11.3   Disorders of acid-base homeostasis

11.3.1   Regulation mechanisms of acid-base homeostasis

One of the conditions to maintain the stability of inner environment is the isohydria, i.e. the stability of hydrogen ion concentration in the organism. Since the concentration of hydrogen ions in body fluids represents a very small number (e.g. in the blood 0.00004 meq/l), it is commonly expressed as pH. The pH is defined as the negative decadic logarithm of the molar H^+ concentration: $pH = -\log H^+$. The pH in biological systems has a specific significance. The electrochemical potential of ions is proportional not to their concentration but to its logarithm. For this reason the responses of the sensors or receptors in the body are more likely to be proportional to pH than to concentration.

The concentration of H^+ is the main determinant of many physiological and biochemical processes. Already in physiological pH range, the activity of enzymes varies due to the changes in protein charge and conformation. The influence of pH values on proteins leads further to consequent changes in membrane transport systems activity for metabolites and ions. The dissociation of many physiologically and pharmacologically important weak acids and bases depends on the value of pH. Changes of their dissociation can lead to alterations in their distribution in compartments separated by lipid membrane. That is why the pathological changes in pH disturb many important functions of organism.

Hydrogen ions are components of chemical - anatomical structures, and their activity in individual compartments varies. The physiological pH value of arterial blood is 7.40, the pH of venous blood and interstitial fluid is 7.35 due to increased amount of carbon dioxide. Intracellular pH depends on the type of cells and their metabolism, it usually reaches the value of 6.9. Subcellular organelles also maintain the value of pH on the level necessary for their optimal function. The inner space of lysosomes and Golgi apparatus is very acidic ($pH < 5.0$). On the contrary, mitochondrial compartment is slightly more basic than the cytosole (pH 6.7–7.2). It is difficult to measure the intracellular pH. As a consequence, only measurements of pH of ECF(blood or plasma) are used in clinical praxis.

11.3.1.1   Sources of hydrogen ions

There are two main sources of hydrogen ions in human body:

1. the metabolism of proteins and phospholipids and the incomplete metabolism of fatty acids and carbohydrates. Formed acids (so called nonvolatile acids) are no further dissociated, and they must be eliminated by kidneys,

2. the complete metabolism of fatty acids and carbohydrates, whereby CO_2 is formed. Even though CO_2 is not an acid, in the solution it is hydrated to carbonic acid which is the source of H^+ : $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$. Carbonic acid is called volatile acid because this reaction is reversible, and the acid can be eliminated by expiration in form of CO_2.

11.3.1.2   Transport and neutralisation of hydrogen ion

Approximately 40 mmol of nonvolatile acids and 20 000 mmol of CO_2 are daily formed in the cells and delivered into the circulation. To maintain a normal value of H^+ concentration (40 nmol/l), the hydrogen ions in body fluids have to be promptly and sufficiently neutralised. There are efficient extracellular (plasma) and intracellular (erythrocytes) buffers acting in the blood. The main intracellular buffer is haemoglobin. The main buffer of plasma is bicarbonate-carbonic acid buffer system followed by other, less important systems (phosphates, plasma proteins). Protein system plays an important role in keeping the pH of tissue cells. Phosphate system is involved in maintaining the pH of tissue cells, erythrocytes, and tubular urine. Bicarbonate-carbonic acid buffer system, consisting of weak carbonic acid and its strong natrium salt, plays an important role in keeping the pH of extracellular fluid.

Henderson–Hasselbalch's equation derives the blood pH from the equation:
$$pH = pK + \log[HCO_3^-]/[H_2CO_3]$$

Since H_2CO_3 is in equilibrium with dissolved CO_2, and CO_2 is in equilibrium with pCO_2, we can use the term pCO_2 instead of H_2CO_3. From the equation follows that the pH of extracellular fluid depends on the reciprocal relation between $[HCO_3^-]$ and pCO_2 and not on their absolute amounts. Bicarbonate-carbonic acid buffer system is very efficient one because of its greatest amount in extracellular fluid, and mainly because it is an "open system" i.e. – both its components are regulated by lungs and kidneys according to the demands of organism.

Except the introduced physical-chemical buffers also others, so called biological buffers, operate in the organism, e.g. metabolic reactions consuming or producing hydrogen ion, if they, as an response to pH shift, change their speed in order to maintain homeostasis. Another mechanism is the transport of protons by proton pumps through the lipid membranes. They maintain the pH of intracellular compartments (cytosole, mitochondria, lysosomes, Golgi apparatus) on a level unresponding to passive distribution according to the electrochemical gradient. The most important proton pumps act in the mitochondrial and lysosomal membrane.

11.3.1.3 Excretion of hydrogen ion

Two basic mechanisms are responsible for definite excretion of hydrogen ions :

1. Removal of CO_2 by lungs. The quantity of ventilation is regulated by respiratory centre in medulla oblongata, responding to changes in pCO_2 and pH. Under physiological condition, the pCO_2 is kept on the value $5.3\,kPa$.

2. Excretion of hydrogen ion by tubular cells of kidneys. The H^+ is formed in the tubular cells of proximal and distal tubule by the dissociation of carbonic acid. Carbonic acid is formed in the reaction of CO_2 and H_2O catalyzed by carbon anhydrase. The amount and activity of carbon anhydrase is one of the factors determining the speed of H^+ production in the tubular cells. It is necessary to realise that also HCO_3^- is formed by the dissociation of carbonic acid. Simultaneously with hydrogen ion elimination to the tubular fluid, HCO_3^- returns to the blood (therefore expression "kidney eliminates H^+" means the same as "kidney saves bicarbonate"). The eliminated hydrogen ion is exchanged for natrium

ion accompanying bicarbonate, phosphate, sulphate anions, and the anions of other nonvolatile acids in the urine.

Immensely important for the excretion of H^+ is ammoniagenesis. It takes place primarily in the proximal tubular cells. Since the excretion of hydrogen ions is limited by tubular fluid acidity (limit of pH 4.5), natrium ion, in excess of strong acid's salts in the urine, is exchanged for H^+ after its connection with NH_3 to NH_4^+. This reaction helps to avoid the rise of strong acids in urine, and excretion of hydrogen ions is not restricted.

11.3.2 Classification of acid-base disturbances

The acid-base disturbances arise as a result of disbalance in production, buffering and final excretion of hydrogen ions.

Increased activity of H^+ (pH < 7.36) is called acidosis.

Decreased activity of H^+ (pH > 7.44) is called alkalosis.

The values of pH that are suitable for living organisms are 7.0 to 7.8. Very important is the speed of development of the disorder. Acute disorders are worsely tolerated.

Using the equation $pH = pK + \log[HCO_3^-]/[CO_2]$, it is obvious that the shift in pH is due not to the absolute amount, but due to the disturbance in reciprocal ratio of these two components in the extracellular fluid. HCO_3^- is the metabolic part of the buffer, and pCO_2 the respiratory part. Therefore the states with primary change in $[HCO_3^-]$ are called metabolic disturbances, and the states with primary change in pCO_2 are respiratory disturbances. From this point of view, we can define four basic acid-base disturbances:

- **metabolic acidosis** (shift in pH to the acidic side due to primary decrease in $[HCO_3^-]$ without a change in pCO_2)

- **respiratory acidosis** (shift in pH to the acidic side due to primary increase in pCO_2 without a change in $[HCO_3^-]$)

- **metabolic alkalosis** (shift in pH to the alkalic side due to primary increase in $[HCO_3^-]$ without a change in pCO_2)

- **respiratory alkalosis** (shift in pH to the alkalic side due to primary decrease in pCO_2 without a change in $[HCO_3^-]$).

11.3.3 Compensation of acid-base disturbances

The organism reacts by compensatory processes to changes in metabolic or respiratory component of the buffer system. The purpose of compensatory process is the appropriate shift of the other, originally unchanged component so that pH returns closer to normal value. This process leads to compensation of the disorder. But even maximal compensatory effort can not return pH on the physiological value (except chronic respiratory alkalosis that can be compensated by kidneys to physiological pH).

11.3.3.1 Participation of respiratory system in compensatory processes

Pathological changes in pH, caused by primary change in HCO_3^- concentration in extracellular fluid (metabolic acidosis and alkalosis), are compensated by the change in depth and frequency of respiration. In this way, the primary change in bicarbonate concentration induces a respiratory response which changes plasma CO_2 in the same direction. Metabolic acidosis is compensated by hyperventilation, metabolic alkalosis, on the contrary, by hypoventilation. However, respiratory compensation for metabolic alkalosis is relatively weak because its limitation by hypoxemic hypoxia. Respiratory centre, regulating the process, is sensitive to changes in pCO_2 and pH. In the compensatory process, the respiratory centre reacts only to the pH shift caused by the change in HCO_3^- concentration, because in primary metabolic disturbances the value of pCO_2 does not change. Bicarbonate anion is slowly diffusible – the equilibration of its changed level between blood and liquor is slow. Therefore, the compensatory process starts 1 hour after the rise of the disorder and is developed to it's maximum in 12 to 24 hours. On the contrary, sudden and total therapeutical correction of bicarbonate plasma level in compensated patient causes dangerous shift of pH to the other side, because of compensatory process sustaining for longer period of time.

11.3.3.2 Participation of kidneys in compensatory processes

The degree of compensation in respiratory disturbances depends on the speed of the respiratory disorder development.

In **acute respiratory disorders** (lasting about 6 hours) only immediately reacting chemical buffers of extracellular fluid help to correct pH. These non-bicarbonate buffers (plasma proteins, haemoglobin, phosphates, sulphates) bind or release H^+, that is demonstrated by an unimportant change in HCO_3^- concentration. Relatively weak total activity of these buffers is the cause of uncomplete compensation of acute respiratory disorders.

In **chronic respiratory disorders**, kidneys take part in the compensation. The compensatory activity of kidneys is held by increased or decreased secretion of H^+ and, simultaneously, by increased and decreased reabsorption of bicarbonate. In this way, the level of bicarbonate adjusts to the changed value of pCO_2, and pH returns toward the normal standard. Regulation processes need enzyme reconstruction of tubular cells (carbon anhydrase). The maximal compensatory effort of kidneys is then achieved after 5 days, and it remains for the same time after the removal of a disorder. Compensation of chronic respiratory disorders by healthy kidneys is very effective.

To understand the typical shifts of several other ions that will be mentioned in individual acid-base disturbances, it is necessary to remember:

1. Hydrogen ions in surplus remove **potassium ions** from the cells to the extracellular fluid. This shift (sc. distributive hyperkalemia) often accompanies metabolic acidosis. On the other hand, in alkalosis potassium enters the cells, but this effect is short lasting. If the alkalosis lasts longer, increased loss of potassium by kidneys occurs, which leads to mild deficiency of potassium in the organism. Typical relationships are acidosis – hyperkalemy, alkalosis – hypokalemy. These relationships are not always present, it depends on underlying cause of the disorder and other circumstances of it's development.

2. To maintain the electroneutrality, the number of cations has to be equal to the number of anions. The major plasma cation is Na^+, while other cations (K^+, Mg^{2+}, Ca^{2+}) form the nonessential part of the cationic pool. The major plasma

anions are HCO_3^- and Cl^-, and there are also anions of nonvolatile acids in the pool. We can express basic relationship: $Na^+ = HCO_3^- + Cl^-$ (+ anions of nonvolatile acids). Therefore, in primary change of **chloride** concentration, appropriate amount of HCO_3^- originates or disappears. This reaction is accompanied with pH change. On the other hand, primary change in bicarbonate will be accompanied with the retention or excretion of chloride (hyper- and hypochloremy in some metabolic acid-base disturbances).

3. Plasma **sodium** plays an important role in keeping pH as well as in maintaining the volume of body fluids. Maintaining the stable volume of body fluids is vitally important, and it has preference in the kidneys before regulation of pH. This fact is the direct cause of some pH disturbances owing to decrease of body fluid volume (see metabolic alkalosis).

4. The activity of H^+ is one of the factors influencing the ionisation of plasma **calcium**. Decrease in H^+ activity lowers the ionisation of plasma calcium (tetany in severe alkalosis); increase in H^+ activity increases the ionisation of calcium (in acidosis with hypocalcemia, symptoms of tetany are "masked", until the moment when acidosis is therapeutically repaired).

11.3.4 Metabolic acidosis

Metabolic acidosis is characterized by decrease of pH below 7.35 due to primary decrease in plasma bicarbonate below 22 mmol/l.

The main reasons of metabolic acidosis:

Intake of substances producing H^+

- Intoxication by salicylates: salicylates create a metabolic block, which leads to production of a mixture of endogenous organic acids. At the same time, salicylates have the additional effect of direct respiratory centre stimulation, which leads to independent respiratory alkalosis.

- Intoxication by inorganic acids: resulting acidosis is characterised by close relation between the decrease in pH and degree of hyperkalemia (decrease of pH by 0.1 causes the increase of potassium in extracellular fluid by cca 0.8 mmol/l).

This close relation is not present in acidosis caused by accumulation of organic acids.

- Administration of ammonium chloride and lysine or arginine hydrochloride. The cations of these drugs enter the metabolism, while chloride anions cause the extinction of adequate amount of bicarbonate anions in order to maintain electroneutrality.

Increased production of nonvolatile acids

Ketoacidosis:

- Diabetic ketoacidosis: In diabetes mellitus, due to altered carbohydrate and lipid metabolism, ketoacids are produced more rapidly than they can be metabolised. Formed nonvolatile ketoacids are the source of H^+ which binds with HCO_3^-. Simultaneously, hydrogen shifts potassium out from the cells into the blood and distributive hyperkalemia occurs. In patients with uncontrolled diabetes, blood glucose can overshoot the renal threshold and osmotic diuresis arises. During osmotic diuresis, normal reabsorption of potassium is impossible because of rapid flow of tubular fluid. Primary distributive hyperkalemia can be gradually decreased what represents, however, total potassium depletion. Drugs, used in treatment of diabetic ketoacidosis (insulin, glucose) cause shift of potassium from extra- to intracellular space and therefore sudden, life-threatening hypokalemia can arise.

- Starvation (i.e. long-lasting fever with anorexia) may cause mild ketoacidosis. Reduced carbohydrate intake leads to low insulin and high glucagon levels. These hormonal changes favour glycolysis and ketogenesis.

- Alcoholic ketoacidosis: The main causes of ketoacidosis are prolonged restriction of food intake, vomiting and alcohol intake.

Lactic acidosis: It arises most often in severe circulatory or respiratory failure as a result of hypoxia due to hypoperfusion of peripheral tissues. During the insufficiency of peripheral circulation, certain degree of acidosis is advantageous since haemoglobin, at lower pH, easier releases oxygen to hypoperfused

tissues. Another cause of lactic acidosis may be severe anaemia because of diminished blood oxygen-carrying capacity, and intoxication by drugs (ethylene glycol, paraldehyde) which are metabolised into lactate. Overproduction of lactate by neoplastic tissue is probably the cause of lactic acidosis associated with tumours.

Reduced excretion of H^+

- Renal failure: It seems that the main defect is the failure of amoniagenesis, decreased renal proton secretion and decreased number of functional nephrons. For this reason the excretion of phosphates, important acceptors of hydrogen in tubular urine, fails. In these, usually chronic conditions, the plasma bicarbonate rarely falls below 10 mmol/l because the formed acids are partially buffered by phosphate and carbonate from bones.

Increased losses of HCO_3^-

- Severe diarrhea or intestinal malabsorption cause loss of bicarbonate, potassium, sodium and water by the stool. Hyperchloremic, hypokalemic acidosis and volume depletion result. Dehydration is very dangerous especially in newborn and infants.

- Chronic vomiting, in which there is a loss of gastric contents accompanied by a loss of alkalic duodenal contents. If the loss of HCO_3^- is higher than the loss of acids (e.g. during hypo- or anacidity of gastric juice), and there is almost no food intake, acidosis, usually accompanied by dehydration, arises.

- Renal tubular acidosis is the term used to describe metabolic acidosis which is caused by a disorder of the renal tubules. It is due to decreased ability of tubular cells to secrete H^+ and therefore to reabsorb an appropriate amount of the filtered bicarbonate. Sodium is in increased amounts exchanged for potassium, and potassium depletion results. Typical clinical finding is hyperchloremic metabolic acidosis and increased urinary HCO_3^- excretion.

- Carbon anhydrase inhibitors, such as acetazolamide, have similar effect. They cause mild to moderate acidosis by increasing bicarbonate loss in the urine.

Clinical pattern in metabolic acidosis is due to underlying disorder. Acidosis per se has a negative inotropic effect on the heart that is, hovewer, hidden by increased production and excretion of katecholamines. It also causes the constriction of veins that results in increased venous return with the risk of pulmonary edema. When pH is lowered to 7.0, depression of CNS ranging from fatigue to confusion and coma is present. The compensation of acidosis is hyperventilation. In acute metabolic acidosis, hyperventilation may be very intensive (Kussmaul's respiration).

11.3.5   Metabolic alkalosis

Metabolic alkalosis is characterized by increased pH above the value 7.45 due to primary increase in plasma bicarbonate above 26 mmol/l.

The basic reasons of metabolic alkalosis:

Increased supply or production of bicarbonate

- Metabolic alkalosis can originate in long-term parenteral application of substances containing organic anions (natrium lactate, natrium citrate). The organic anions are metabolised, and remaining cations are the reason of corresponding increase of bicarbonate to maintain the electroneutrality. Transfusion of larger amount of conserved blood, that contains natrium citrate, ammonium and potassium, can lead to metabolic alkalosis. Therapeutical correction of metabolic acidosis or an overdose of bicarbonate and other alkalising substances can lead to the development of metabolic alkalosis.

Chloride depletion

- Loss of hydrochloric acid in gastric contents by vomiting (e.g. patients with increased gastric acid secretion or pyloric stenosis),or by gastric aspirate, leads to increased concentration of bicarbonate to maintain the electroneutrality.

- Low intake of chlorides in patients with restriction of NaCl in the diet. The kidneys, in order to maintain the volume of ECF reabsorb sodium in increased amounts. If only small amount of

sodium in form of NaCl is available, its reabsorption is increased by exchanging for H^+, what however leads to increased reabsorption of bicarbonate and to the shift of pH to alkalic values.

- An overdose of diuretics that primarily suppresses the reabsorption of chlorides ("loop" diuretics). Kidneys, that cannot reabsorb sodium in form of NaCl in sufficient amounts, compensate its reabsorption by exchange for H^+ that leads to increase in blood bicarbonate.

- Metabolic alkalosis is most often formed as a result of extracellular volume depletion. During volume depletion, renal conservation of sodium takes priority over the other homeostatic mechanisms. Kidneys maximally increase the reabsorption of sodium in the form of NaCl, by exchange for H^+ and by exchange for K^+ influenced by aldosterone.

Reduced elimination of HCO_3^-

- Primary hyperaldosteronism. Aldosterone stimulates the reversed reabsorption of Na^+ in the tubular cells by stimulating the secretion of K^+, H^+, Mg^{2+}, and ammonium ions. Pathological graduation of this mechanism leads to minimal or moderate hypokalemic alkalosis. Patients are not volume- or chloride-deficient.

- Primary potassium depletion causes increased loss of H^+ by kidneys. It seems that there is a relation between the elimination of K^+ and H^+ that compete for common transport mechanism. It means that the deficit of one cation leads to increased elimination of another one. Hypokalemia is the reason for increased secretion of H^+. However, only chronic and severe hypokalemia may generate metabolic alkalosis.

Clinical pattern. Metabolic alkalosis directly enhances neuromuscular irritability. This effect, rather than the decrease in ionized plasma calcium induced by alkalosis, is the major cause of tetany. Alkalosis may cause slight increase of myocardial contractility as well as increased sensibility of myocardium to heart glycosides. Severe alkalemia has been associated with cardiac arrhytmias. The relationship between alkalosis and potassium depletion is complex, and it is still not sufficiently explained. Symptoms of metabolic alkalosis are generally inexpressive, and in most cases the symptoms of underlying disorder are dominating.

11.3.6 Respiratory acidosis

Respiratory acidosis is characterized by decrease in pH below 7.36 due to primary increase in pCO_2 (hypercapnia) over 5.8 kPa.

There is no disorder known characterized by overproduction of CO_2. Thus, all causes of respiratory acidosis have in common a defect in the excretion of CO_2.

Central depression of respiration. The causes of decreased activity of respiratory centre may be:

- drugs (hypnotics, sedatives, morphium) supressing the activity of respiratory centre

- local damage of the respiratory centre by inflammation, tumour, trauma, as well as by ischemia during embolisation or during thrombosis of a. vertebralis

Impaired respiratory mechanics: deformities of thorax, high position of diaphragm, morbus Bechterev, pain after chest traumas etc.

Pulmonary disorders. The most common cause of chronic respiratory acidosis is chronic obstructive lung disease (chronic bronchitis and emphysema), in which ventilation and perfusion are mismatched and effective alveolar ventilation is decreased. Other diseases (pneumonia, pulmonary edema, bronchial asthma, pneumothorax, haemothorax, atelectasis, chronic pulmonary fibrosis) usually cause respiratory alkalosis. In these conditions, hypoxia stimulates ventilation and since CO_2 is much more diffusible than oxygen, excretion of CO_2 is enhanced (hypocapnia). Respiratory acidosis occurs only with respiratory fatigue in advanced stages of the above mentioned disease.

Neuromuscular disorders: muscular dystrophy, myasthenia, poliomyelitis, botulism etc.

Clinical manifestations of respiratory acidosis depend on the speed of it's development. In acute disorders dominate confusion up to loss of consciousness. If the respiratory acidosis develops more slowly, it is characterized by symptoms that are typical for cerebral vasodilation caused by hypercapnia: somnolence, headache, papilledema, dilatation of conjunctival and superficial facial blood vessels. Influence of

acidemia on cardiovascular system was described in the part considering metabolic acidosis.

Acute respiratory acidosis is nearly always accompanied by hypoxemia, i.e. cardiopulmonary arrest is a combination of respiratory acidosis and metabolic lactic acidosis.

11.3.7 Respiratory alkalosis

Respiratory alkalosis is characterised by increase in pH over 7.44 due to primary decrease of pCO_2 (hypocapnia) under 4.8 kPa.

The basic reasons of respiratory alkalosis:

Disorders of CNS

- Cerebrovascular incidents with hypoxia in the surroudings of the respiratory centre. Local decrease of pH in the area of respiratory centre causes hyperventilation and consequent decrease of pCO_2 in the blood

- Trauma, tumour and inflammation of CNS when causing an irritation of respiratory centre

- Drugs (salicylates, progesterone) cause hyperventilation by direct stimulation of medullary respiratory centre

- Extreme anxiety and hysterical fit. Strong hyperventilation is conditioned by the sensation of air shortage, and it may be as intensive as to cause the tetanic spasm.

Diseases of lungs with the failure of alveolo-capillar oxygen transfer or with reduced respiratory surface area. Decrease of pO_2 causes irritation of the chemoreceptors, leading to hyperventilation. Respiratory alkalosis occurs during initial stages of the diseases, e.g. during mild pulmonary embolism, pneumonia, mild pulmonary edema or asthma. If the disorder causes failure of CO_2 exhalation, respiratory acidosis with hypoxia arises.

Irritation of the respiratory centre from the peripheral receptors during localized pulmonary and pleural diseases.

Mountain sickness. Lower pO_2 in the inhaled air stimulates the medullar respiratory centre. During hyperventilation, highly diffusible carbon dioxide escapes in greater amounts and hypocapnia occurs.

Clinical manifestations of respiratory alkalosis depend on its severity and acuteness. Hyperventilation may or may not be clinically apparent. Acute hypocapnia causes constriction of small vessels in the brain. This condition is clinically manifested by headache, dizziness and light-headedness. Severe respiratory alkalosis may cause confusion or loss of consciousness. Alkalosis, in combination with hypocapnia, enhances neuromuscular excitability that is typically manifested by paresthesias around mouth and on the fingers. In some cases, severe symptoms of CNS irritation may occur. Irritation is manifested e.g. as extreme nervousness or convulsions (in epileptics purposely performed hyperventilation may induce seizures that are clinically used to determine the degree of seizure emergency).

11.3.8 Therapeutical principles of acid-base disturbances

Disorders of acid-base balance may accompany various diseases and they are not detectable by clinical observation alone. It is necessary, especially in acutely ill patients, to determine the value of pH, pCO_2, and bicarbonate in capillary blood. Analysators of blood gases measure pH and pCO_2 directly by specific electrodes. The equipment automatically calculates the concentration of bicarbonate using Henderson-Hasselbalch equation. The value is usually expressed as "standard bicarbonate" that represents the theoretical concentration of bicarbonate in the blood saturated with oxygen, at pCO_2 5.3 kPa and temperature of 37°C. After applying the obtained value to nomogram, we can determine the concentration of "actual bicarbonate", the concentration at actual pH, pO_2, pCO_2, and temperature of patient's blood. This determination, in clinical practice, is sufficient for accurate and relatively rapid classification of pure or combined acid-base disturbances.

The appropriate therapy is choosed considering the type and the stage of the disorder. As discussed above, acid-base disturbance is in almost all cases secondary one. Therefore, the optimal therapy is the elimination of the underlying disorder. If it is not possible and patient's health requires a rapid correction of pH, the application of substances normalising the surplus of acids or bases is justified.

Immediate and rapid arrangement of acidosis is indicated only in acute intoxication. Alkalisation of extracellular fluid, and hence of urine, simultaneously helps to eliminate the acids more quickly.

Intravenous application of sodium bicarbonate is recommended if pH falls below 7.2, or plasma bicarbonate falls below 10 mmol/l. Intravenous application of bicarbonate requires considerable attention because it changes the pH very strongly and suddenly. We apply only one third or one half of calculated amount over the period of 24 hours, and we lean on the activity of compensatory mechanisms of the body.

For slowlier neutralisation of acid surplus in acidosis, a larger amount of sodium bicarbonate per os can be applied. After absorption from GIT to the blood, pH is shifted to the alkalic side.

For slow alkalisation of body fluids, substances metabolised in the body (sodium lactate or sodium gluconate) can be used. Lactate or gluconate part of the molecule is metabolised, and sodium remains in the extracellular fluid as sodium bicarbonate.

To correct the alkalosis, ammonium chloride per os can be used. After the resorption into the blood, the NH_4 is metabolised to urea in the liver. This reaction releases HCl that immediately reacts with the buffers of extracellular fluid and shifts pH to the acidic side. Intravenous application of ammonium chloride is dangerous because of its toxicity. Another substance commonly used, is monohydrochlorid lysine. During acidifying therapy, enhancement of diuresis for the elimination of bicarbonate is required.

In therapeutical approach of acid-base disturbance, it is necessary to regulate other components of body fluids simultaneously (potassium, calcium, sodium, chlorides). It is important to think of the outlast of compensatory processes and to eliminate the underlying disorder to maximal possible extent.