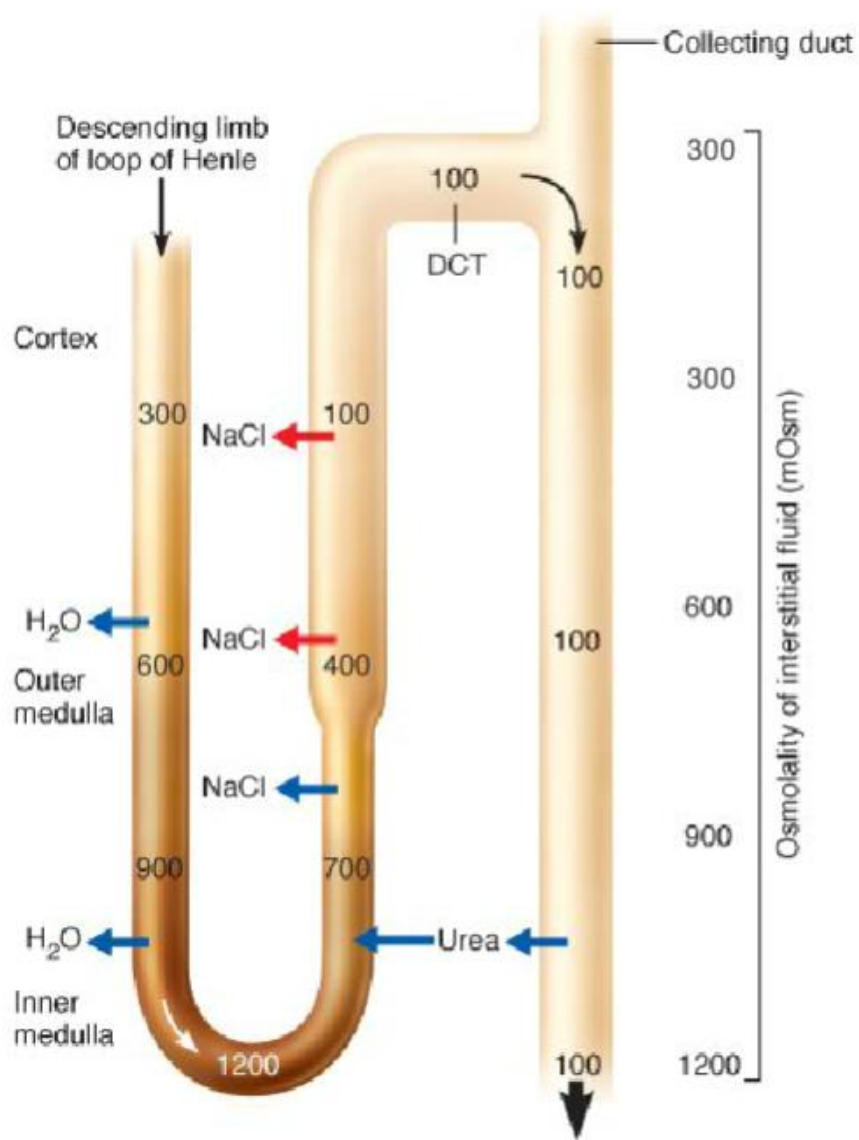
dr. Katja Adam

UP FAMNIT



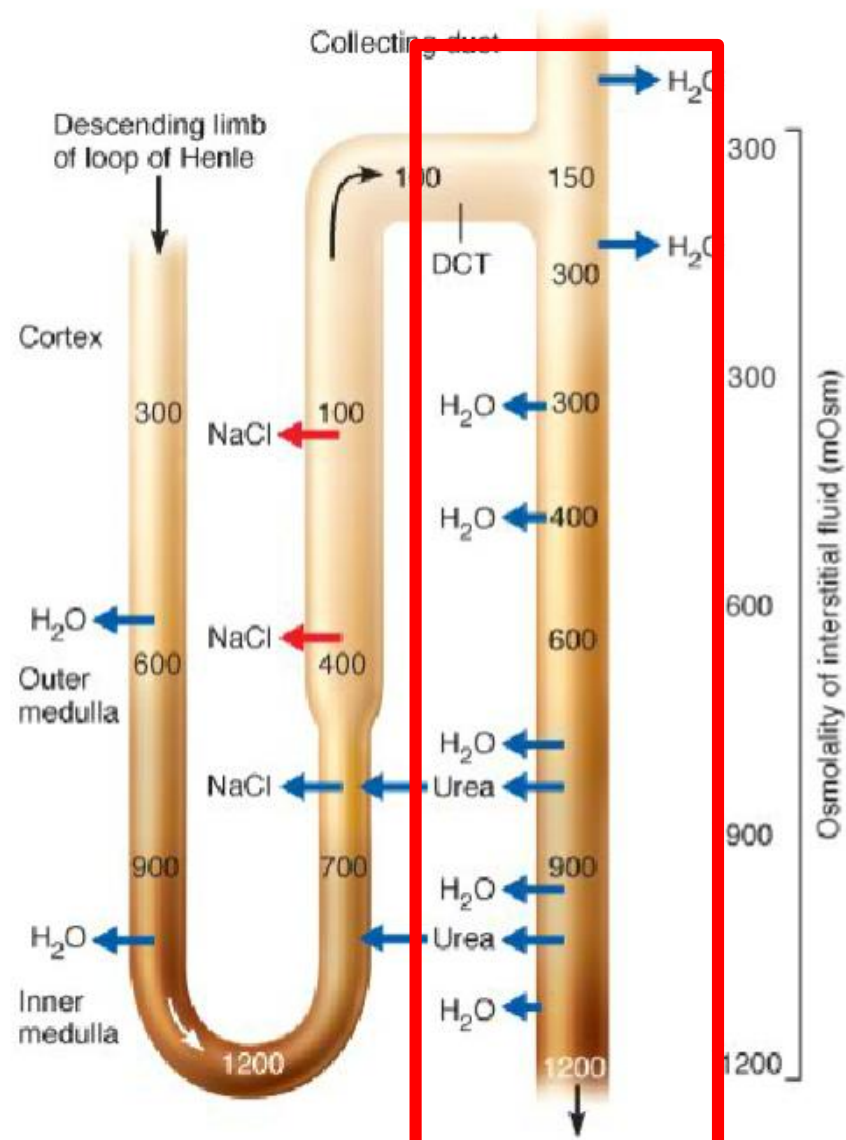
4. VPLIV HORMONA ADH NA KOLIČINO FILTRATA

- **ADH (antidiuretični) hormon** poveča permeabilnost za vodo v zbirnih cevkah → voda gre zato v območja z večjo koncentracijo topljenca (*spomnite se na osmozo!), iz zbirne cevke v intersticijsko območje → količina seča se na ta račun zmanjša, osmolarnost poveča
- Diuretik poveča diurezo (izločanje seča), anti-diuretik pa to zmanjša
- **osmolarnost** = koncentracija osmozno aktivnih delcev, merilo koncentracije topljenca



(a) Absence of ADH

Henleyeva pentlja – zelo prepustna za H₂O, slabo za toplience

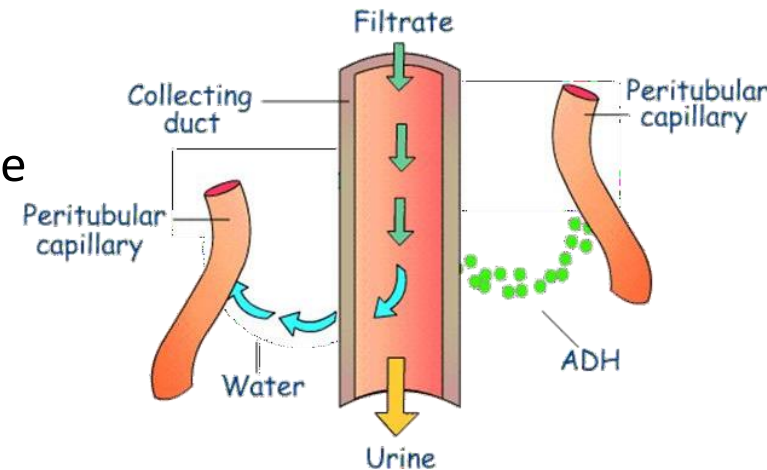
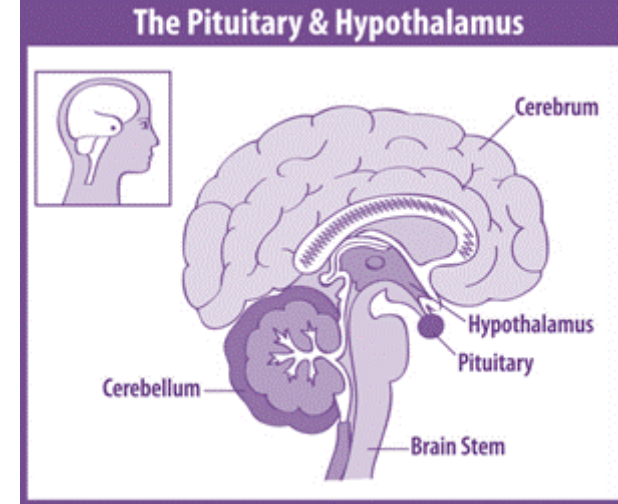


(b) Maximal ADH

ADH poveča premeabilnost zbirnih cevkc za vodo

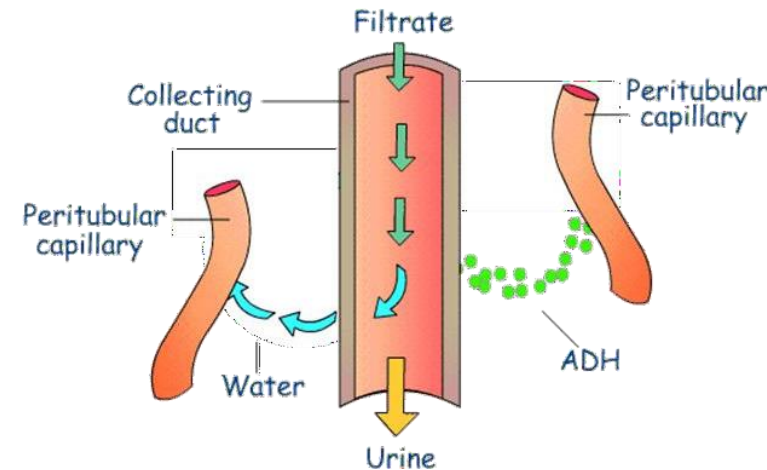
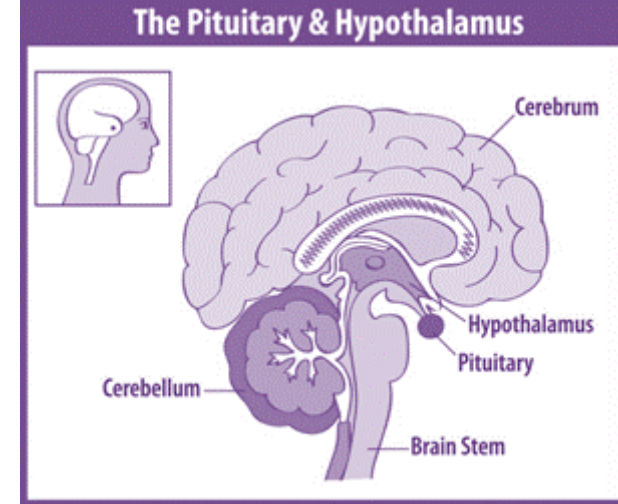
6. VPLIV HORMONOV NA OBLIKOVANJE URINA

- **ADH** – proizvaja ga hipotalamus in shranjen je v hipofizi (pituitary gland)
- gl. naloga: povečanje permeabilnosti v **zbirni cevki** za vodo, tako da vstavlja akvaporine (kanalčke) v apikalno membrano → več vode je resorbirane v telo
- voda gre do območij z večjo koncentracijo topljenca: iz lumna cevke v okoliški intersticij



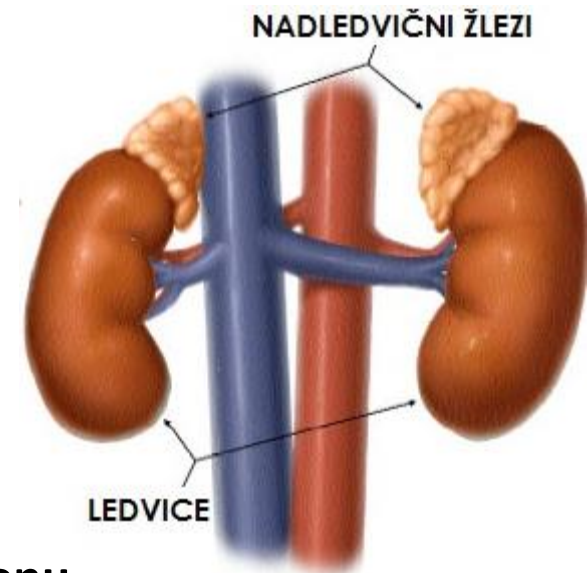
6. VPLIV HORMONOV NA OBLIKOVANJE URINA

- OSMOLARNOST TELESNIH TEKOČIN ter volumni in tlaki v obtočilnem sistemu vplivajo na izločanje ADH
- že samo **1% sprememba osmolarnosti** povzroči izločanje ADH
- sprememba v elektrolitih + dodatek antidiuretičnega hormona (ADH) → več vode je resorbirane v kri → koncentriran urin, krvni tlak naraste zaradi večje vsebnosti vode v krvi



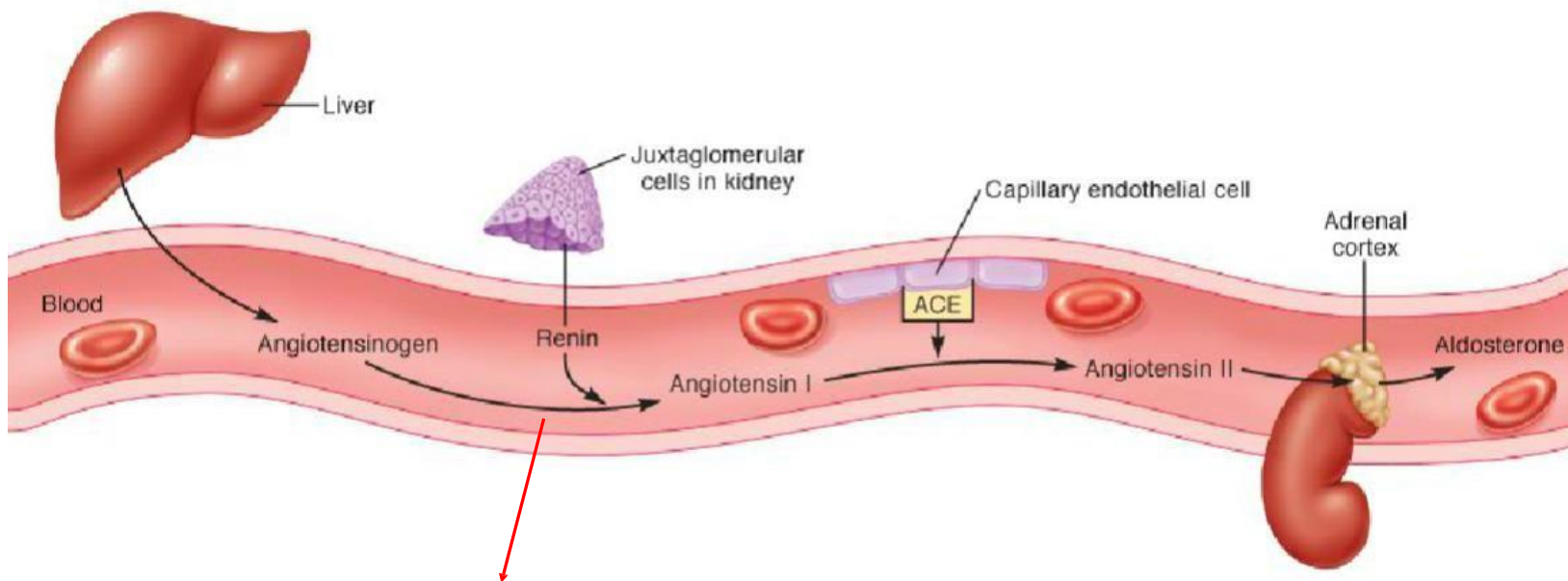
6. VPLIV HORMONOV NA OBLIKOVANJE URINA

- **ALDOSTERON** – proizvaja ga skorja nadledvičnih žlez
- vpliva na **distalne zavite cevke (in zbrine cevke) v nefronu** – spodbuja resorpcijo Na^+ iz filtrata (iz cevke) v telo in izločanje K^+ iz telesa v cevke – z NaCl se izloči tudi nekaj vode (**osmoza!**)
- Pod vplivom aldosterona se v distalnih cevkah:
 - reabsorbirajo - Na^+ in Cl^- ioni, ker so osmotsko aktivni, HCO_3^- in voda
 - izločajo iz intersticija v filtrat - K^+ , H^+ in amonijevi ioni, kar vzdržuje kislinsko-bazično ravnovesje krvi



PROIZVODNJA ALDOSTERONA

- proizvaja ga skorja nadledvične žleze v tako imenovanem **RENIN-ANGIOTENZIN SISTEMU**



KO SE ZNIŽA PRITISK KRVI – to zaznajo celice v aferentni arterioli in povzročijo izločanje **renina** → renin povzroča spremembo angiotenzinogena v angiotenzin I
endotelne celice povzročijo spremembo angiotenzina I v angiotenzin II → ta stimulira skorjo nadledvične žleze, da izloči **ALDOSTERON**

REGULACIJA IZLOČENE VODE/TOPLJENCEV

- ledvice regulirajo količino vode in topljencev, ki se izločajo, da vzdržujejo ravnovesje vode v telesu
- majhen vnos vode, izguba telesnih tekočin – ledvice delajo na shranjevanju vode, “naredijo” urin zelo **hiperosmotski** (ima visoko koncentracijo topljenca)
- velik vnos tekočin – urin je zelo **hipoosmotski**
- normalen urin – osmolarnost med 50-1200 miliosmolov/kg vode

FIZIOLOGIJA ŽIVALI

Laboratorijske vaje

KISLINSKO-BAZIČNO RAVNOVESJE

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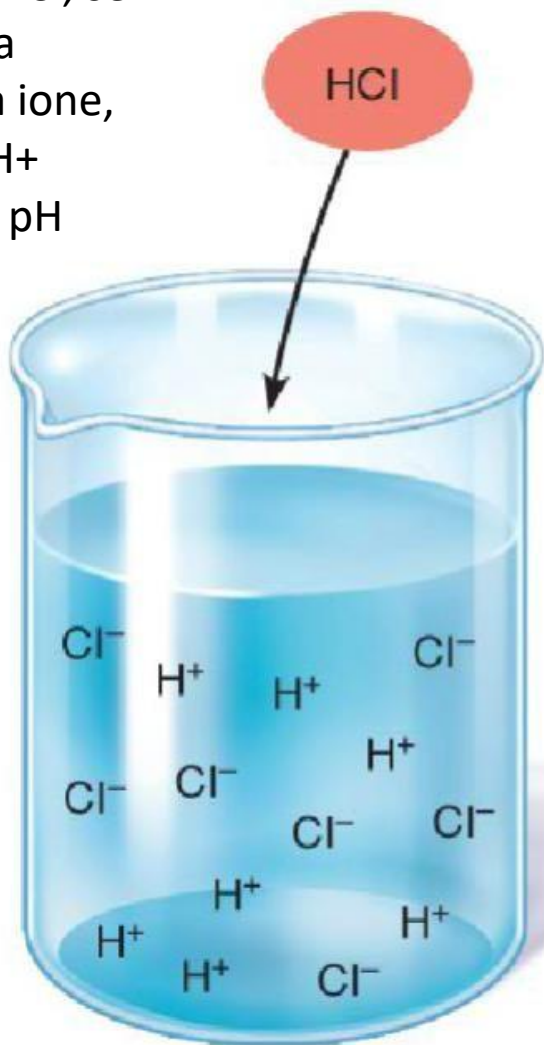
KISLINSKO-BAZIČNO RAVNOVESJE

- **pH** = koncentracija vodikovih ionov (H^+) v (telesni) tekočini
- pH in količina H^+ ionov sta obratnosorazmerna:
 - več H^+ ionov - nižji pH, bolj kislina tekočina
 - manj H^+ ionov – višji pH, manj kislina oz. bolj bazična tekočina
- pH telesnih tekočin je izražen tudi kot kislinsko-bazično ravnovesje
 - kislina – snov, ki oddaja H^+ ione v tekočino
 - baza – snov, ki veže H^+ ione (npr. OH^- ali HCO_3^-)

MOČNA VS. ŠIBKA KISLINA

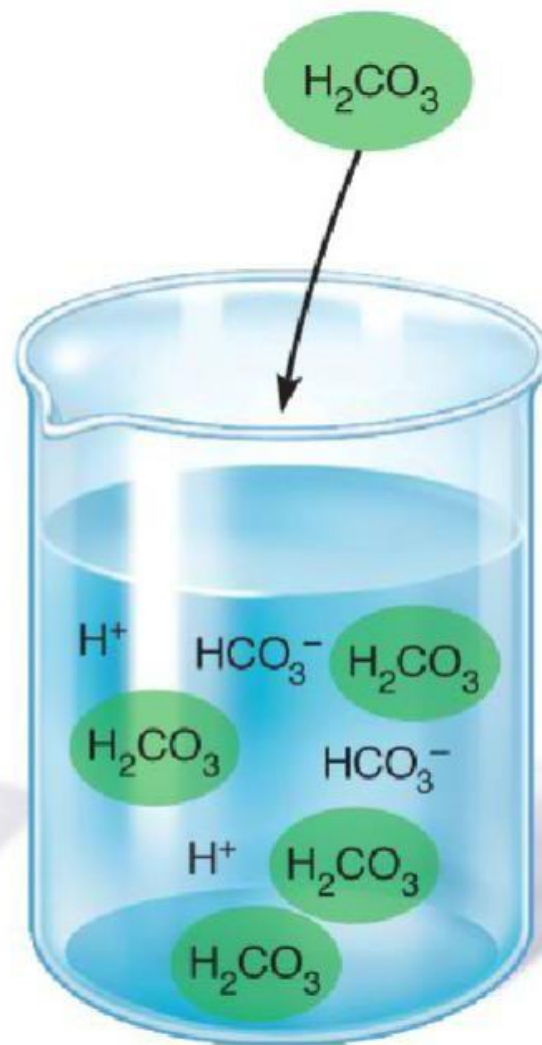
MOČNA KISLINA

kot je npr. HCl, se popolnoma razgradi na ione, odda VSE H⁺ ione, zniža pH tekočin



(a) A strong acid such as HCl dissociates completely into its ions.

ŠIBKA KISLINA kot je npr. H₂CO₃, se NE razgradi popolnoma na ione, ne odda vseh H⁺ ionov, manjši vpliv na pH tekočine

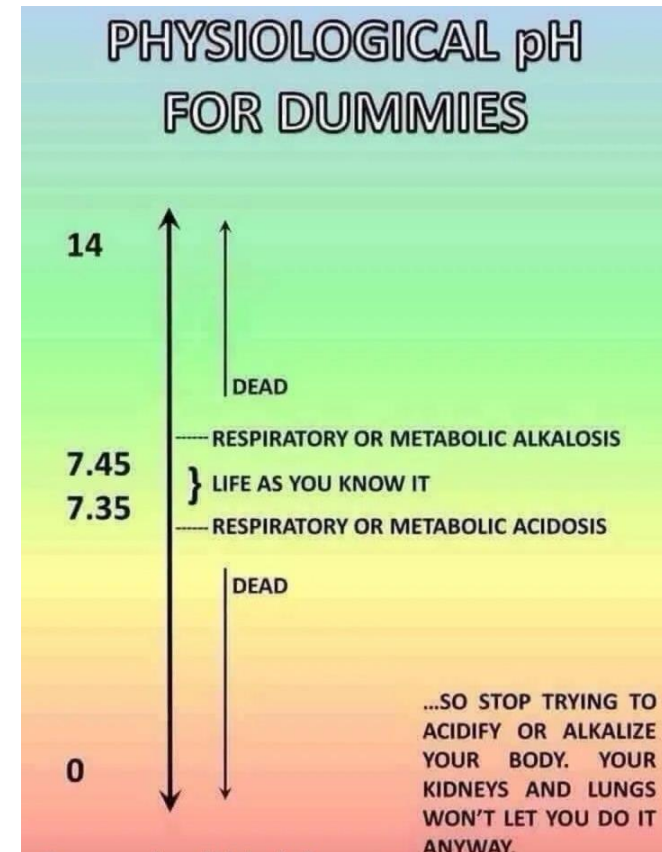


(b) A weak acid such as H₂CO₃ does not dissociate completely.

pH TELESNIH TEKOČIN

- je zelo dobro reguliran
- normalen pH v krvi in tkivnih tekočinah je med **7,35 - 7,45**
 - patološko: 6,9 – 7,8 (manj/več smrtno)
- majhen razpon → veliko reakcij za vzdrževanje mora biti vključenih
- H^+ se namreč v telesu proizvaja zelo veliko v različnih reakcijah (metabolizem maščob, sladkorjev, aminokislin)

→ *uravnavanje relativno konstantnega notranjega pH je ena izmed glavnih fizioloških nalog organskih sistemov v telesu!!!*



VZDRŽEVANJE pH

- lahko je KEMIJSKO ALI FIZIOLOŠKO – telo za vzdrževanje pH uporablja oba sistema istočasno

KEMIJSKO (poteka v celicah):

- kemijski pufri so sestavljeni iz šibkih baz in njihovih soli ter šibkih kislin in njihovih soli
- regulirajo pH z vezavo H^+ ionov in izločanjem, ko je pH prenizek, oziroma oddajanjem H^+ ionov, ko je pH previsok
- najhitrejši sistem, lahko “normalizira” pH v delcu sekunde

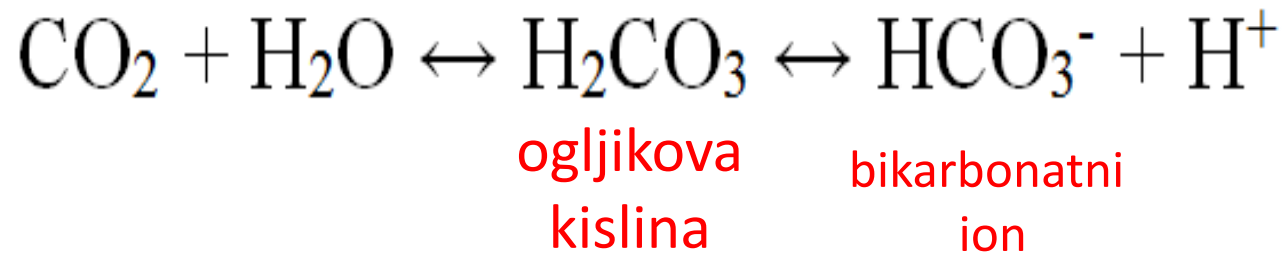
VZDRŽEVANJE pH - FIZIOLOŠKO

- ledvični in dihalni sistem sta dva največja fiziološka sistema za uravnavanje pH v telesu
 1. **LEDVIČNI SISTEM** – zelo počasen, ure-dnevi za opravljanje naloge, opravi nalogo popolnoma
 2. **DIHALNI SISTEM** – hiter (v nekaj minutah), ampak ne more uravnavati takih sprememb pH kot ledvice
- prenizek pH v telesu – ledvični sistem izloča več H^+ iz telesa z urinom
- preveč CO_2 v krvi – dihalni sistem poveča ventilacijo, da gre višek CO_2 ven

vpliv CO₂ na pH

- CO₂ neposredno vpliva na pH – dodatek CO₂ v tekočino (kri) poveča količino H⁺ ionov

OGLJIKOVA ANHIDRAZA

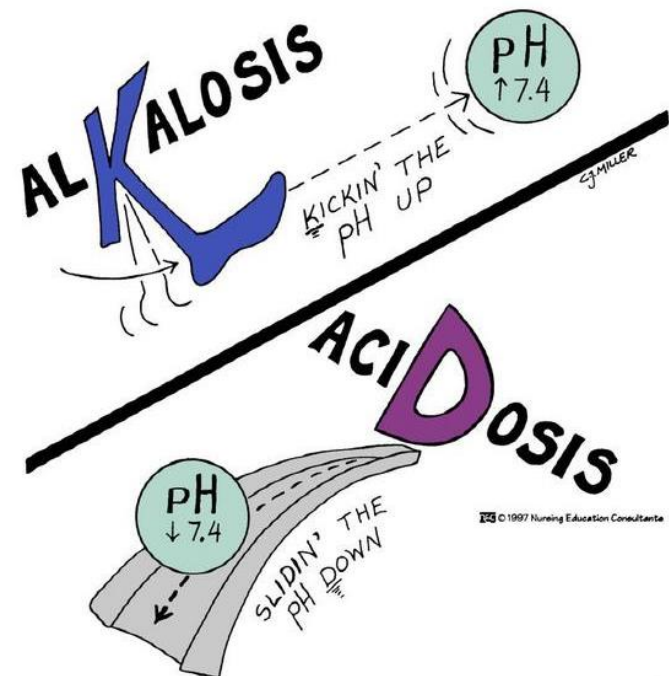


NERAVNOVESJE pH TELESNIH TEKOČIN

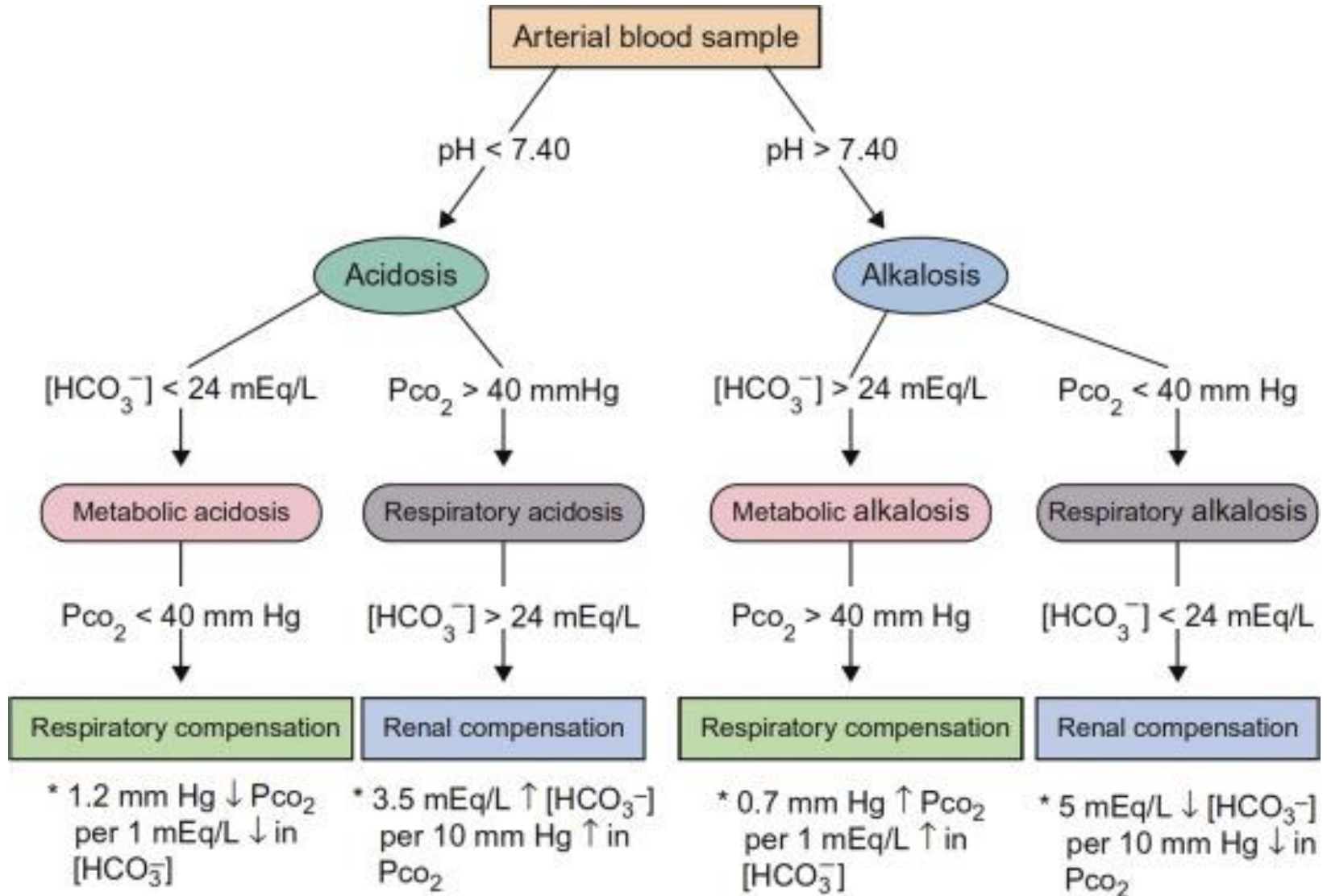
- do neravnovesja pH lahko pride zaradi **respiratornih ali metabolnih motenj** (ali kombinacije obojega), ki imajo za posledico porušenje kislinsko-baznega ravnovesja
- pri diagnosticiranju ocenjujemo:
 - parcialni tlak CO₂ v krvi (normalno med 35-45 mmHg)
 - pH: normalno **7,35 - 7,45**
 - pH > 7,45 - **ALKALOZA**
 - pH < 7,35 - **ACIDOZA**

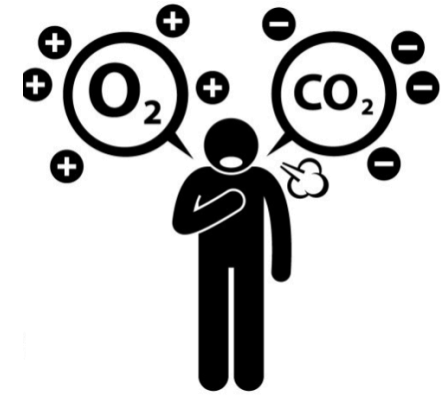
LOČIMO:

- respiratorno alkalozo oz. acidozo
- metabolno alkalozo oz. acidozo



POVZETEK ALKALOZ IN ACIDOZ





RESPIRATORNA ALKALOZA

- do respiratorne alkaloze pride zaradi **premalo CO₂** v krvi
- npr. ob potovanju na visoke nadmorske višine ali ob hiperventilaciji
- **HIPERVENTILACIJA** – povečanje globine in frekvence dihanja zaradi npr. vročine, napadov panike, tesnobe
- CO₂ se iz krvi odstranjuje hitreje, kot ga celice proizvajajo
- **manj CO₂ = zmanjšanje H⁺ v krvi – povišanje pH = imenujemo ALKALOZA**
- **LEDVIČNI SISTEM kompenzira** alkalozo z zadrževanjem H⁺ ionov in izločanjem bikarbonatnih ionov za znižanje pH nazaj na normalne vrednosti (enačba!)

RESPIRATORNA ACIDOZA

- pH < 7,35
- respiratorna acidoza je posledica motenega dihanja – **HIPOVENTILACIJE**
– zaradi oviranega dihanja, depresije dihalnega centra, obolelih pljuč, prevelikega doziranja zdravil, nezadostne alveolarne ventilacije pri paralizi dihalnih mišic ali hudem kroničnem bronhitisu, zadrževanja zraka pod vodo
- prihaja do akumulacije prevelike količine CO₂ v krvi → nivo H⁺ ionov v krvi se poveča, pH se zniža



RESPIRATORNA ACIDOZA



- razlog hipoventilacije je tudi ponovno dihanje – “rebreathing” = vdihanje zraka, ki je bil ravnokar izdihan iz pljuč (npr. ko pihamo v vrečko ob anksioznosti)
- zaradi tega prihaja do akumulacije CO_2 v krvi
- vpliv na pH in nivo CO_2 ???
- **LEDVIČNI SISTEM** kompenzira acidozo z izločanjem H^+ ionov in zadrževanjem bikarbonatnih ionov za povišanje pH nazaj na normalne vrednosti

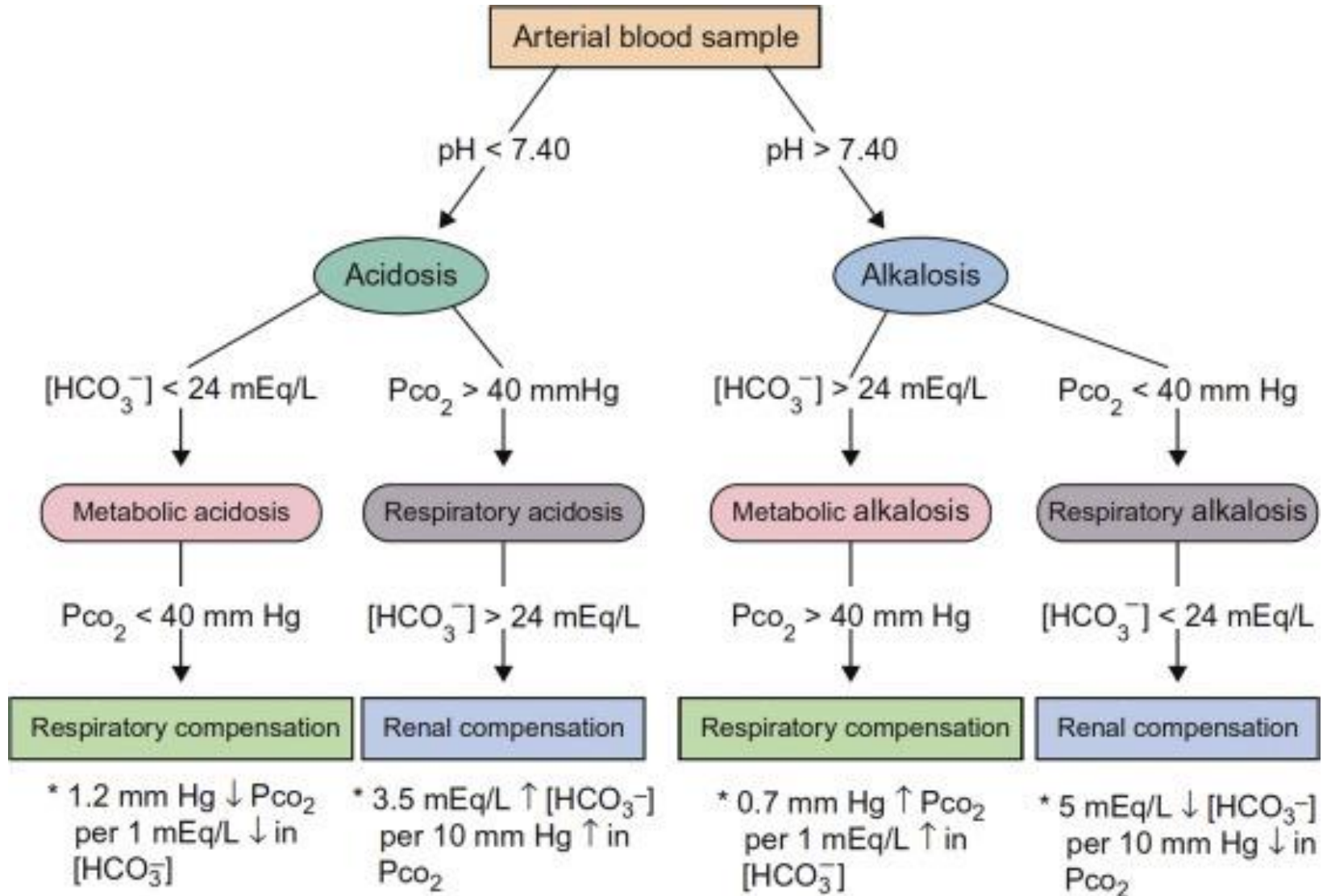
ODZIV LEDVIC NA R. ALKALOZO IN R. ACIDOZO

LEDVICE

- uravnavajo količino **vode** v urinu → obramba pred preveliko hidracijo/dehidracijo
- uravnavajo kislost urina in **stopnjo izločanja elektrolitov** – ledvice vzdržujejo pH in nivo elektrolitov v mejah normale
- **KOMPENZACIJA LEDVIC** – primarna metoda za kompenzacijo respiratorne alkaloze/acidoze
 - uravnavajo nivo H⁺ in HCO₃ ionov, ki jih izločajo v urin



POVZETEK ALKALOZ IN ACIDOZ



- čeprav lahko **ledvični sistem delno kompenzira** pH neravnovesje zaradi respiratornih razlogov, ledvice ne morejo čisto popolnoma kompenzirati, če se nivo dihanja ne vrne na normalno!

VAJE

- Kako povišanje/znižanje $p\text{CO}_2$ vpliva na nivo H^+ in HCO_3^- , ki jih ledvice izločajo z urinom

METABOLNA ACIDOZA IN ALKALOZA

- acidoze in alkaloze, ki niso respiratornega nastanka
- CO₂ – odpadni produkt metabolizma – meša se z vodo v plazmi, tvori se ogljikova kislina, tvori se H⁺
- dejavniki, ki vplivajo na stopnjo cel. metabolizma – vročina, stres, zaužitje hrane
- *povišanje normalne metabolne stopnje* – več CO₂ se tvori → več H⁺ se tvori → nižji pH plazme **metabolna acidoza**
- *znižanje normalne metabolne stopnje* – manj CO₂ se tvori → manj H⁺ se tvori → višji pH plazme **metabolna alkaloz**



METABOLNA ACIDOZA

- *povišanje normalne metabolne stopnje* – več CO_2 se tvori → več H^+ se tvori → nižji pH plazme **metabolna acidoza**
- nizek nivo HCO_3^- in pH v plazmi, **VELIKO H^+**
- **VZROKI:**
 - ketoacidoza – nastanek keto teles (kislin) kot posledica diabetesa
 - zastrupitev s salicilatom – toksično stanje, posledica npr. preveč aspirina
 - zaužitje prevelike količine alkohola
 - driska – izguba bikarbonatov
 - naporena vadba – nastanek mlečne kisline iz anaerobnega metabolizma mišic
- **kompenzira DIHALNI SISTEM:** dihanje se poveča – poveča se izdihavanje CO_2 iz pljuč za izločanje CO_2 iz krvi - to zniža pCO_2 v krvi,
- **kompenzirajo tudi LEDVICE** s povečanim izločanjem H^+ in povečano reabsorpcijo bikarbonata

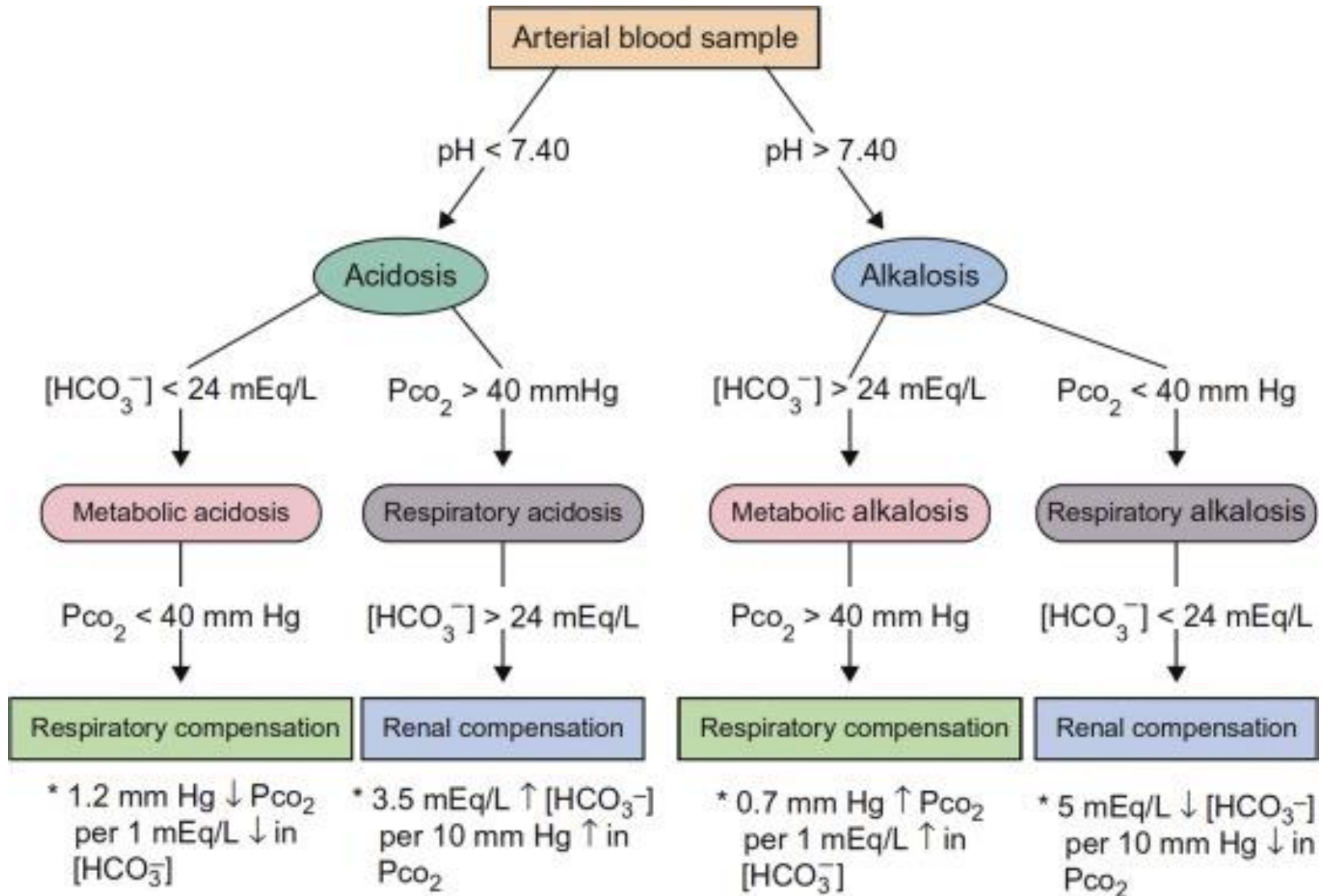
METABOLNA ALKALOZA

- *znižanje normalne metabolne stopnje* – manj CO_2 se tvori \rightarrow manj H^+ se tvori \rightarrow višji pH plazme **metabolna alkaloz**
- povišan nivo HCO_3^- ionov in pH, malo H^+

VZROKI:

- bruhanje – izguba preveč H^+ , K^+ in vode
- zaprtje – reabsorpcija HCO_3^-
- diuretična zdravila
- zaužitje baz (bikarbonatov)
- **kompensira DIHALNI SISTEM**: zmanjša izdihavanje CO_2 iz pljuč, CO_2 se akumulira v krvi – povišanje H^+ , znižanje pH, povečanje pCO_2 v krvi,
- **kompensirajo tudi LEDVICE** s povečanim izločanjem bikarbonatnih ionov

POVZETEK ALKALOZ IN ACIDOZ



VAJE

- 9_4
- 9_6
- 10_1-4

Exercise Overview

Acid-Base Balance

pH denotes the hydrogen ion concentration, $[H^+]$, in a solution (such as body fluids). The reciprocal relationship between pH and $[H^+]$ is defined by the following equation.

$$\text{pH} = \log(1/[H^+])$$

Because the relationship is reciprocal, $[H^+]$ is higher at *lower* pH values (indicating higher acid levels) and lower at *higher* pH values (indicating lower acid levels).

The pH of a body's fluid is also referred to as its **acid-base balance**. An **acid** is a substance that releases H^+ in solution. A **base**, often a hydroxyl ion (OH^-) or bicarbonate ion (HCO_3^-), is a substance that binds, or buffers, the H^+ .

A **strong acid** completely dissociates in solution, releasing all of its hydrogen ions and, thus, lowering the solution's pH. A **weak acid** dissociates incompletely and does not release all of its hydrogen ions in solution, producing a lesser effect on the solution's pH (view [Figure 10.1](#)).

A **strong base** has a strong tendency to bind to H^+ , raising the solution's pH. A **weak base** binds less of the H^+ , producing a lesser effect on the solution's pH.

The pH of body fluids is very tightly regulated. Blood and tissue fluids normally have a pH between 7.35 and 7.45. Under pathological conditions, blood pH as low as 6.9 or as high as



Exercise Overview

7.8 has been recorded, but a higher or lower pH cannot sustain human life. The narrow range from 7.35 to 7.45 is remarkable when you consider the vast number of biochemical reactions that take place in the body. The human body normally produces a large amount of H^+ as the result of metabolic processes; ingested acids; and the products of fat, sugar, and amino acid metabolism. The regulation of a relatively constant internal pH is one of the major physiological functions of the body's organ systems.

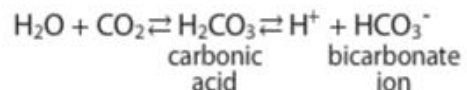
To maintain pH homeostasis, the body utilizes both *chemical* and *physiological* buffering systems. Chemical buffers are composed of a mixture of weak acids and weak bases. They help regulate the body's pH levels by binding H^+ and removing it from solution as its concentration begins to rise or by releasing H^+ into solution as its concentration begins to fall. The body's three major chemical buffering systems are the *bicarbonate*, *phosphate*, and *protein buffer systems*. We will not focus on chemical buffering systems in this exercise, but keep in mind that chemical buffers are the fastest form of compensation and can return pH to normal within a fraction of a second.

The body's two major physiological buffering systems are the **renal system** and the **respiratory system**. The renal system is the slower of the two, taking hours to days to do its work. The respiratory system usually works within minutes, but cannot handle the amount of pH change that the renal system can. These physiological buffer systems help regulate body pH by controlling the output of acids, bases, or carbon dioxide (CO_2) from the body. For



Exercise Overview

example, if there is too much acid in the body, the renal system may respond by excreting more H^+ from the body in urine. Similarly, if there is too much carbon dioxide in the blood, the respiratory system may respond by increasing ventilation to expel the excess carbon dioxide. Carbon dioxide levels have a direct effect on pH because the addition of carbon dioxide to the blood results in the generation of more H^+ . The following equation shows what happens in the respiratory system when carbon dioxide combines with water in the blood, producing carbonic acid.

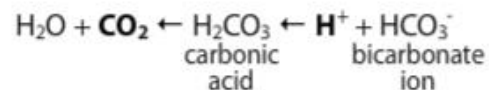


Introduction

Acid-base imbalances can have respiratory and metabolic causes. When diagnosing these disorders, two key signs are evaluated: the pH and the partial pressure of carbon dioxide in the blood (P_{CO_2}). The normal range for pH is between 7.35 and 7.45, and the normal range for P_{CO_2} is between 35 and 45 mm Hg. When the pH falls below 7.35, the body is said to be in a state of **acidosis**. When the pH rises above 7.45, the body is said to be in a state of **alkalosis**.

Respiratory alkalosis is the condition of too little carbon dioxide in the blood. Respiratory alkalosis commonly results from traveling to high altitude (where the air contains less oxygen) or hyperventilation, which can be brought on by fever, panic attack, or anxiety.

Hyperventilation, defined as an increase in the rate and depth of breathing, removes carbon dioxide from the blood faster than it is being produced by the cells of the body, reducing the amount of H^+ in the blood and, thus, increasing the blood's pH. The following equation shows the shift in the equilibrium that results in the increase in blood pH due to less carbon dioxide in the blood.



The renal system can compensate for alkalosis by retaining H^+ and excreting bicarbonate ions to lower the blood pH levels back to the normal range (view [Figure 10.2](#)).



Introduction

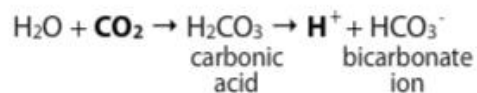
Equipment Used

- Simulated lung chamber
- pH meter
- Oscilloscope
- Two breathing patterns: normal and hyperventilation

Introduction

The body is said to be in a state of **acidosis** when the pH of the blood falls below 7.35 (although a pH of 7.35 is technically not acidic). Respiratory acidosis is the result of impaired respiration, or *hypoventilation*, which leads to the accumulation of too much carbon dioxide in the blood. The causes of impaired respiration include airway obstruction, depression of the respiratory center in the brain stem, lung disease (such as emphysema and chronic bronchitis), and drug overdose.

Recall that carbon dioxide contributes to the formation of carbonic acid when it combines with water through a reversible reaction catalyzed by carbonic anhydrase. The carbonic acid then dissociates into hydrogen ions and bicarbonate ions. Because hypoventilation results in elevated carbon dioxide levels in the blood, the equilibrium shifts, the H^+ levels increase, and the pH value of the blood decreases.



Rebreathing is the action of breathing in air that was just expelled from the lungs. Rebreathing results in the accumulation of carbon dioxide in the blood. Breathing into a paper bag is an example of rebreathing. (Note that breathing into a paper bag can deplete the body of oxygen and is therefore not the best therapy for hyperventilation because it can mask other life-threatening emergencies, such as a heart attack or asthma). In this activity you will observe

Introduction

what happens to pH and carbon dioxide levels in the blood during rebreathing. In the body, the kidneys regulate the acid-base balance by altering the amount of H^+ and HCO_3^- excreted in the urine (view [Figure 10.3](#)).

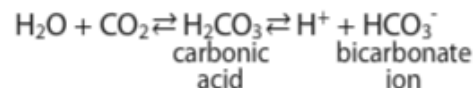
Equipment Used

- Simulated lung chamber
- pH meter
- Oscilloscope
- Two breathing patterns: normal and rebreathing

Introduction

The kidneys play a major role in maintaining fluid, electrolyte, and acid-base balance in the body's internal environment. By regulating the amount of water lost in the urine, the kidneys defend the body against excessive hydration or dehydration. By regulating the acidity of urine and the rate of electrolyte excretion, the kidneys maintain plasma pH and electrolyte levels within normal limits.

Renal compensation is the body's primary method of compensating for conditions of respiratory acidosis or respiratory alkalosis. The kidneys regulate the acid-base balance by altering the amount of H^+ and HCO_3^- excreted in the urine. If we revisit the equation for the dissociation of carbonic acid, a weak acid, we see that the conservation of bicarbonate ion (base) has the same net effect as the loss of acid, H^+ .



In this activity you will examine how the renal system compensates for respiratory acidosis or respiratory alkalosis. Respiratory acidosis is generally caused by the accumulation of carbon dioxide in the blood from hypoventilation, but it can also be caused by rebreathing. Acidosis results in a lower-than-normal blood pH. Respiratory alkalosis is caused by a depletion of carbon dioxide, often caused by an episode of hyperventilation, and results in an elevated blood pH.



Introduction

You will primarily be working with the variable P_{CO_2} . Recall that the normal range for pH is between 7.35 and 7.45 and the normal range for P_{CO_2} is between 35 and 45 mm Hg. You will observe how increases and decreases in P_{CO_2} affect the levels of H^+ and HCO_3^- that the kidneys excrete in urine. The functional unit for adjusting the plasma composition is the **nephron**. View [Figure 10.4](#) to see an uncoiled nephron similar to the one you will use in this activity. Remember that, although the renal system can partially compensate for pH imbalances with a respiratory cause, the kidneys cannot fully compensate if respirations have not returned to normal because the carbon dioxide levels will still be abnormal.

Equipment Used

- Source beaker for blood (first beaker on left side of screen)
- Drain beaker for blood (second beaker on left side of screen)
- Simulated nephron (The filtrate forms in Bowman's capsule, flows through the renal tubule—the tubular components, and empties into a collecting duct, which, in turn, drains into the urinary bladder.)
 - ♦ Nephron tank
 - ♦ Glomerulus—"ball" of capillaries that forms part of the filtration membrane
 - ♦ Glomerular (Bowman's) capsule—forms part of the filtration membrane and a capsular space where the filtrate initially forms
 - ♦ Proximal convoluted tubule

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- Loop of Henle
- Distal convoluted tubule
- Collecting duct
- Drain beaker for filtrate (beaker on right side of screen)—simulates the urinary bladder

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Conditions of acidosis and alkalosis that do not have respiratory causes are termed **metabolic acidosis** and **metabolic alkalosis**.

Metabolic acidosis is characterized by low plasma HCO_3^- and pH. The causes of metabolic acidosis include:

- **ketoacidosis**, a buildup of keto acids that can result from diabetes mellitus;
- **salicylate poisoning**, a toxic condition resulting from ingestion of too much aspirin or oil of wintergreen (a substance often found in laboratories);
- the ingestion of too much alcohol, which metabolizes into acetic acid;
- diarrhea, which results in the loss of bicarbonate with the elimination of intestinal contents; and
- strenuous exercise, which can cause a buildup of lactic acid from anaerobic muscle metabolism.

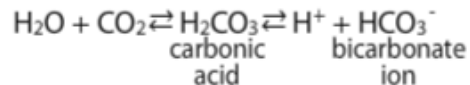
Metabolic alkalosis is characterized by elevated plasma HCO_3^- and pH. The causes of metabolic alkalosis include:

- ingestion of alkali, such as antacids or bicarbonate;
- vomiting, which can result in the loss of too much H^+ ;
- constipation, which may result in significant reabsorption of HCO_3^- .



Introduction

Increases or decreases in the body's normal metabolic rate can also result in metabolic acidosis or alkalosis. Recall that carbon dioxide—a waste product of metabolism—mixes with water in plasma to form carbonic acid, which, in turn, forms H^+ .



Therefore, an increase in the normal metabolic rate causes more carbon dioxide to form as a metabolic waste product, resulting in the formation of more H^+ and, therefore, lower plasma pH, potentially causing acidosis. Other acids that are also normal metabolic waste products (such as ketone bodies and phosphoric, uric, and lactic acids) would likewise accumulate with an increase in metabolic rate.

Conversely, a decrease in the normal metabolic rate causes less carbon dioxide to form as a metabolic waste product, resulting in the formation of less H^+ and, therefore higher plasma pH, potentially causing alkalosis. Many factors can affect the rate of cell metabolism. For example, fever, stress, or the ingestion of food all cause the rate of cell metabolism to *increase*. Conversely, a fall in body temperature or a decrease in food intake causes the rate of cell metabolism to decrease.

The respiratory system compensates for metabolic acidosis or alkalosis by expelling or retaining carbon dioxide in the blood. During metabolic acidosis, respiration increases to expel carbon

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dioxide from the blood, thus decreasing $[H^+]$ and raising the pH. During metabolic alkalosis, respiration decreases to promote the accumulation of carbon dioxide in the blood, thus increasing $[H^+]$ and decreasing the pH.

The renal system also compensates for metabolic acidosis and alkalosis by conserving or excreting bicarbonate ions. Nevertheless, in this activity, you will focus on respiratory compensation of metabolic acidosis and alkalosis.

Equipment Used

- Simulated heart pump
- Simulated lung chamber
- Oscilloscope

