

# Acid – Base Balance

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Monitoring of acid – base balance is essential for biochemical changes in the organism and the hydrogen ion concentration in plasma and other water spaces

*Sirker AA, Rhodes A, Grounds RM, Bennett ED: Acid–base physiology: the traditional and the modern approaches. Anaesthesia 2002; 57:348–356*

Acid–base equilibrium is a pivotal topic in the biomedical sciences and clinical medicine.

Studied by literally millions of people it is often perceived as difficult.

This may be because the commonly taught approaches to acid–base physiology are confusing and illogical.

*Paul WG Elbers and John A Kellum, Stewart's Textbook of Acid–Base, ISBN: 978-1-4092-5470-6 LCCN: 20099200, 2009*

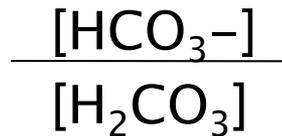
# Learning objectives (1)

1. Body organism all the time produces some acids as lactic acid, uremic acid or  $\text{H}_2\text{CO}_3$ ...
2. During the activity the total amount of acids is rapidly increased
3. The second place of acid release is digestive system which can produce gastric acid
4. Intake of acid with food and transport them into the blood

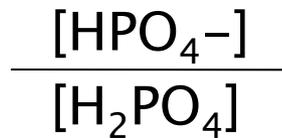
# Learning objectives (2)

Acid - base balance depends mainly in the activity of buffers in the blood

1. bicarbonate



2. phosphate



3. plasma proteins

4. red blood cells

# Learning objectives (3)

## ▶ Red blood cell buffer

### 1. in the lungs

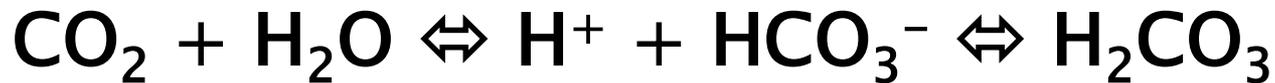
oxyhemoglobin is stronger acid than hemoglobin and release  $\text{Cl}^-$  from red blood cells into the plasma

### 2. in the tissues

in venous blood  $\text{Cl}^-$  return to red blood cells and this process is responsible for the constant pH of venous plasma

# History 1

- ▶ 1908 Lawrence Joseph Henderson used for the dissociation equation of carbonic acid



This equation is characterised by the following:

- \* the law of mass action
- \* the speed of chemical reaction is proportional to the concentration of reagents

# After transformation: equation is as follow:

- ▶ The substitution of bicarbonate ion with carbon dioxide ( $\text{CO}_2$  is an easier parameter to evaluate)

$$\text{H}^+ = \frac{K_1 \times [\text{CO}_2]}{\text{HCO}_3^-}$$

# History 2

- ▶ In 1916 Karl Albert Hasselbach converted the Henderson equation into the form corresponding to the pH equation introduced by Sorensen 6 years earlier and replaced the concentration of dissolved, molecular carbon dioxide with its tension leading to:

$$\text{pH} = \text{pK} + \log \frac{\text{HCO}_3^-}{\text{S}\text{CO}_2 \times \text{P}\text{CO}_2}$$

$\text{S}\text{CO}_2$  is the solubility coefficient for  $\text{CO}_2$ , being  $0.03 \text{ mmol l}^{-1}\text{mmHg}^{-1}$  at  $37^\circ\text{C}$

$\text{pK}$  a negative decimal logarithm of the constant  $K$  from equation =  $6.1$  at  $37^\circ\text{C}$

# H<sup>+</sup> concentration

- ▶ **H<sup>+</sup> concentration** is normally maintained within tight limits around a normal value of about **0.00004 mEq/L = 40 nEq/L**

Normal variations are only about 3 to 5 nEq/L, but under extreme conditions, the H<sup>+</sup> concentration can vary from as low as 10 nEq/L to as high as 160 nEq/L without causing death

- ▶ Because H<sup>+</sup> concentration normally is low is necessary to express H<sup>+</sup> concentration on a logarithm scale, using pH units

- ▶ pH is related to the actual H<sup>+</sup> concentration by the following formula

(H<sup>+</sup> concentration [H<sup>+</sup>] is expressed in *equivalents per liter*):

$$\text{pH} = \log \frac{1}{[\text{H}^+]} = -\log [\text{H}^+]$$

$$[\text{H}^+] = 40 \text{ nEq/L (0.00000004 Eq/L)}$$

$$\text{pH} = -\log [0.00000004]$$

$$\text{pH} = 7.4$$

Haselbach introduced the term „standard pH” as value of pH of oxygen-saturated blood at PaCO<sub>2</sub> 40 mmHg (5.33 kPa) and temperature 37°C

# pH is related to the $H^+$ concentration

- ▶ low pH corresponds to:  
high  $H^+$  concentration
- ▶ high pH corresponds to:  
low  $H^+$  concentration

# Body fluids...

# pH and H<sup>+</sup> Concentration of Body Fluids

	H <sup>+</sup> Concentration (mEq/L)	pH
Extracellular fluid		
Arterial blood	4.0 \ 10 <sup>-5</sup>	7.40
Venous blood	4.5 \ 10 <sup>-5</sup>	7.35
Interstitial fluid	4.5 \ 10 <sup>-5</sup>	7.35
Intracellular fluid	1 \ 10 <sup>-3</sup> to 4 \ 10 <sup>-5</sup>	6.0 to 7.4
Urine	3 \ 10 <sup>-2</sup> to 1 \ 10 <sup>-5</sup>	4.5 to 8.0
Gastric HCl	160	0.8

# Extracellular fluid – pH

- ▶ pH of **arterial** blood – **7.4**
- ▶ pH of **venous** blood and **interstitial** fluids – **7.35**  
because of the extra amounts of carbon dioxide ( $\text{CO}_2$ ) released from the tissues to form  $\text{H}_2\text{CO}_3$  in these fluids
- ▶ **acidosis** – pH falls **<7.4**  
The lower limit of pH at which a person can live more than a few hours is about 6.8
- ▶ **alkalosis** – pH rises above **>7.4**  
The lower limit of pH at which a person can live more than a few hours is about 6.8, and the upper limit is about 8.0

# Extracellular fluid – pH

$$\text{pH} = 7.4$$

$$\text{PaCO}_2 = 40 \text{ mmHg (5.3 kPa)}$$

$$\text{Bicarbonates} = 25 \text{ mmol/l}$$

# Intracellular fluid

- ▶ **Intracellular pH** usually is slightly **lower** than plasma pH because the metabolism of the cells produces acid, especially  $\text{H}_2\text{CO}_3$
- ▶ Depending on the type of cells, the pH of intracellular fluid has been estimated to range between **6.0 and 7.4**
- ▶ **From the clinical point of view!!!**



# Urine

- ▶ The pH of **urine** can range from **4.5 to 8.0**, depending on the acid–base status of the extracellular fluid
- ▶ Kidneys play a major role in correcting abnormalities of extracellular fluid  $H^+$  concentration by excreting acids or bases at variable rates

# Gastric acid

- ▶ **HCl secretion** into the stomach by the oxyntic (parietal) cells of the stomach mucosa is an extreme example of an acidic body fluid
- ▶ The  $H^+$  concentration in these cells is about 4 million times greater than the hydrogen concentration in blood, with a **pH of 0.8**

# Homeostasis

# Homeostasis

balance between  
the intake or production of  $H^+$



and the net removal of  $H^+$  from the body

# How to achieve acid–base homeostasis?

# Acid is...

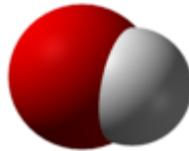
- ▶ A strong acid is one that rapidly dissociates and releases especially large amounts of  $H^+$  in solution (HCl)
- ▶ Weak acids have less tendency to dissociate their ions and, therefore, release  $H^+$  with less vigor

# Acid is...

- ▶ Molecule containing hydrogen atoms that can release hydrogen ions in solutions
  - **HCL** – hydrochloric acid, which ionizes in water to form hydrogen ions ( $H^+$ )
    - \* *strong acid*
  - **Cl** – chloride ions
  - **H<sub>2</sub>CO<sub>3</sub>** – carbonic acid ionizes in water to form  $H^+$  and bicarbonate ions ( $HCO_3^-$ )
    - \* *weak acid*

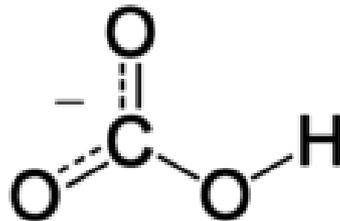
# Base is...

- ▶ A strong base is one that reacts rapidly and strongly with  $H^+$  and, therefore, quickly removes these ion from a solution ( $OH^-$ )



hydroxide ion

- ▶ weak base is  $HCO_3^-$  - because it binds with  $H^+$  much more weakly than does  $OH^-$



bicarbonate

# Base is...

- ▶ an ion or a molecule that can accept an  $H^+$ 
  - $HCO_3^-$  is a base because it can combine with  $H^+$  to form  $H_2CO_3$   
*weak base*
  - $OH^-$   
*strong base*
  - $HPO_4^{2-}$ , the *hydrogen phosphate* anion, is a base because it can accept an  $H^+$  to form  $H_2PO_4^-$
  - Proteins, amino acids that make up proteins have net negative charges that readily accept  $H^+$

# Alkali is...

- ▶ Molecules formed by the combination of one or more of the alkaline metals –  
sodium, potassium, lithium  
and so forth—with a highly basic ion such as a hydroxide ion ( $\text{OH}^-$ )

## *Alkalosis*

refers to excess removal of  $H^+$  from the body fluids

## *Acidosis*

*is a* contrast to the excess addition of  $H^+$

# Approach methods

changes in the hydrogen ion concentration  
in blood  
results from changes in concentration  
of **volatile and non-volatile acids**

**Volatile** – CO<sub>2</sub>

eliminated by the lungs – changes in them are classified as **respiratory**

**Non-volatile** – hydrochloric, lactic, sulphuric etc.

changes are classified as **metabolic**

# Copenhagen approach

- ▶ Conventional method of interpretation, based on Henderson–Hasselbach equation
- ▶ Focuses on the excess / deficiency of bases
- ▶ Classical theory – disturbance is classified as
  1. **respiratory** if the change originally concerns the tension of  $\text{CO}_2$
  2. **metabolic** if it concerns metabolic **acids**

# Copenhagen evaluation

## ▶ Buffer bases (BB)

- \* difference between the sum of all strong (i.e. completely dissociated) cations and the sum of all strong anions
- \* their levels increase in metabolic alkalosis and decrease in metabolic acidosis

## ▶ Standard bicarbonates

- \* concentration of bicarbonates in the blood sample at PaCO<sub>2</sub> 40 mmHg (5.33 kPa) and temperature 37°C

## ▶ Base excess

- \* the amount of a strong acid or base required to return the in vitro pH of 1 litre of completely oxygen-saturated human blood to 7.4 at 37°C (originally 38°C) assuming PaCO<sub>2</sub> of 40 mmHg (5.33 kPa)
- \* in vivo – some inaccuracies occur – e.g. changes of CO<sub>2</sub> tension and influence of hemoglobin concentration changes is ignored

# Boston approach

- ▶ Essential is analysis of bicarbonate ion concentration
- ▶ Disturbances are determined by assessing whether the changes in the concentration of  $\text{HCO}_3^-$  and  $\text{PaCO}_2$  coincide with the expected ones

# Evaluation of $\text{HCO}_3^-$ and $\text{PCO}_2$

- ▶ Decreased  $\text{HCO}_3^-$  and  $\text{PCO}_2$  suggests metabolic acidosis or respiratory alkalosis  
mixed disturbances cannot be excluded
- ▶ Increased  $\text{HCO}_3^-$  and  $\text{PCO}_2$  suggests metabolic alkalosis and respiratory acidosis  
mixed disturbances cannot be excluded
- ▶ When  $\text{HCO}_3^-$  and  $\text{PCO}_2$  change in opposite directions, some mixed disturbances should be considered

And finally...

Modern theory is leading to...

# The essence of modern theory:

Only three elements  
*(called independent variables)*  
influence the hydrogen ion concentration:

the mentioned CO<sub>2</sub> tension

SID

*SID - strong ion difference*

A<sub>TOT</sub>

A<sub>TOT</sub> - total concentration  
of weak acids

# SID (strong ion difference)

- ▶ Difference between the sum of all strong cations and the sum of all strong anions
- ▶ Correlates with BB (buffer bases described 50 years ago) – but concerns only plasma and ignores the effects of hemoglobin
- ▶ Normal ranges 40 – 42 mmol/l

# $A_{TOT}$ (total concentration of weak acids)

- ▶ Determine the concentration of hydrogen ions
- ▶ Could be affected by proteins (particularly albumins) and phosphates
- ▶ The influence on acid–base balance depends on their total amount and dissociation balance
- ▶ Difficulties in calculating  $A_{TOT}$  limit its usefulness for acid–base evaluation

*Kellum JA: Determinants of blood pH in health and disease. Critical Care 2000; 4: 6–14*

# Concept of anion gap (AG)

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

12 mmol/l

$$AG = (Na^+ + K^+) - (Cl^- + HCO_3^-) = \text{Albumin} + PO_4^- + XA$$

- ▶ Reflects anions in this equation:  
proteins, phosphates, and other anions (XA - anion from unidentified organic acid)
- ▶ Limits:
  1. critically ill patients - the concentration of plasma proteins is particularly important as a decrease in serum albumin concentrations reduces the anion gap
  2. hypoalbuminemia and hypophosphatemia - AG could be normal even the unmeasured ions are present

	PO4
	HCO3
Na	
K	Cl

	XA
	PO4
	HCO3
Na	
K	Cl

# Regulation of $H^+$ concentration

# Defenses Against Changes in Hydrogen Ion Concentration: Buffers, Lungs, and Kidneys

There are three primary systems that regulate the  $H^+$  concentration in the body fluids to prevent acidosis or alkalosis:

- buffers

- lungs

- kidneys

# Buffers

the *chemical acid–base buffer systems of the body fluids, which immediately* combine with acid or base to prevent excessive changes in  $H^+$  concentration

Buffer systems do not eliminate  $H^+$  from or add them to the body but only keep them tied up until balance can be reestablished

“Buffer Power” is determined by the amount and relative concentrations of the buffer components

# Lungs

The *respiratory center*, which regulates the removal of  $\text{CO}_2$  (and, therefore,  $\text{H}_2\text{CO}_3$ ) from the extracellular fluid

The *respiratory system*, also acts within a few minutes to eliminate  $\text{CO}_2$  and, therefore,  $\text{H}_2\text{CO}_3$  from the body

# Kidneys

Can excrete either acid or alkaline urine, thereby readjusting the extracellular fluid  $H^+$  concentration toward normal during acidosis or alkalosis

*The kidneys, the third defense line, can eliminate the excess acid or base from the body. Although they are relatively slow to respond compared with the other defenses, over a period of hours to several days, they are by far the most powerful of the acid–base regulatory systems*

# Buffers

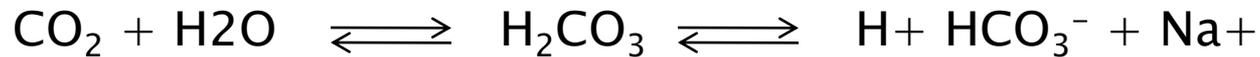
# Buffering of Hydrogen Ions in the Body Fluids (*general formula*)



- ▶ free H<sup>+</sup> combines with the buffer to form a weak acid (H buffer) that can either remain as an unassociated molecule or dissociate back to buffer and H<sup>+</sup>
- ▶ When the H<sup>+</sup> concentration **increases**, the reaction is forced to the right, and more H<sup>+</sup> binds to the buffer, as long as buffer is available
- ▶ Conversely, when the H<sup>+</sup> concentration **decreases**, the reaction shifts toward the left, and H<sup>+</sup> is released from the buffer

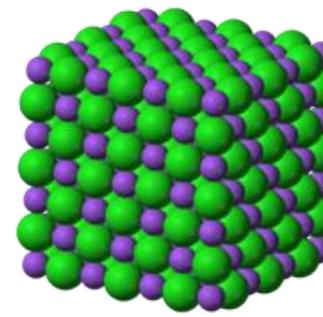
# Bicarbonate Buffer System

- ▶ quantitatively the most important in the extracellular fluid
- ▶ consists of a water solution that contains two ingredients:
  - (1) a weak acid,  $\text{H}_2\text{CO}_3$
  - (2) a bicarbonate salt,  $\text{NaHCO}_3$

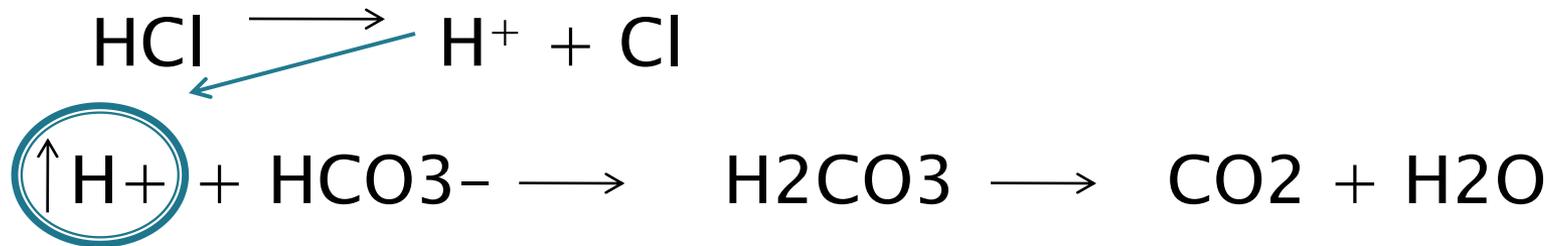


**Bicarbonate Buffer System Is the Most Important Extracellular Buffer**

# Acidosis...adding HCl

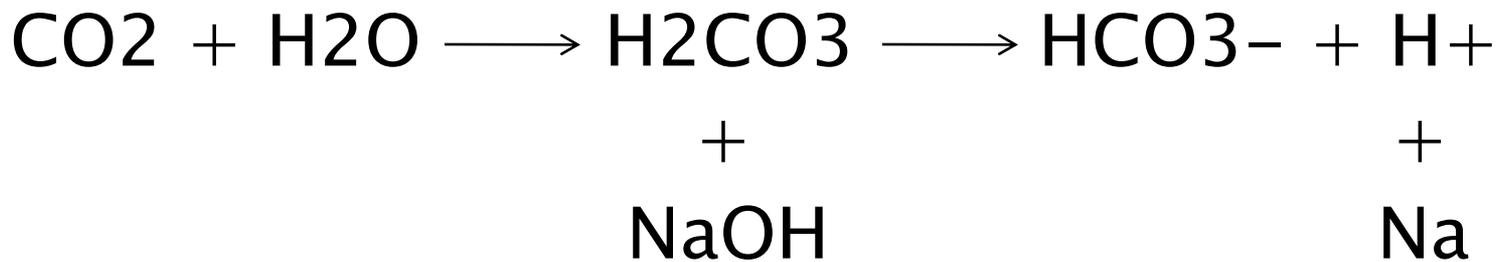


- ▶ When a strong acid such as HCl is added to the bicarbonate buffer solution, the increased  $H^+$  released from the acid is buffered by  $HCO_3^-$



- ▶ As a result, more  $H_2CO_3$  is formed, causing increased  $CO_2$  and  $H_2O$  production.  
From these reactions, one can see that  $H^+$  from the strong acid HCl reacts with  $HCO_3^-$  to form the very weak acid  $H_2CO_3$ , which in turn forms  $CO_2$  and  $H_2O$ .  
The excess  $CO_2$  greatly stimulates respiration, which eliminates the  $CO_2$  from the extracellular fluid

# Alkalosis...adding NaOH



## explanation

In this case, the  $\text{OH}^-$  from the NaOH combines with  $\text{H}_2\text{CO}_3$  to form additional  $\text{HCO}_3^-$ .

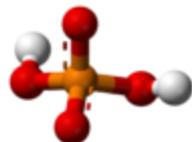
Thus, the weak base  $\text{NaHCO}_3$  replaces the strong base NaOH.

At the same time, the concentration of  $\text{H}_2\text{CO}_3$  decreases (because it reacts with NaOH), causing more  $\text{CO}_2$  to combine with  $\text{H}_2\text{O}$  to replace the  $\text{H}_2\text{CO}_3$ .

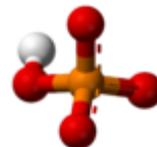
# Phosphate Buffer System

- ▶ plays a major role in buffering renal tubular fluid and intracellular fluids
- ▶ The main elements of the phosphate buffer system are  $\text{H}_2\text{PO}_4^-$  and  $\text{HPO}_4^{2-}$
- ▶ The phosphate buffer system has a pK of 6.8, which is not far from the normal pH of 7.4 in the body fluids
- ▶ phosphate usually becomes greatly concentrated the tubules, thereby increasing the buffering power of the phosphate system
- ▶ the tubular fluid usually has a considerably lower pH than the extracellular fluid does, bringing the operating range of the buffer closer to the pK (6.8) of the system

**Phosphate buffer is especially important in the tubular fluids of the kidneys**

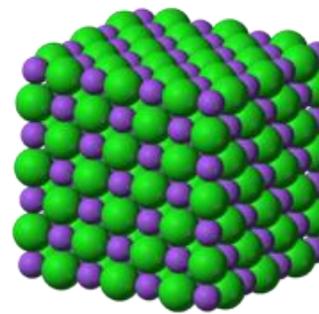


$\text{H}_2\text{PO}_4^-$

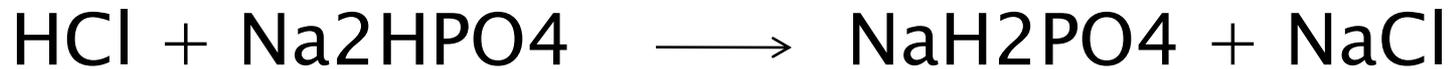


$\text{HPO}_4^{2-}$

# Acidosis...adding HCl

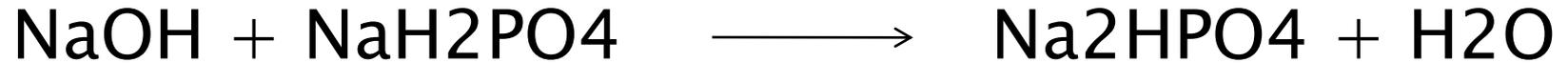


- ▶ When a strong acid such as HCl is added to a mixture of these two substances, the hydrogen is accepted by the base  $\text{HPO}_4^{2-}$  and converted to  $\text{H}_2\text{PO}_4^-$



- ▶ As a result, strong acid, HCl is replaced by an additional amount of a weak acid  $\text{NaH}_2\text{PO}_4$ , and the decrease in pH is minimized

# Alkalosis...adding NaOH



## explanation

- ▶ strong base, NaOH, is traded for a weak base, NaH<sub>2</sub>PO<sub>4</sub>, causing only a slight increase in pH

# Proteins: Important Intracellular Buffers

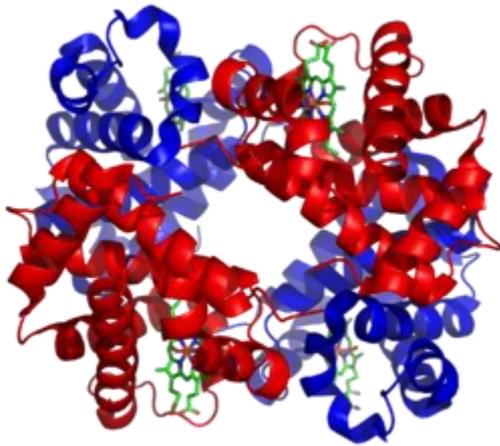
- ▶ The buffer systems within the cells help prevent changes in the pH of extracellular fluid but may take several hours to become maximally effective

*There is a slight amount of diffusion of  $H^+$  and  $HCO_3^-$  through the cell membrane, although these ions require several hours to come to equilibrium with the extracellular fluid, except for rapid equilibrium that occurs in the red blood cells.*

*$CO_2$ , however, can rapidly diffuse through all the cell membranes*

The pH in intracellular fluid is able to change when there are changes in extracellular pH

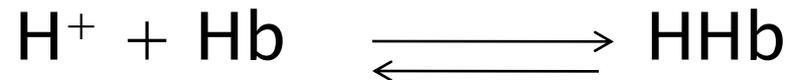
# Hemoglobin



Hemoglobin, human, adult  
(heterotetramer,  $(\alpha\beta)_2$ )

Structure of human hemoglobin. The protein's  $\alpha$  and  $\beta$  subunits are in red and blue, and the iron-containing heme groups in green.

# Hemoglobin (Hb) as an important buffer



- ▶ In the red blood cell, hemoglobin (Hb) is an important buffer
- ▶ except for the red blood cells, the slowness with which  $\text{H}^+$  and  $\text{HCO}_3^-$  move through the cell membranes often delays for several hours the maximum ability of the intracellular proteins to buffer extracellular acid–base abnormalities

# Respiratory regulation

# CO<sub>2</sub> metabolic pathway

CO<sub>2</sub> production in metabolic intracellular processes



diffusion from the cells into the interstitial fluids and blood



blood transports it to the lungs



diffusion into the alveoli and then transfer to the atmosphere by pulmonary ventilation

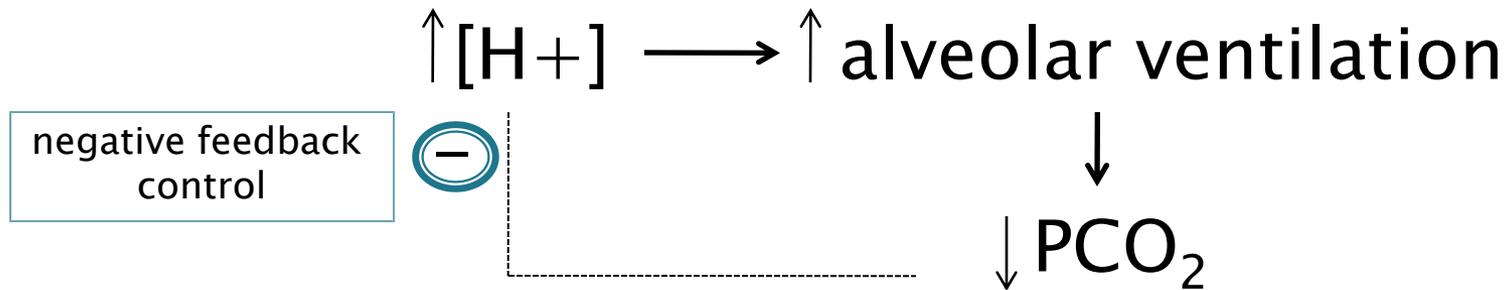
\*\*\* About 1.2 mol/L of dissolved CO<sub>2</sub> normally is in the extracellular fluid, corresponding to a P<sub>co2</sub> of 40 mm Hg

# Hemoglobin-CO<sub>2</sub>

## Carbaminohemoglobin

- ▶ **Carbaminohemoglobin** (or **Carbaminohaemoglobin**, also known as carbhemoglobin and carbohemoglobin) is a compound of hemoglobin and carbon dioxide, which is one of the forms in which carbon dioxide exists in the blood.  
Binding to carbon dioxide lowers hemoglobin's affinity for oxygen when carbaminohemoglobin is formed, via the **Bohr Effect**.  
When hemoglobin is not bound to oxygen, it has a higher tendency to become carbaminohemoglobin; this is known as the **Haldane effect**.  
Carbaminohemoglobin is blueish in color, so the veins, whose blood contains the compound, appears blue.
- ▶ Binding of carbon dioxide in carbaminohemoglobin is not always agreed upon with certain biochemistry texts.  
⇒ 4 carbon dioxide molecules bind to hemoglobin.  
This binding does not occur at the same place as oxygen binding although 4 oxygen molecules do bind to hemoglobin.  
Other biochemistry texts suggest that carbon dioxide does not bind at all and is found only floating in the cytoplasm of the red blood cell. The need of further studies seems to be necessary.

# Feedback Control of Hydrogen Ion Concentration by the Respiratory System



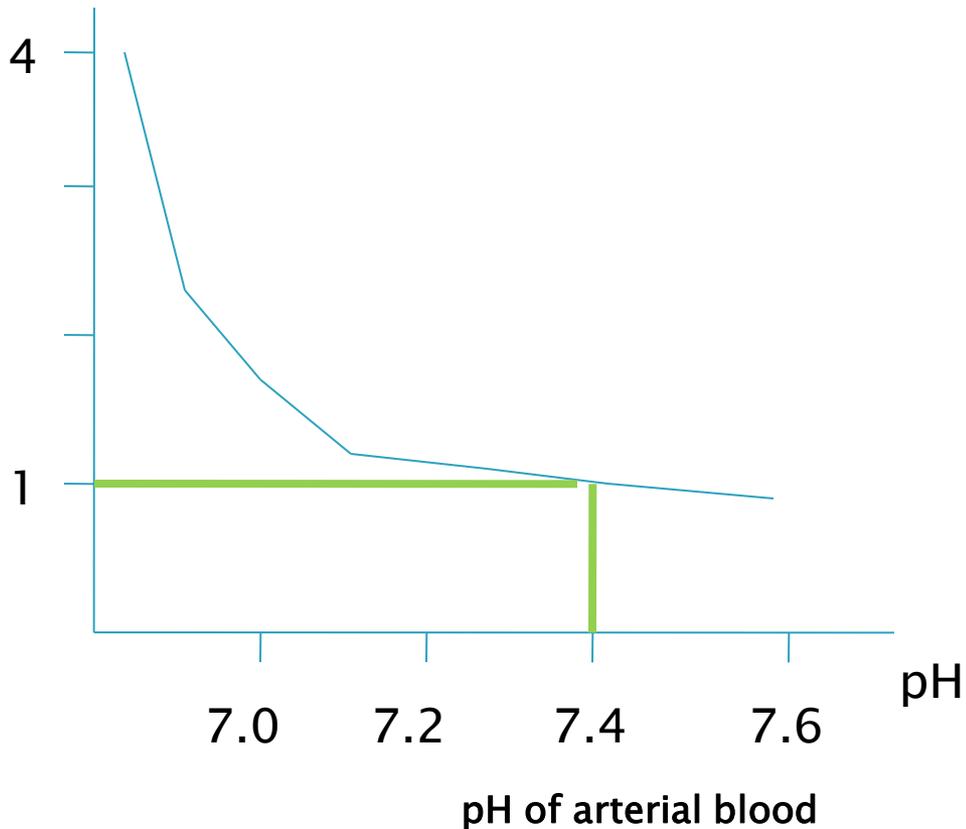
- ▶ acts rapidly
- ▶ keeps the  $H^+$  concentration from changing too much until the slowly responding kidneys can eliminate the imbalance
- ▶ one to two times as great as the buffering power of all other chemical buffers in the extracellular fluid combined

# Efficiency of Respiratory Control

- ▶ if the  $H^+$  concentration is suddenly increased by adding acid to the extracellular fluid and pH falls from 7.4 to 7.0, the respiratory system can return the pH to a value of about 7.2 to 7.3.
- ▶ This response occurs within 3 to 12 minutes

# Effect of blood pH on the rate of alveolar ventilation

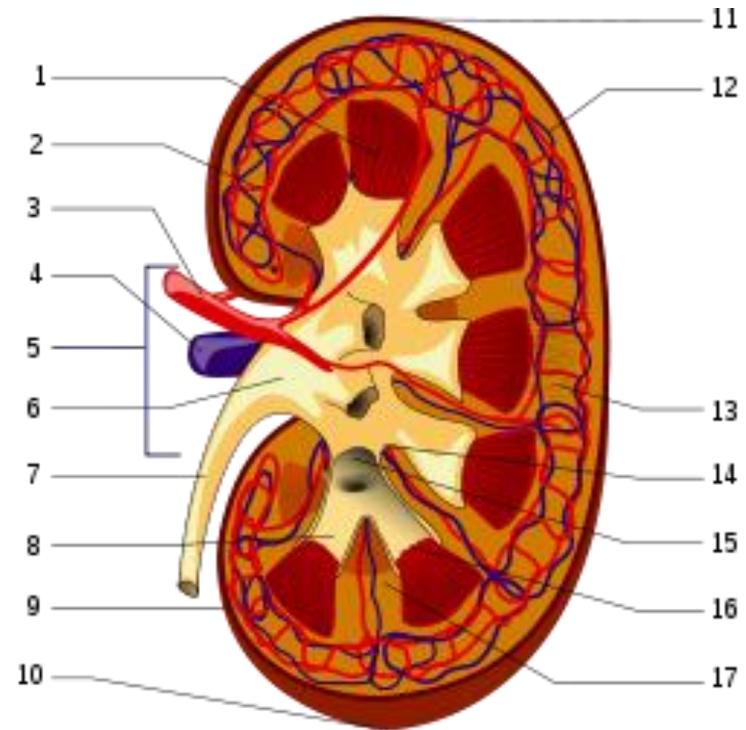
Alveolar ventilation  
Normal = 1



# Renal Control

# Kidneys

1. Renal pyramid
2. Interlobar artery
3. Renal artery
4. Renal vein
5. Renal hilum
6. Renal pelvis
7. Ureter
8. Minor calyx
9. Renal capsule
10. Inferior renal capsule
11. Superior renal capsule
12. Interlobar vein
13. Nephron
14. Minor calyx
15. Major calyx
16. Renal papilla
17. Renal column



- ▶ The kidneys control acid–base balance by excreting either an acidic or a basic urine
- ▶ Excreting an acidic urine reduces the amount of acid in extracellular fluid, whereas excreting a basic urine removes base from the extracellular fluid
- ▶ Excretion of either an acidic or a basic urine

# Kidneys mechanism

kidneys regulate extracellular fluid  $H^+$  concentration through three fundamental mechanisms:

1. secretion of  $H^+$
2. reabsorption of filtered  $HCO_3^-$
3. production of new  $HCO_3^-$

# H<sup>+</sup> secretion

- ▶ **normal conditions**

the kidney tubules must secrete at least enough H<sup>+</sup> to reabsorb almost all HCO<sub>3</sub><sup>-</sup> that is filtered

- ▶ **alkalosis**

tubular secretion of H<sup>+</sup> must be reduced to a level that is too low to achieve complete HCO<sub>3</sub><sup>-</sup> reabsorption, enabling the kidneys to increase HCO<sub>3</sub><sup>-</sup> excretion

- ▶ **acidosis**

the tubular H<sup>+</sup> secretion must be increase sufficiently to reabsorb all the filtered HCO<sub>3</sub><sup>-</sup>

# Reabsorption of filtered $\text{HCO}_3^-$

## Factors That Increase or Decrease $\text{H}^+$ Secretion and $\text{HCO}_3^-$ Reabsorption by the Renal Tubules

### Increase $\text{H}^+$ Secretion and $\text{HCO}_3^-$ Reabsorption

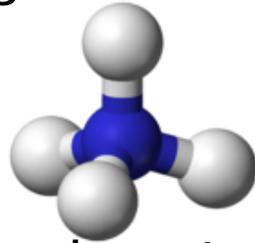
↑  $\text{PCO}_2$   
↑  $\text{H}^+$ , ↓  $\text{HCO}_3^-$   
↓ Extracellular fluid volume  
↑ Angiotensin II  
↑ Aldosterone  
Hypokalemia

### Decrease $\text{H}^+$ Secretion and $\text{HCO}_3^-$ Reabsorption

↓  $\text{PCO}_2$   
↓  $\text{H}^+$ , ↑  $\text{HCO}_3^-$   
↑ Extracellular fluid volume  
↓ Angiotensin II  
↓ Aldosterone  
Hyperkalemia

# Production of new $\text{HCO}_3^-$

- ▶ The amount of new bicarbonate contributed to the blood at any given time is equal to the amount of  $\text{H}^+$  secreted that ends up in the tubular lumen with nonbicarbonate urinary buffers e.g.  $\text{NH}_4^+$  and phosphate



*Ammonium cation*

- ▶ in acidosis, there is a net addition of  $\text{HCO}_3^-$  back to the blood as more  $\text{NH}_4^+$  and urinary titratable acid are excreted
- ▶ In alkalosis, there is a negative net acid secretion  
net loss of  $\text{HCO}_3^-$  from the blood (which is the same as adding  $\text{H}^+$  to the blood)  
no new  $\text{HCO}_3^-$  is generated by the kidneys

# Clinical Causes of Acid–Base Disorders

# Summarize of acid–base disturbances

## Characteristics of Primary Acid–Base Disturbances

	pH	H+	PCO <sub>2</sub>	HCO <sub>3</sub> <sup>-</sup>
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
Respiratory acidosis	↓	↑	↑↑	↑
Respiratory alkalosis	↑	↓	↓↓	↓
Metabolic acidosis	↓	↑	↓	↑↑
Metabolic alkalosis	↑	↓	↑	↓↓

# Respiratory Acidosis

- ▶ **Decreased Ventilation**
- ▶ **Increased PCO<sub>2</sub>**



Remember!!!  
Increased PCO<sub>2</sub> dilatates cerebral vessels causing ↑ICP

damage the respiratory center

vertebral column fracture  
brain trauma  
brain stem death  
  
intracranial haematoma  
  
neuro-muscular disease

decrease the ability of the lungs to eliminate CO<sub>2</sub>

pneumonia  
emphysema  
decreased pulmonary  
    membrane surface area  
ARDS / IRDS

# Respiratory Alkalosis

## ▶ Increased Ventilation

## ▶ Decreased PCO<sub>2</sub>

- Controlled hyperventilation
- Uncontrolled hyperventilation (mistakes in ventilator parameters by doctor or technician)
- Overventilation by the lungs
- Psychoneurosis
- Sepsis
- Pregnancy
- Lung diseases
- Severe anemia
- Liver insufficiency

PaCO<sub>2</sub> < 36 mmHg  
↓ H<sup>+</sup>  
↑ pH



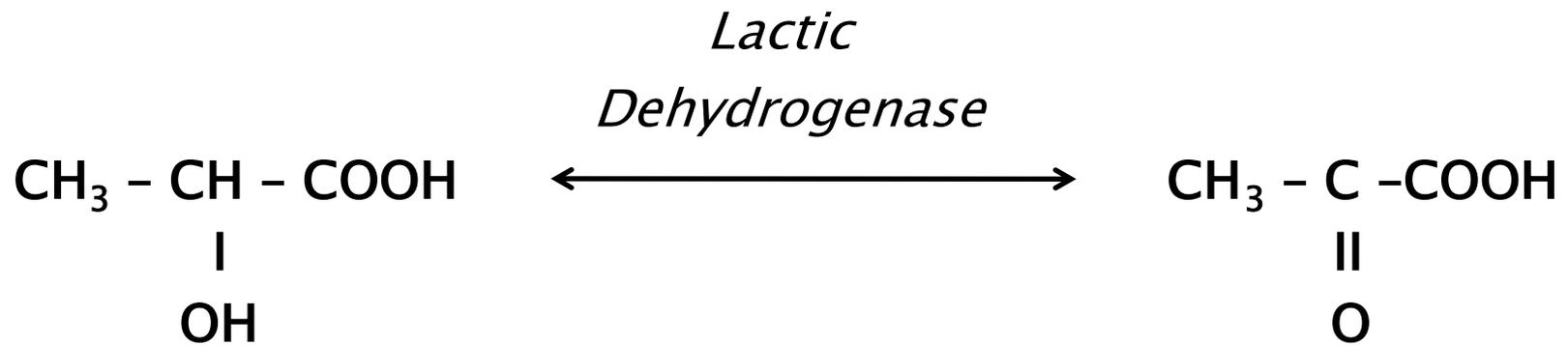
# Metabolic acidosis

- ▶ **Decreased extracellular fluid bicarbonate concentration**
- ▶ **Defect in renal secretion of  $H^+$**
- ▶ **Defect in reabsorption of  $HCO_3^-$** 
  - failure of the kidneys to excrete metabolic acids normally formed in the body
  - formation of excess quantities of metabolic acids in the body
  - addition of metabolic acids to the body by ingestion or infusion of acids
  - loss of base from the body fluids, which has the same effect as adding an acid to the body fluids
  - Diarrhea
  - Vomiting of intestinal contents
  - Diabetes mellitus
  - Chronic kidney disease

**Remember!!!**  
**The risk of death from  $pH=7.2$**

# Lactic acidosis

- ▶ Lactates are produced during anaerobic metabolism of glucose
- ▶ Normal plasma values: 1 mmol/l  
during maximal physical activity could rise to 20 mmol/l
- ▶ The most important acidosis among critically ill patients in ICU-s  
very prognostic value depending on the MOF (Multi Organ Failure) and Poor Outcome



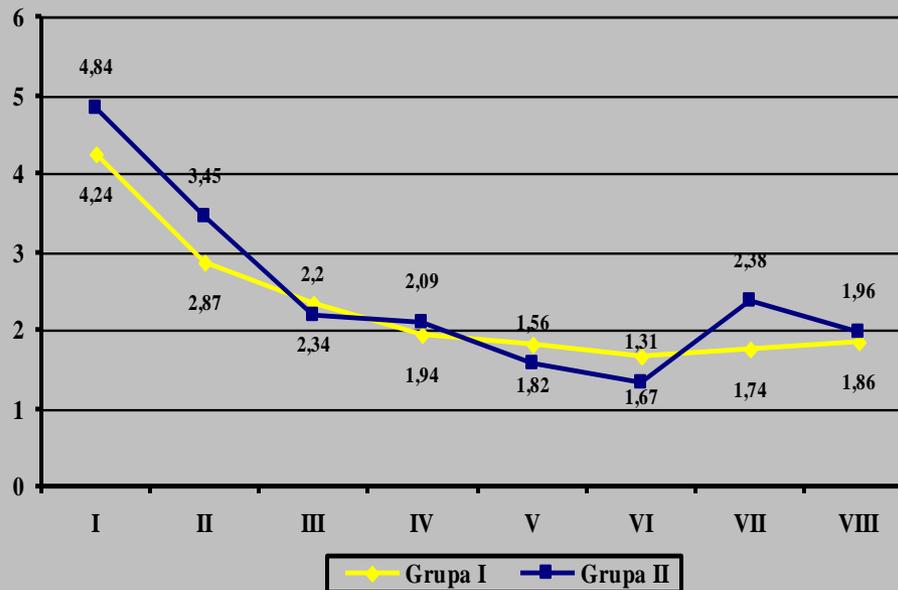
# Clinical course of lactic acidosis

- ▶ **Type A: severe hypoperfusion**
  - severe multiple trauma
  - sepsis
  - heart insufficiency
  - haemorrhage or severe anemia
  - CO intoxication
  - epilepsy grand mal
  - pheochromocytoma
- ▶ **Type B: without hypoperfusion**
  - uraemia
  - liver insufficiency
  - diabetes mellitus
  - sepsis
  - cancer
  - intoxication: ethanol, methanol, adrenaline, terbutaline...

# Clinical study – stress adult reaction leads into the severe multiple trauma (SIRS and MOF)

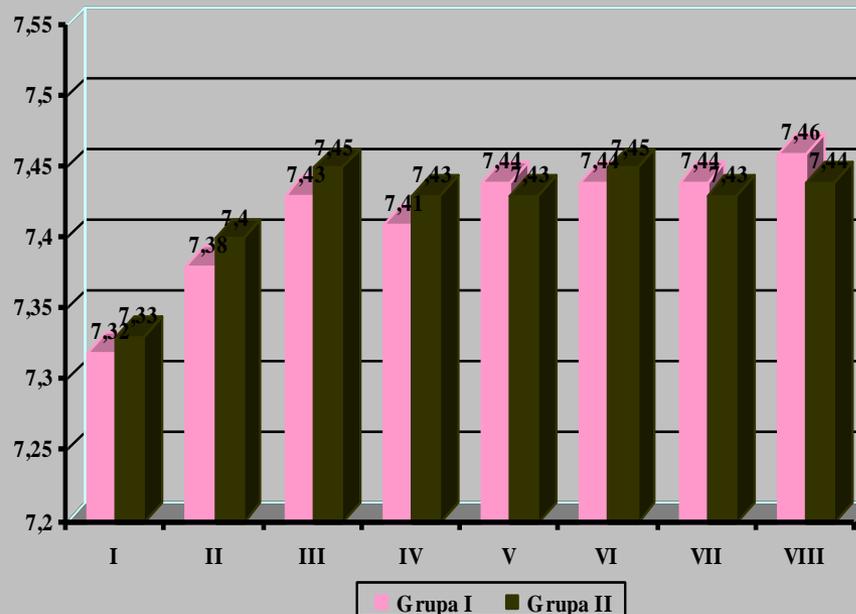
## Lactate plasma concentration

Normal values  
0,63-2,44 mmol/l



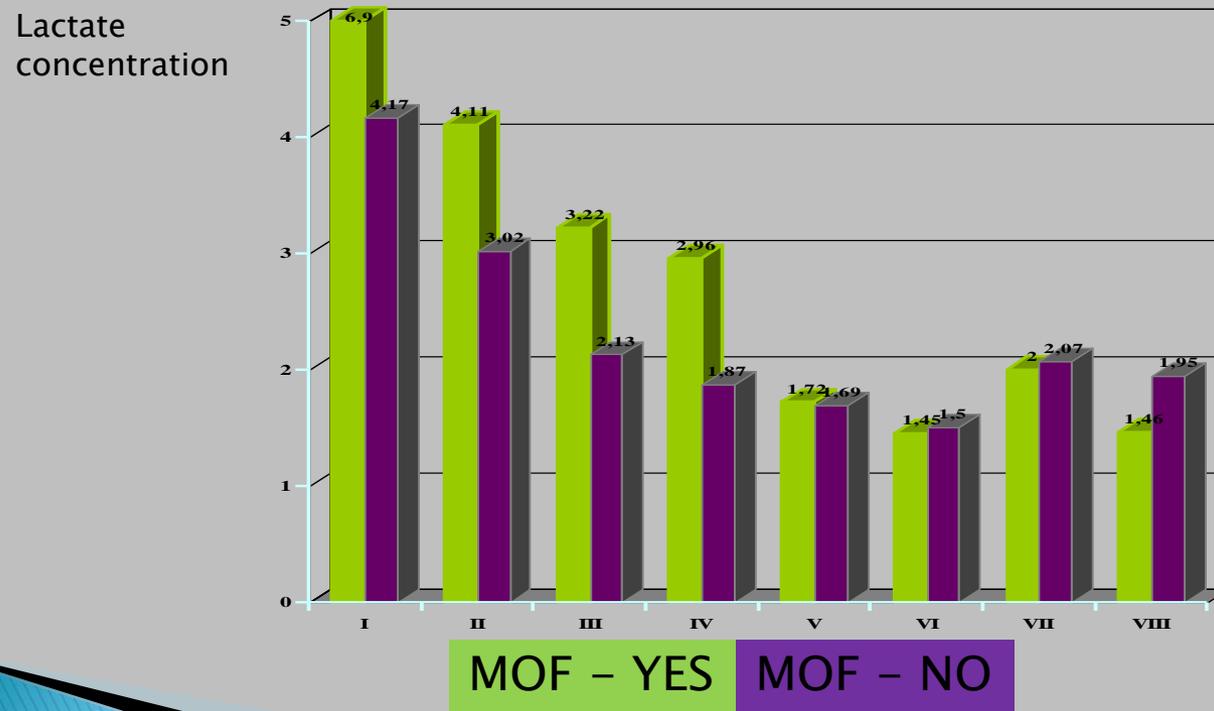
# Clinical study – stress adult reaction leads into the severe multiple trauma (SIRS and MOF)

Plasma pH



# Clinical study – stress adult reaction into the severe multiple trauma (SIRS and MOF)

Correlation between MOF and lactate concentration



# Metabolic alkalosis

- ▶ **excess retention of  $\text{HCO}_3^-$**
- ▶ **loss of  $\text{H}^+$  from the body**
  - administration of diuretics (except the carbonic anhydrase inhibitors)
  - excess aldosterone
  - diarrhea
  - vomiting of gastric contents
  - ingestion of alkaline drugs
  - after compensation of chronic hypokalemia
  - Severe hypokalemia

**pH > 7.4**

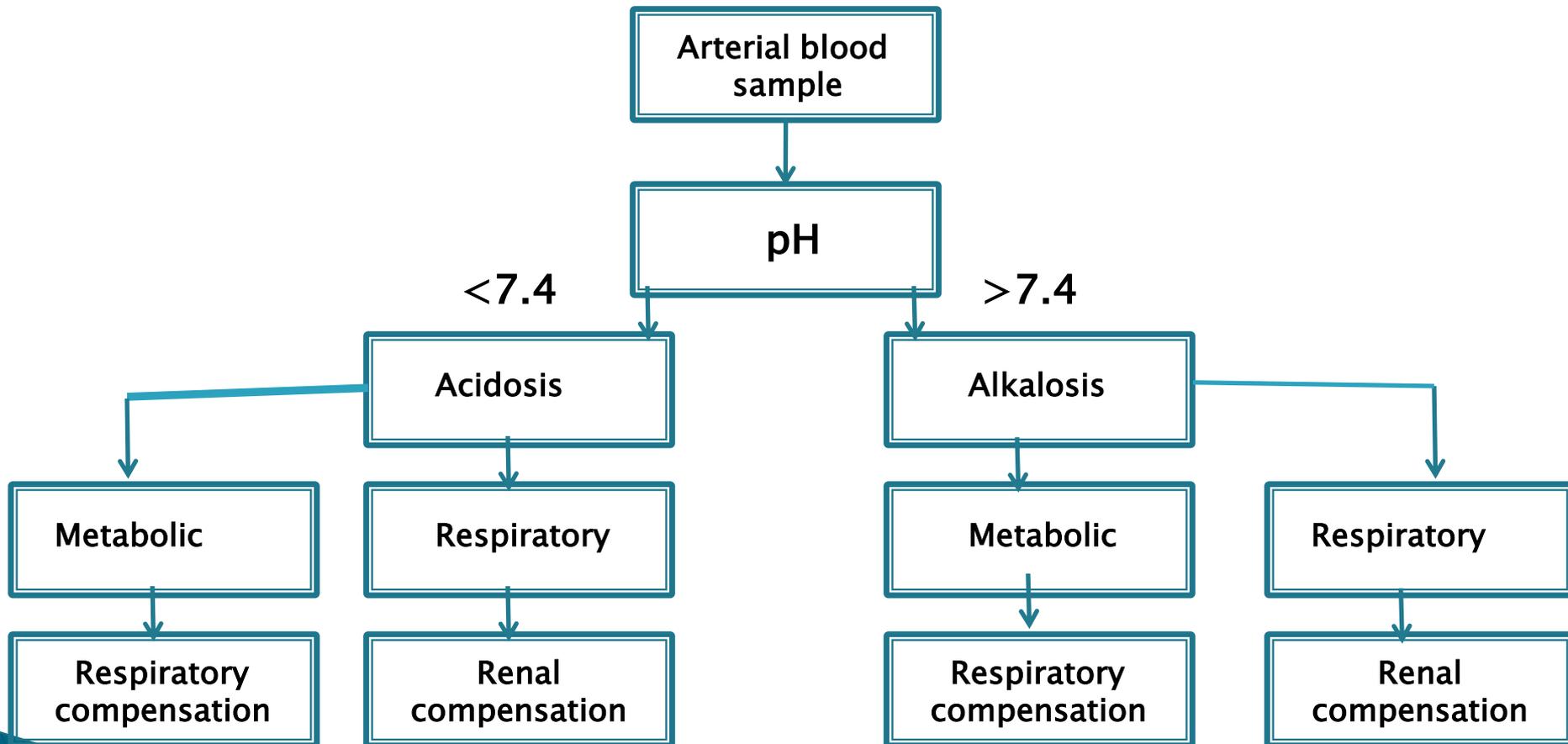
**$\text{HCO}_3^- > 26 \text{ mmol/l}$**

**BE > 2**

**$\text{PaCO}_2$  increases 0.7 mmHg for every 1 mmol/l of increasing  $\text{HCO}_3^-$  in plasma**

# Acid–Base Balance Monitoring

# Analysis of simple acid–base disorders



# Diagnosis

**Appropriate therapy of acid–base disorders  
requires  
proper diagnosis**

# Arterial blood gases analysis

1. pH
2. Plasma bicarbonates concentration
3. PaCO<sub>2</sub>
4. BE (Base excess)

# Important steps

1. Step  
pH assessment       $< 7.4$  means acidosis  
                                  $> 7.4$  means alkalosis
2. Step  
pCO<sub>2</sub> assessment  
HCO<sub>3</sub><sup>-</sup> assessment
3. Step  
\* assessment if disturbance could be metabolic  
acidosis or alkalosis  
\*\* assessment if disturbance could be  
respiratory acidosis or alkalosis  
\*\*\* ...

# Example of... metabolic acidosis

pH = 7.25  
HCO<sub>3</sub> = 18 mmol/l  
pCO<sub>2</sub> = 30 mmHg

*In simple metabolic acidosis, one would expect to find a low pH, a low plasma HCO<sub>3</sub><sup>-</sup> concentration, and a reduction in PCO<sub>2</sub> after partial respiratory compensation*

# Treatment

The aims of therapy

1. correction of acidosis
2. elimination of the cause

Ad1.

is necessary to administer basic fluids if pH below 7.15–7.20  
bicarbonates – i.v.

$$\text{mmol} = \text{BE} \times 0.3 \times \text{kg b.w.}$$

*Remember* 1 ml of 8.4%  $\text{HCO}_3^-$  = 1 mmol  $\text{HCO}_3^-$

→ first only correction to increase pH above 7.2

**complications**

increase of Na

hyperosmolarity

increase of  $\text{PaCO}_2$  and intracellular acidosis

left shift of oxygen–hemoglobin dissociation curve

# Treatment

Ad1

**i.v. TRIS Buffer (THAM, Trometamol)**

connects the H<sup>+</sup> and decrease PaCO<sub>2</sub>

remember

- \* TRIS is without Na – indication in hypernatremia
- \* causes respiratory depression (decrease PaCO<sub>2</sub>)  
– contraindication among the patient with himself  
ventilation

**ml = BE x 0.3 x kg b.w.**

**Max speed of i.v. – 10 ml/min**

**Max dose 750 ml / 24 hours**

# Example of... Respiratory acidosis

pH = 7.29  
pCO<sub>2</sub> = 52 mmHg  
HCO<sub>3</sub> = 28 mmol/l

expected values for a simple respiratory acidosis would be reduced plasma pH, increased PCO<sub>2</sub>, and increased plasma HCO<sub>3</sub><sup>-</sup> concentration after partial renal compensation

# Treatment

- ▶ Acute
  1. remove the cause of respiratory insufficiency
  2. oxygenation
  3. mechanical ventilation
  
- ▶ Chronic
  1. long lasting therapy
  2. be very carefull in mechanical ventilation – you could never disconnect the patient...

# Example of... Respiratory alkalosis

pH = 7.51

pCO<sub>2</sub> = 24 mmHg

after several hours increased HCO<sub>3</sub><sup>-</sup>

simple respiratory alkalosis, one would expect to find increased pH, decreased PCO<sub>2</sub>

# Treatment

Is necessary if pH is above 7.55

1. remove the cause

for example change the parameters in the ventilator

if hypoxemia is present try to treat the basic disturbance

...

# Example of... **Metabolic alkalosis**

pH = 7.55  
HCO<sub>3</sub><sup>-</sup> = 33 mmol/l  
pCO<sub>2</sub> = 56 mmHg

In simple metabolic alkalosis, one would expect to find increased pH, increased plasma HCO<sub>3</sub><sup>-</sup>, and increased PCO<sub>2</sub>

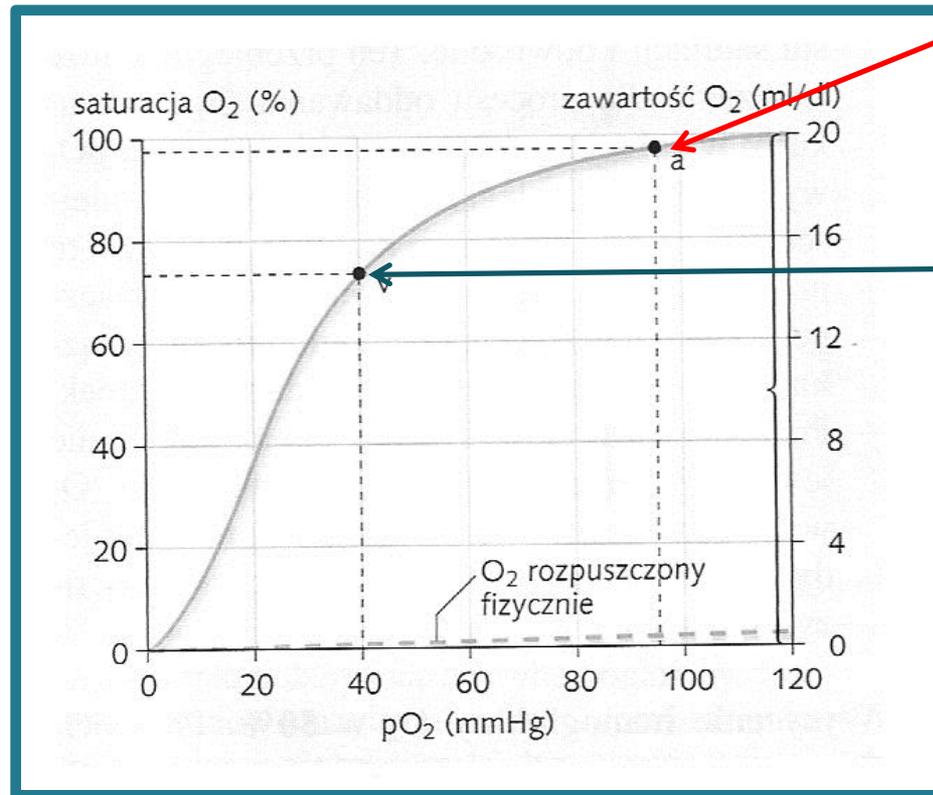
# Treatment

You have time to correct the metabolic alkalosis

1. Diagnosis and cause treatment
2. ↓ CL<sup>-</sup> i.v. NaCl, KCl, HCL - only severe alkalosis

# New concept of treatment critically ill patients

# Influence of pH and PCO<sub>2</sub> on oxygen-hemoglobin dissociation curve



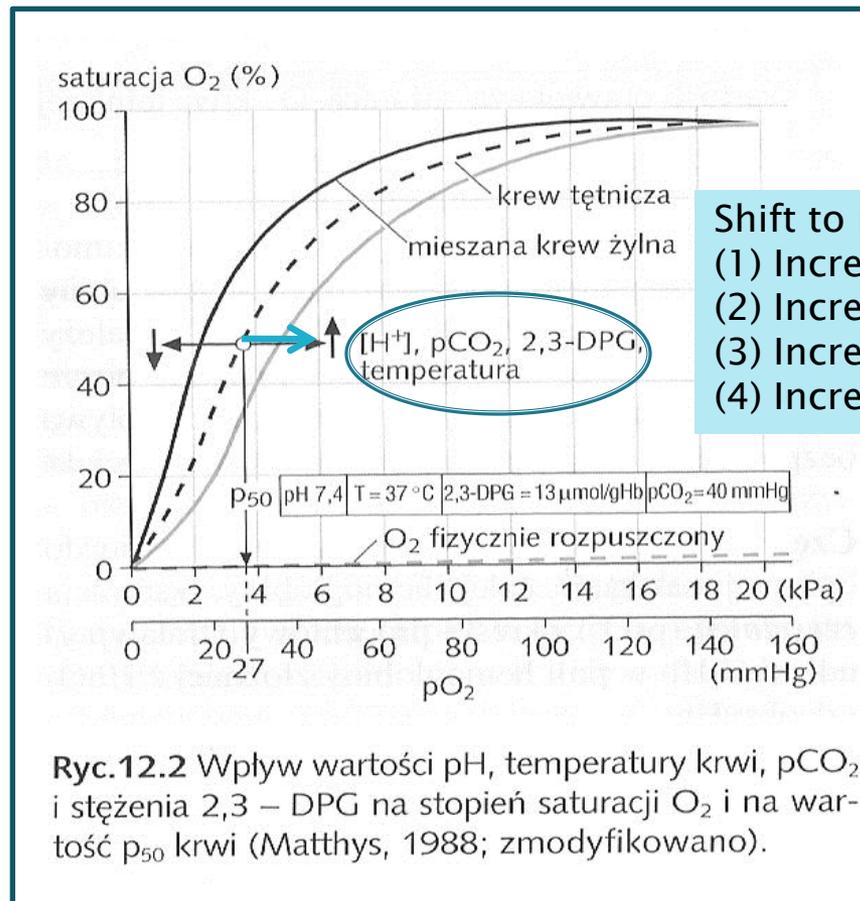
arterial point  
*oxygen saturation  
of systemic arterial  
blood averages 97 per  
cent*

venous point  
*the saturation of  
hemoglobin  
averages 75 per cent*

Normal condition

# Influence of pH and PCO<sub>2</sub> on oxygen-hemoglobin dissociation curve

Saturation is percentage of hemoglobin bound with oxygen  
1g Hb = 1,34 ml O<sub>2</sub>



Shift to right:  
(1) Increased hydrogen ions  
(2) Increased CO<sub>2</sub>  
(3) Increased temperature  
(4) Increased BPG

- ▶ Shift to the right  
the amount of O<sub>2</sub> connected with hemoglobin at accurate PO<sub>2</sub> is decreased
- ▶ Shift to the left  
at accurate PO<sub>2</sub> the bigger amount of O<sub>2</sub> is connected with hemoglobin and O<sub>2</sub> is also released more difficult

# Consequences of right shift the curve – Bohr effect

## ▶ Tissues

forcing oxygen away from the hemoglobin and delivering increased amounts of oxygen to the tissues

As the blood passes through the tissues, carbon dioxide diffuses from the tissue cells into the blood. This increases the blood  $P_{O_2}$ , which in turn raises the blood  $H_2CO$  (carbonic acid) and the hydrogen ion concentration

## ▶ Lungs

quantity of oxygen that binds with the hemoglobin at any given alveolar  $P_{O_2}$  becomes considerably increased, thus allowing greater oxygen transport to the tissues

Carbon dioxide diffuses from the blood into the alveoli and reduces the blood  $P_{CO_2}$  and decreases the hydrogen ion concentration, shifting the oxygen–hemoglobin dissociation curve to the left

# www.AcidBase.org

**What do you want to do?**

**Enter new data:**

**Please, please be careful choosing the units, especially for PCO<sub>2</sub> and albumin!**  
**(choosing the wrong units leads to grossly false results)**

**(test data will be deleted from time to time)**

**or**

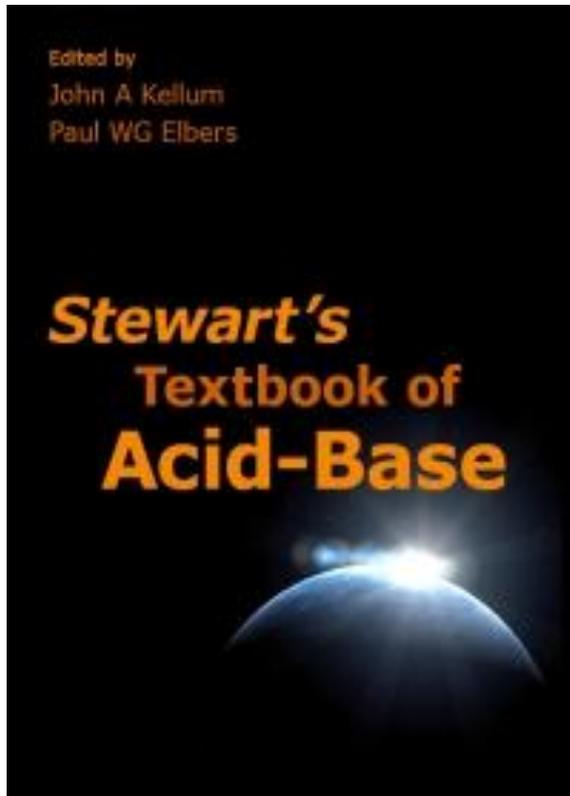
**register and calculate osmolality-related data only**

**(minimal data required: Na, glucose; better with urea, K and osmolality measured with the freeze-point method, best with a full acid-base and electrolyte dataset)**

**this part of the scripts is under development right now - be patient with imperfections ....**

**or**

**take a look at existing data:**



The Stewart model predicts that changes in the proportion of anions and cations will result in changes in pH. So we will have to change our definitions of acids and bases.

Stewart hypothesized that water dissociates into  $H^+$  and  $OH^-$  to a greater or a lesser extent when  $[SID]$ ,  $[ATOT]$  or  $PCO_2$  change.

But the Stewart hypothesis has no empiric support.

Although experience is the only judge of scientific theories, scientific knowledge does not exclusively arise from experience.

Throughout this book, we refer to the Stewart hypothesis as a ready explanation for the observed association between the variables  $[SID]$ ,  $[ATOT]$  and  $PCO_2$  and the variable pH. We recognize that this theoretic construct is only one of a number of possible explanations.

# Summary

- ▶ Increased  $\text{PCO}_2$
- ▶ Decreased pH (acidosis)
- ▶ Fever
- ▶ Anemia (increased 2,3-DPG)

Easier  $\text{O}_2$  releasing in the tissues  
and better connection in the lungs

- ▶ Decreased  $\text{PCO}_2$
- ▶ Alkalosis
- ▶ Hypothermia
- ▶ Decreased 2,3-DPG

More difficult  $\text{O}_2$  releasing in the  
tissues

**Thank You for Your  
Attention**