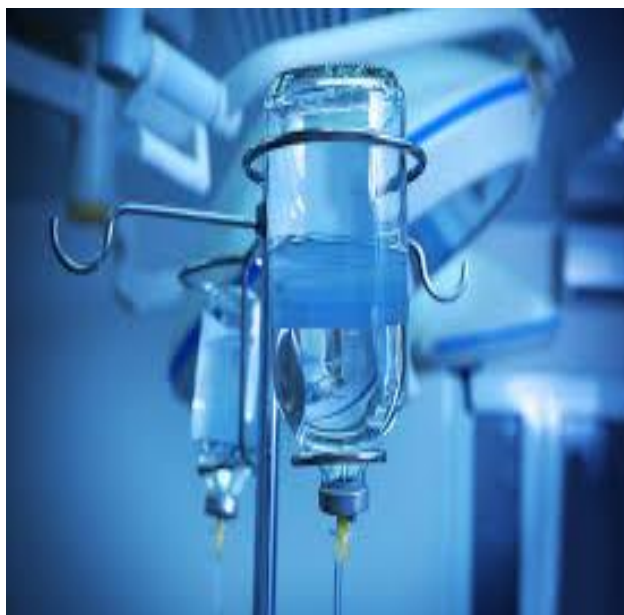**Tkachenko Y. A., Redko S. I., Kasyan S. M.**

INTRODUCTION TO INFUSION THERAPY

Study guide

Ministry of Education and Science of Ukraine
Ministry of Health of Ukraine
Sumy State University

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Recommended by the Academic Council of Sumy State University

Sumy
Sumy State University
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The study guide dedicated to infusion therapy, which has become an integral part of intensive care for critically ill patients. A detailed approach to the diagnosis and treatment of the main types of disorders of electrolyte metabolism and acid-base balance. The provisions of international minutes on issues related to parenteral nutrition are used..
The study guide corresponds to the Curriculum approved by the Ministry of Health of Ukraine, the Ministry of Education and Science of Ukraine and intended for students of higher medical (pharmaceutical) educational institutions of Ukraine of III–IV levels of accreditation.

Contents

INTRODUCTION

The manual is devoted to the issues of infusion therapy, which is firmly entrenched in the medical practice of doctors of various clinical specialties in all countries of the world.

Infusion therapy is an integral part of the fight against massive blood loss or hypovolemia for emergency specialists. Internal medicine physicians also use this powerful treatment method to eliminate intoxication, improve microcirculation and rheological properties of blood, and so on.

The purpose of this guide is to help physicians identify pathological disorders that require infusion therapy, to make optimal choices for infusion according to specific circumstances, to provide appropriate and safe infusion techniques, and to objectively evaluate the effectiveness of therapy. The manual consistently considers the main pathophysiological mechanisms of regulation of water-salt metabolism and acid-base balance. The main principles of providing parenteral nutrition and correction of deficiency of cells and individual blood components are given.

Also extremely important today is the training of market-competitive professionals who provide modern innovative clinical thinking, the appropriate authority needed to provide medical care effectively, including a competent approach to the preparation of infusion and transfusion therapy programs. Therefore, the appearance of a textbook on this issue is timely, the information contained in it – actual.

The manual is intended for students of higher medical educational institutions of Ukraine of III–IV levels of accreditation, and can be useful for anesthesiologists, doctors of intensive care units, students, paramedics, emergency services, as well as specialists of related specialties involved in the treatment of patients requiring infusion therapy.

PHYSIOLOGY AND PATHOPHYSIOLOGY
OF WATER METABOLISM
Role of water in the human body

Living organisms, to maintain existence and stability, need continuous support for the constancy of their internal environment – homeostasis. Homeostasis (homeo – the same, similar; stasis – stability, balance) is the process of regulating or maintaining the system in a stable state relative to the changing external environment.

The most important component of maintaining homeostasis is maintaining the constancy of the water – electrolyte composition of the body. Water is one of the main components of the body, is a universal solvent for organic and inorganic substances. Water with substances dissolved in it is a functional unity in both biological and physico-chemical relations. Most chemical reactions in our cells require water. Water is needed to transport nutrients and oxygen to all cells of the body. It helps to convert food into energy and absorb nutrients. Water maintains stability of body temperature and protects vital organs, participates in maintaining the shape of cells and organs. Water helps the body get rid of waste and promotes respiration.

Water performs the following physiological functions in the body:

• is a transport medium during the exchange of substances between cells, between the external environment and the internal environment, between the internal environment and cells;

• is the structural basis of the optimal physiologically active volume of the cell and the internal environment of the body;

• determines the structural ordering of biomolecules;

• acts as a substrate in a number of enzymatic reactions and provides substrate specificity of the action of enzymes;

• forms a directed flow of substances inside the cell;

• plays the role of a hemodynamic factor in the work of the cardiovascular system;

• the main regulator of energy and osmotic balance in the body;

• participates in the processes of thermoregulation.

The interactions of various aqueous solutions-solutions in which water is the solvent-are continuously monitored and adjusted by a large suite of interconnected feedback systems in our body. Understanding the ways in which the body maintains these critical balances is key to understanding good health.

General principles:

− diffusion: movement of the particles in a solution from the area of high concentration to the area of lower concentration;

− electrolyte: inorganic substance that dissociates into ions;

− osmosis: diffusion of solvent molecules (water) into region in which there is a higher concentration of a solute (electrolyte) to which the membrane is impermele;

− osmotic pressure: the pressure necessary to prevent solvent migration;

− osmol: concentration of osmotic active particles;

− osmolarity: number of osmoles per liter of solution;

− osmolality: number of osmoles per kilogram of solvent;

− measurement: depression of freezing point;

− calculation (plasma): 2Na + glucose + BUN (mmol/l);

− tonicity: effective osmolality of a solution relative to plasma;

− colloids: high molecular weight particles (> 20 000 D);

− oncotic pressure (colloidal osmotic pressure): the pressure required to prevent the diffusion of solvent molecules

(water) to the area with a higher concentration of colloid, for which the membrane is impermeable.

Body fluid compartments

The average adult male is approximately 60 % water by weight; females are 50 %. In newborns, it is 75–80 % of body weight. As the body ages, the total amount of water decreases to 50 % of body weight in men and 42–44 % in women. In this case, the amount of intracellular water decreases, and extracellular water increases.

This water is distributed between two major fluid compartments separated by cell membranes: intracellular fluid (ICF) and extracellular fluid (ECF). In turn, extracellular water subdivided of interstitial (IF) 15 %, intravascular (plasma) 5 % and transcellular (0.5–1 %). The interstitial fluid includes all fluid that is both outside cells and outside the vascular endothelium. Transcellular fluid includes chamber moisture in the eyes, cerebrospinal fluid, articular and synovial fluid, the contents of the renal tubules, and digestive juices. In clinical calculations, transcellular water is not separately positioned. Distribution of water by fluid compartments given in Table 1.

Table 1 – **Distribution of water by fluid compartments**

Compartment	Fluid as Percent Body Weight (%)	Total Body Water (%)	Fluid Volume (l)
Intracellular	40	67	28
Extracellular			
Interstitial	15	25	10.5
Intravascular	5	8	3.5
Total	60	100	42

Intracellular Fluid (ICF) = Fluids within cells ~ 2/3 of total body water

Extracellular Fluid (ECF) = Fluid outside of cells ~ 1/3 of total body water

The volume of water compartments are calculated by with the following formulas:

– intracellular space (l) = body weight (kg) × 0.4;
– extracellular space (l) = body weight (kg) × 0.2;
– plasma volume (l) = body weight (kg) × 0.043;
– plasma water (l) = body weight (kg) × 0.040.

Composition of Body Fluids

The fluids of the body are primarily composed of water, which in turn contains a multitude of substances. One such group of substances include electrolytes such as sodium, potassium, magnesium, phosphate, chloride, and others. Another group includes metabolites, such as oxygen, carbon dioxide, glucose, urea, etc. A third important group of substances contained within the water of our body, which includes proteins, most of which are vital for our existence.

The volume of fluid (water) within a compartment is determined by its solute composition and concentrations. The compositions of plasma and IF are similar to one another but are quite different from the composition of the ICF. The ionic composition of the interstitial fluid and plasma is approximately the same, but the protein content in the interstitial fluid is small – about 4 g/l, in plasma the protein content is normal 70–75–80 g/l.

The ionic composition of intracellular fluid is significantly different from ionic composition of interstitial fluid and plasma. Main cation in cells – potassium (77 %), in interstitium and plasma – sodium (92 %); the main anions in the cells are phosphates, proteins and sulfates (94 %), in interstitium and in plasma – chlorides and bicarbonates (83 %).

Ionic composition of different water compartments given in Table 2.

Table 2 – **Ionic composition of different water compartments (mmol/l)**

Ions	Intravascular	Interstitial	Intracellular
Na^+	142	132	14
K^+	5	5	154
Ca^{2+}	2.5	2.5	1.5
Mg^{2+}	1.5	2.5	12.5
Cl^-	101	110	6
HCO_3^-	27	10	10
HPO_4^{2-}	1	1	110
SO_4^{2-}	1	1	20
Organic acids	6	5	–
Proteins	16	0.5	75

Intracellular fluid

The outer membrane of cells plays an important role in regulating intracellular volume and composition. A membrane-bound adenosine-triphosphate (ATP) – dependent pump exchanges Na^+ for K^+ in a 3:2 ratio. Because cell membranes are relatively impermeable to sodium and to a lesser extent – potassium ions, potassium is concentrated intracellularly, whereas sodium is concentrated extracellularly. As a result, potassium is the most important determinant of intracellular osmotic pressure, whereas sodium is the most important determinant of extracellular osmotic pressure.

The impermeability of cell membranes to most proteins results in a high intracellular protein concentration. Because proteins act as nondiffusible solutes (anions), the unequal

exchange ratio of 3 Na^+ for 2 K^+ by the cell membrane pump is critical in preventing relative intracellular hyperosmolality. Interference with $Na^+–K^+$ ATPase activity, as occurs during ischemia or hypoxia, results in progressive swelling of cells.

Extracellular fluid

The principal function of extracellular fluid is to provide a medium for cell nutrients and electrolytes and for cellular waste products. Maintenance of a normal extracellular volume-particularly the circulating component (intravascular volume) – is critical. For the reasons described above, sodium is quantitatively the most important extracellular cation and the major determinant of extracellular osmotic pressure and volume. Therefor changes in extracellular fluid volume are related to changes in total body sodium content. The latter is a function of sodium intake, renal sodium excretion, and extrarenal sodium losses.

Interstitial Fluid

Very little interstitial fluid is normally in the form of free fluid. Most interstitial water is in chemical association with extracellular proteoglycans, forming a gel. Interstitial fluid pressure is thought to be negative (about – 5 mm Hg). As interstitial fluid volume increases, interstitial pressure also rises and eventually becomes positive. When the latter occurs, the free fluid in the gel increases rapidly and appears clinically as edema.

Because only small quantities of plasma proteins can normally cross capillary clefts, the protein content of interstitial fluid is relatively low (20 g/l). Protein entering the interstitial space returns to the vascular system via the lymphatic system.

Intravascular Fluid

Intravascular fluid, commonly referred to as plasma, is restricted to the intravascular space by the vascular endothelium. Most electrolytes (small ions) freely pass between plasma and the interstitium, resulting in nearly

identical electrolyte composition. However, the tight intercellular junctions between adjacent endothelial cells impede the passage of plasma proteins outside the intravascular compartment. As a result, plasma proteins (mainly albumin) are the only osmotically active solutes in fluid not normally exchanged between plasma and interstitial fluid.

Increases in extracellular volume are normally proportionately reflected in intravascular and interstitial volume. When interstitial pressure becomes positive, continued increases in ECF result in expansion of only the interstitial fluid compartment. In this way, the interstitial compartment acts as an overflow reservoir for the intravascular compartment. This can be seen clinically in the form of tissue edema.

The movement of water between fluid compartments.

Molarity, osmolarity and equivalency

One mole of a substance represents 6.02×10^{23} molecules. The weight of this quantity in grams is commonly referred to as gram-molecular weight. Molarity is the standard SI unit of concentration that expresses the number of moles of solute per liter of solution. Molality is an alternative term that expresses moles of solute per kilogram of solvent. Equivalency is also commonly used for substances that ionize: the number of equivalents of an ion in solution is the number of moles multiplied by its charge (valence). Thus, a 1 M solution of $MgCl_2$ yields 2 equivalents of magnesium per liter and 2 equivalents of chloride per liter.

Osmotic pressure is the pressure that must be applied to the side with more solute to prevent a net movement of water across the membrane to dilute the solute. Osmotic pressure is generally dependent only on the number of nondiffusible solute particles. This is because the average kinetic energy of particles in solution is similar regardless of their mass. One osmole

equals 1 mol of nondissociable substances. For substances that ionize, however, each mole results in n Osm, where n is the number of ionic species produced. Thus, 1 mol of a highly ionized substance such as NaCl dissolved in solution should produce 2 Osm. A difference of 1 mOsm/L between two solutions results in an osmotic pressure of 19.3 mm Hg. The osmolarity of a solution is equal to the number of osmoles per liter of solution, whereas its osmolality equals the number of osmoles per kilogram of solvent. Tonicity refers to the effect a solution has on cell volume. An isotonic solution has no effect on cell volume, whereas hypotonic and hypertonic solutions increase and decrease cell volume, respectively.

Plasma osmolarity

The osmolality of ECF is equal to the sum of the concentrations of all dissolved solutes. Because Na^+ and its anions account for nearly 90 % of these solutes, the following approximation is valid:

Calculated osmolarity = 2 Na + Glucose + Urea (all in mmol/l).

Osmolality can be measured on an analytical instrument called an osmometer. It works on the method of depression of freezing point

Plasma osmolality normally varies between 285 and 295 mOsm/l. A discrepancy between the measured and calculated osmolality is referred to as an osmolal gap. Significant osmolal gaps indicate a high concentration of an abnormal osmotically active molecule in plasma such as ethanol, mannitol, methanol, ethylene glycol, or isopropyl alcohol.

Diffusion is the random movement of molecules due to their kinetic energy and is responsible for the majority of fluid and solute exchange between compartments. The rate of diffusion of a substance across a membrane depends on the permeability of that substance through that membrane, the

concentration difference for that substance between the two sides, the pressure difference between either side because pressure imparts greater kinetic energy, and the electrical potential across the membrane for charged substances.

Exchanges between the interstitial fluid and intracellular fluid

Exchanges between the interstitial fluid and intracellular fluid occur across plasma membranes. Exchanges across the plasma membrane depend on its permeability properties. As a general rule, two – way osmotic flow of water is substantial. But ion fluxes are restricted and, in most cases, ions move selectively, by active transport or through channels. Movements of nutrients, respiratory gases, and wastes are typically unidirectional (both ways). For instance, glucose and oxygen move into the cells and metabolic wastes move out.

Fluid exchange between the intracellular and interstitial spaces is governed by the osmotic forces created by differences in nondiffusible solute concentrations. Relative changes in osmolality between the intracellular and interstitial compartments result in a net water movement from the hypoosmolar to the hyperosmolar compartment.

Oxygen, CO_2, water, and lipid-soluble molecules penetrate the cell membrane directly. Cations such as Na^+, K^+, and Ca^{2+} penetrate the membrane poorly because of the cell transmembrane voltage potential (which is positive to the outside) created by the Na^+–K^+ pump. Therefore, these cations can diffuse only through specific protein channels. Passage through these channels is dependent on membrane voltage and the binding of ligands (such as acetylcholine) to the membrane receptors. Glucose and amino acids diffuse with the help of membrane-bound carrier proteins.

Exchanges between plasma and interstitial fluid

Exchanges between plasma and interstitial fluid occur across capillary walls**.** The hydrostatic pressure of blood forces nearly protein-free plasma out of the blood into the interstitial space. The filtered fluid is then almost completely reabsorbed into the bloodstream in response to the colloid osmotic pressure of plasma proteins.

Capillary walls are typically 0.5 mm thick, consisting of a single layer of endothelial cells with their basement membrane. Intercellular clefts, 6–7 nm wide, separate each cell from its neighbors. Oxygen, CO_2, water, and lipid-soluble substances can penetrate directly through both sides of the endothelial cell membrane. Only low-molecular-weight water-soluble substances such as sodium, chloride, potassium, and glucose readily cross intercellular clefts. High-molecular-weight substances such as plasma proteins penetrate the endothelial clefts poorly.

Fluid exchange across capillaries differs from that across cell membranes in that it is governed by significant differences in hydrostatic pressures in addition to oncotic forces (Fig. 1). The hydrostatic pressure within the circulation tends to drive fluid out, the oncotic pressure of the plasma proteins, e. g. albumin, draws fluid in and maintains the relative constancy of the plasma volume as a proportion of the ECF (Starling effect).

Capillary hydrostatic pressure (CHP) → forces fluid out of capillaries into interstitium.

Colloid osmotic pressure (COP) → tends to draw fluid back into capillaries.

Interstitial fluid hydrostatic pressure (IFHP) → forces fluid out of interstitium into capillaries.

Interstitial fluid osmotic pressure (IFOP) → tends to draw fluid back out of capillaries.

These forces are operative on both arterial and venous ends of capillaries. As a result, there is a tendency for fluid to move out of capillaries at the arterial end and back into capillaries at the venous end.
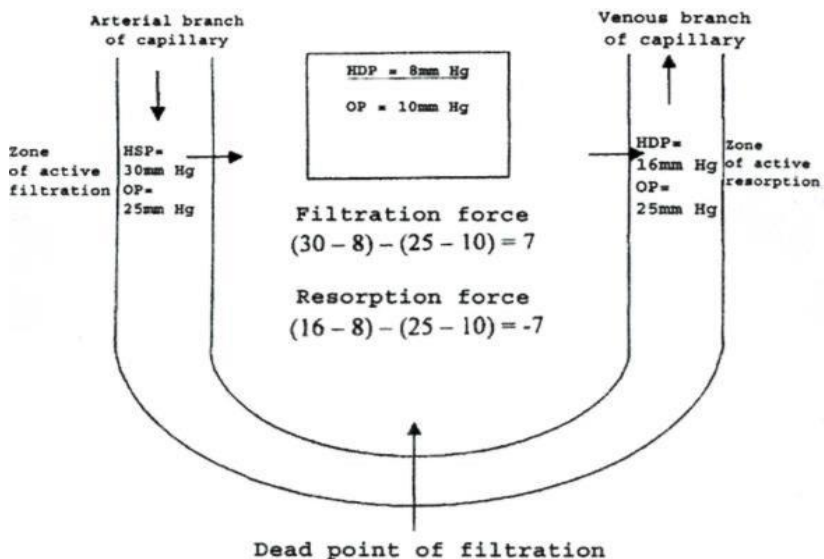
Figure 1 – **Mechanism of vascular –interstitial fluid circulation**

Many factors can change ECF and ICF volumes. Because water moves freely between compartments, however, the osmolarities of all body fluids are equal. Increasing the ECF solute content (mainly sodium chloride) causes osmotic and volume changes in the ICF – generally, a shift of water out of cells. Conversely, decreasing ECF osmolarity causes water to move into the cells. Thus, ECF solute concentration determines ICF volume.

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Types of edema, common manifestations, and treatment goals

Five types of edema have been identified as a result of impaired balance between fluid compartments:

1. Increased hydrostatic pressure.
2. Reduced oncotic pressure.
3. Lymphatic obstruction.
4. Sodium retention.
5. Inflammation / increased vascular permeability.

Increased hydrostatic pressure may result from conditions that alter actual volume or pressure of the blood within the vasculature. Aggressive intravascular volume loading, fluid overloading, backward heart failure, or impaired venous return may result in increased hydrostatic pressure. Examples would include respectively: fluid diuresis in treatment of anuric renal failure, overzealous fluid replacement, left sided heart failure, or pericardial fluid accumulations. Pulmonary edema is a very common manifestation of the fluid shifting that occurs due to increased hydrostatic pressure. Left sided heart failure is the most commonly seen cause of pulmonary edema. As mentioned earlier, several inciting factors may be present concurrently and result in edema formation. Hydrostatic edema during renal failure will also have contributing edema caused by sodium retention. A blood clot causing venous congestion will also produce inflammation and cause edema from increased vascular permeability.

Edema often results from a reduced oncotic pressure and manifests during many disease processes. Edema due to hypoproteinemia is a commonly recognized form. Hypoproteinemia is defined as total serum protein of < 55gm/l. Decreased COP is commonly due to hypoalbuminemia. The most commonly seen causes of hypoproteinemia are usually related to protein loss from the vasculature or organs

(gastrointestinal or renal systems), or decreased production from the liver. Remember that as proteins are either lost from organs or are at too low number the oncotic pull of the remaining proteins in the vasculature is less and fluid will be attracted to those areas that have higher concentrations (peritoneum or pleural space). Examples include: protein losing enteropathy, protein losing nephropathy, and liver failure. The resulting edema manifests as third spacing of fluids into the pleural or peritoneal cavity or accumulation within the interstitium.

Edema formation due to lymphatic obstruction can be exemplified in patients that have a neoplastic disease process or postsurgical swelling that obstructs lymphatic flow. Lymphoma patients with large lymph nodes in the neck or groin area may have facial, airway, or rear leg swelling. Chemotherapeutics to shrink lymph node size and external warm packs to promote blood flow would be beneficial.

Sodium retention is an inciting cause of edema formation. Sodium is a solute that is freely transportable across cell membranes meaning that it will attempt to equalize in both the intracellular and extracellular space. In cases of renal failure where the kidneys cannot excrete sodium adequately, increasing levels of sodium will occur in the extracellular space. As a result, the osmotic pressure of the interstitial space may become greater than the osmotic pressure of the intravascular space. A pressure gradient will form that serves to pull fluid out into the interstitial space.

And finally, edema may form as a result of inflammation, ischemia, or sepsis causing increased permeability of cell membranes. Insults to the vascular endothelium, result in cellular membranes that become increasingly permeable or "leaky" and allow larger size particles to exude into the interstitium. Once the larger size particles leak out into the interstitium, osmotic pressure

gradients are created and serve to pull more fluids out of the vasculature. Any disease process causing ischemia to tissues or systemic inflammation response may manifest with complications of edema.

Edema can present as a life-threatening condition or a more chronic complication of disease. In cases of heart failure and pleural effusion immediate action is necessary. The use of diuretic drugs and thoracic drainage would be indicated. Treatment for nonemergent presentations would be focused on treating the underlying disease while attempting management of tissue or cavitary edema. Diuretics are very commonly used to manipulate increased hydrostatic pressure and increased sodium retention edemas. Local management of edema is indicated in some cases of lymphatic obstruction edema where very large lymph nodes or swelling of an extremity may be involved. In cases of hypoproteinemia, administration of large molecular weight colloid solutions or commercially available human albumin solutions may be indicated. The large size protein molecules will increase the intravascular oncotic pressure and function to retain fluid within the vessels. When inflammation or sepsis has altered membrane permeability the focus of treatment would be identification and alleviation of the inflammatory condition responsible. Typically, the prognosis for successful management of edema is dependent on the ability to treat and resolve the underlying disease.

Water intake and output

Most of the water the body requires comes from the ingestion of liquids; this amount averages 1 200 ml per day. The food we eat also contains water. Even foods we think of as somewhat dry, such as bread, contain significant amounts of water. The daily water total from food averages 1 000 ml. The last source of water, about 300 ml per day, is the metabolic water that is a product of cell respiration. The total intake of water per day, therefore, is about 2 500 ml, or 2.5 litres.

Most of the water lost from the body is in the form of urine produced by the kidneys; this averages 1 500 ml per day. About 500 ml per day is lost in the form of sweat, another 400 ml per day is in the form of water vapor in exhaled air, and another 100 ml per day is lost in faeces. The total output of water is thus about 2 500 ml per day.

The amount of water coming into the body each day must equal the amount of water eliminated from the body over the same period.

Output insensible loss: evaporation of water from the lungs and skin occurs all the time without us being aware of it. In our temperate climate the amount so lost is 0.5–1 liter/day. In a warm environment, during fever, or with exertion, we produce additional sweat containing up to 50 mmol/l of salt. GI losses: normally, the intestine absorbs water and electrolytes very efficiently so that fluid loss in the stool is as little as 100–150 ml/day, although, in the presence of disease this may be greatly increased. Kidney: this is the main organ for regulating fluid and electrolyte balance as well as excreting the waste products of metabolism, e. g. urea.

Table 3 – **Water intake and output**

Water Intake	Water Output
Food and drink: 2 200 ml	Kidneys: 1 500 ml
Metabolic water:300 ml	Skin: 500 ml, Lungs: 400 ml– perspiration or insensible loss, GI tract: 100 ml
Total 2 500 ml	**Total 2 500 ml**

Control of water balance

The multiple mechanisms involved in regulating ECF volume and sodium balance normally complement one

another but can function completely independently of one another. In addition to altering renal Na^+ excretion, some mechanisms also produce more rapid compensatory hemodynamic responses when "effective" intravascular volume is reduced.

Secretion of Antidiuretic Hormone

Plasma osmolality is closely regulated by osmoreceptors in the hypothalamus. These specialized neurons control the secretion of antidiuretic hormone (ADH) and the thirst mechanism. Plasma osmolality is therefore maintained within relatively narrow limits by varying both water intake and water excretion.

Specialized neurons in the supraoptic and paraventricular nuclei of the hypothalamus are very sensitive to changes in extracellular osmolality. When ECF osmolality increases, these cells shrink and release ADH (vasopressin) from the posterior pituitary. ADH markedly increases water reabsorption in renal-collecting tubules, which tends to reduce plasma osmolality to normal again. Conversely, a decrease in extracellular osmolality causes osmoreceptors to swell and suppresses the release of ADH. Decreased ADH secretion allows a water diuresis, which tends to increase osmolality to normal. Peak diuresis occurs once circulating ADH is metabolized (90–120 min). With complete suppression of ADH secretion, the kidneys can excrete up to 10–20 L of water per day.

The carotid baroreceptors and possibly atrial stretch receptors can also stimulate ADH release following a 5–10 % decrease in blood volume. Other nonosmotic stimuli include pain, emotional stress, and hypoxia.

Thirst

Osmoreceptors in the lateral preoptic area of the hypothalamus are also very sensitive to changes in extracellular osmolality. Activation of these neurons by increases in ECF

osmolality induces thirst and causes the individual to drink water. Conversely, hypoosmolality suppresses thirst.

Thirst is the major defense mechanism against hyperosmolality and hypernatremia, because it is the only mechanism that increases water intake. Unfortunately, the thirst mechanism is only operative in conscious individuals who are capable of drinking.

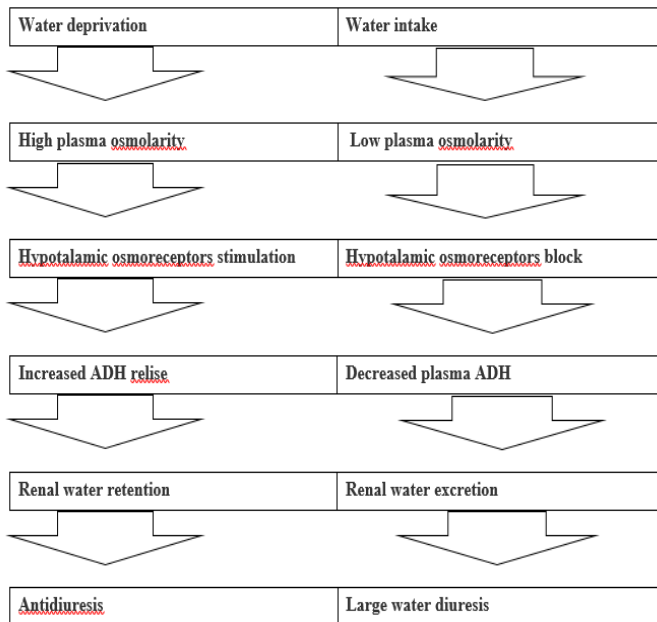| Water deprivation	Water intake
High plasma osmolarity	Low plasma osmolarity
Hypotalamic osmoreceptors stimulation	Hypotalamic osmoreceptors block
Increased ADH relise	Decreased plasma ADH
Renal water retention	Renal water excretion
Antidiuresis	Large water diuresis

Figure 2 – **Osmoregulation of water balance**

Renin-Angiotensin-Aldosterone

The principal volume receptors in the body are really baroreceptors. Because blood pressure is the product of cardiac output and systemic vascular resistance, significant changes in intravascular volume (preload) not only affect cardiac output but also transiently affect arterial blood pressure. Thus, the

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baroreceptors at the carotid sinus and afferent renal arterioles (juxtaglomerular apparatus) indirectly function as sensors of intravascular volume. Changes in blood pressure at the carotid sinus modulate sympathetic nervous system activity and nonosmotic ADH secretion, whereas changes at the afferent renal arterioles modulate the renin-angiotensin-aldosterone system.

Regardless of the mechanism, effectors of volume change ultimately alter urinary Na^+ excretion. Decreases in "effective" intravascular volume decrease urinary Na^+ excretion, whereas increases in the "effective" intravascular volume increase urinary Na^+ excretion. These mechanisms include the following:

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┌──────────────────────────────────────────┐
│      Insufficient H₂O in the body         │
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                    ↓
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│        Increases blood osmolarity          │
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┌──────────────────────────────────────────┐
│              Osmoreceptors                 │
│           in the hypothalamus              │
└──────────────────────────────────────────┘
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┌──────────────────────────────────────────┐
│        Stimulates thirst cetnter           │
│           in the hypothalamus              │
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│             Increases thirst               │
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│              H₂O taken in                  │
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│        Decreases blood osmolarity          │
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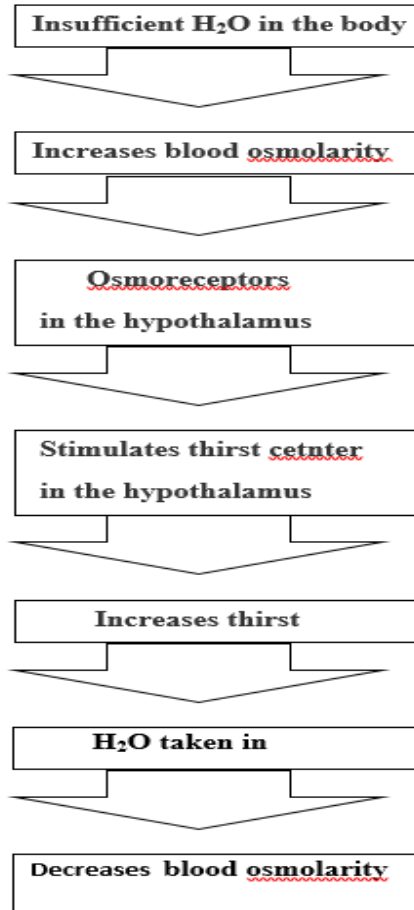
Figure 3 – **Thirst mechanism**

Renin secretion increases the formation of angiotensin II. The latter increases the secretion of aldosterone and has some direct effect in enhancing Na^+ reabsorption in the proximal renal tubules. Angiotensin II is also a potent direct vasoconstrictor and potentiates the actions of norepinephrine. Secretion of aldosterone enhances Na^+ reabsorption in the

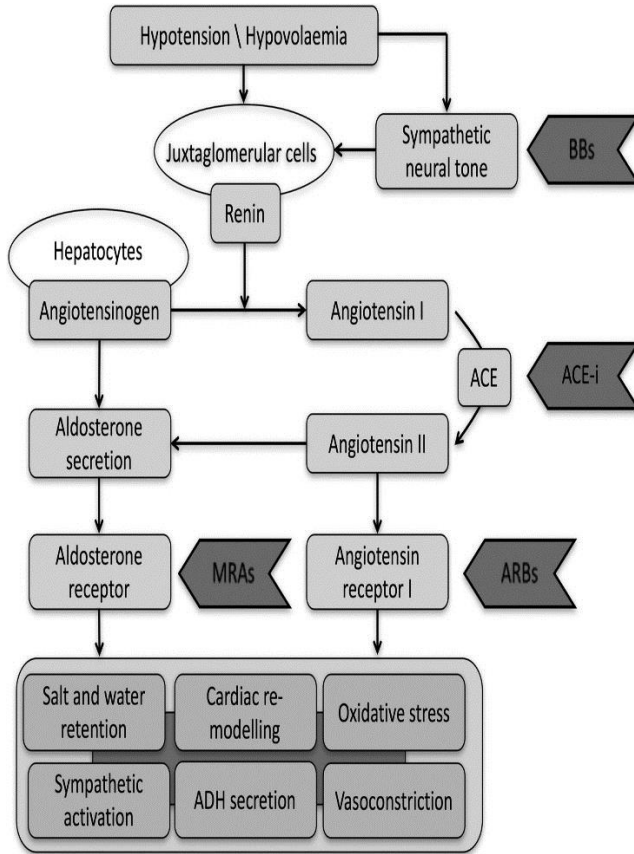distal nephron and is a major determinant of urinary Na^+ excretion.

Figure 4 – **Renin-Angiotensin-Aldosterone mechanism**
Atrial Natriuretic Peptide (ANP)

This peptide is normally released from both right and left atrial cells following atrial distention. Atrial natriuretic peptide appears to have two major actions: arterial vasodilation and increased urinary sodium and water excretion in the renal collecting tubules. Na^+-mediated afferent arteriolar dilation and

efferent arteriolar constriction can also increase glomerular filtration rate (GFR). Other reported effects include the inhibition of both renin and aldosterone secretion and antagonism of ADH.

Brain Natriuretic Peptide (BNP)

ANP, BNP, and C-type natriuretic peptide are structurally related peptides. BNP is released by the ventricles in response to increased ventricular volume and pressure, and ventricular overdistention. BNP levels are usually ~ 20 % of ANP levels, but during an episode of acute congestive heart failure BNP levels may exceed those of ANP. BNP levels can be measured clinically, and a recombinant form of BNP, nesiritide (Natrecor), is available to treat acute decompensated congestive heart failure.

Sympathetic Nervous System Activity

Enhanced sympathetic activity increases Na^+ reabsorption in the proximal renal tubules, resulting in Na^+ retention, and mediates renal vasoconstriction, which reduces renal blood flow. Conversely, stimulation of left atrial stretch receptors results in decreases in renal sympathetic tone and increases renal blood flow (cardiorenal reflex) and, potentially, glomerular filtration.
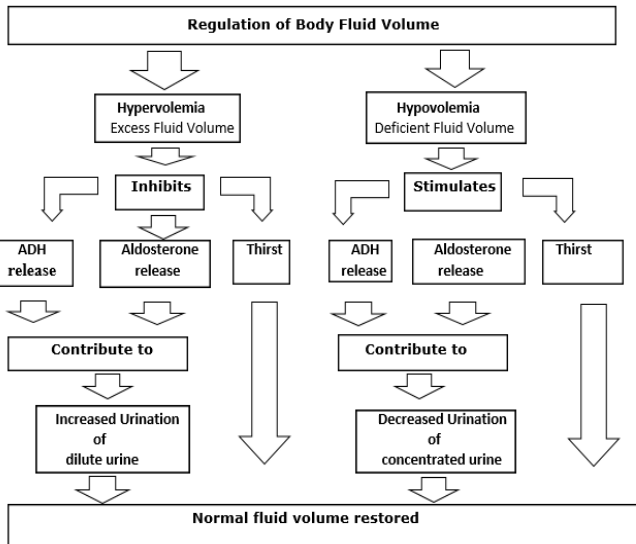
Figure 5 – **Regulation of Body Fluid Volume**

Test tasks for checking the final level of knowledge:

1. The average need for water in adults is normally (ml / kg body weight / day):

A. 70–80.

B. 50–60.

C. 30–40.

D. 15–20.

2. The volume of intravascular fluid (plasma) relative to body weight is roughly:

A. 5 %.

B. 10 %.

C. 15 %.

D. 20 %.

3. The volume of endogenous water per day is approximately equal to:

A. 100 ml.

B. 300 ml.

C. 750 ml.

D. 1 000 ml.

4. The walls of the capillaries are normally low – permeable for solutions:

A. Proteins.

B. Glucose.

C. Calcium chloride.

D. Potassium and sodium chloride.

5. The intensity of urination normally ranges from:

A. 0.1–0.3 ml/kg/h.

B. 0.3–0.7 ml/kg/h.

C. 0.7–1.2 ml/kg/h.

D. 1.0–1.9 ml/kg/h.

6. The "third" body fluid compartment is:

A. Pathological accumulation of fluid in the interstitium and in the transcellular water basins.

B. Normal fluid content in the gastrointestinal tract.

C. Urinary retention in the bladder.

D. Only edema in the focus of inflammation.

7. The mechanism of antiuretic action of vasopressin (antidiuretic hormone) is due to:

A. Increased reabsorption of sodium ions in the tubules.

B. Increased reabsorption of water in the distal nephron.

C. A decrease in the intensity of the renal plasma flow.

D. reduction of natriuresis.

8. Thirst is regulated:

A. Osmoreceptors.

B. Baroreceptors.

C. Volumoreceptors.

D. Sympathetic nervous system.

8. A 18-year-old patient was taken to a medical institution in serious condition. Depressed, complains of general weakness, intense thirst, dry mouth. This condition is due to the fact that, having lost his way in the desert, within 6 hours he traveled over 30 km at an air temperature of 44 °C (there was no water with him). Blood pressure 100/70 mm Hg. Pulse 132 per minute. CVP – 5cm water column. Frequent breathing 34 per minute and occasionally periodic. Body temperature 38.3 °C. Body weight decreased by 6 kg. An analysis of blood revealed an increase in the content of red blood cells (6.0×10^{12}) and hemoglobin (170 g/l). Hematocrit – 54 %. Potassium – 5.0 mmol/l; sodium – 150 mmol/l; chlorine – 104 mmol/l; calcium – 3.0 mmol/l; blood glucose – 5.4 mmol/l; plasma creatinine concentration – 0.6 mmol/l, urea – 6.0 mmol/l. Water intake significantly improved the patient's condition.

1. What water space dehydration are we ascertaining on the basis of increased hematocrit, increased content of red blood cells and hemoglobin?

2. The appearance of thirst indicates dehydration mainly in what compartment of water?

3. What type of dehydration does the patient have (cellular, extracellular, general)?

4. Calculate plasma osmolarity.

TYPICAL WATER BALANCE DISTURBANCES

Disorders of sodium (Na+) and water balance commonly are encountered in critically ill patients. Critical illness, multiple-organ dysfunction, fluid therapy, and the numerous additional interventions applied in the routine care of patients admitted to the intensive care unit can interfere with the complex mechanisms that maintain total body sodium and water homeostasis.

Classifications of water balance disorders

Water metabolism disorders (dyshydria) can manifest as dehydration (water deficiency syndromes) or hyperhydration (excess water syndromes).

Each typical form of dyshydria can be characterized by means of two basic criteria. The first is the osmolality of extracellular fluid. On the basis of this criterion three forms of dyshydria are singled out:

1. Hypoosmolar (with plasma osmolality under 280 mosm/kg H_2O).

2. Hyperosmolar (with plasma osmolality above 300 mosm/kg H_2O).

3. Isoosmolar (with normal plasma osmolality).

The second criterion is the fluid compartment in which dyshydria predominantly develops. On the basis of this criteria:

– cellular;

– extracellular;

– mixed (associated) forms of hypo- and hyperhydration are singled out.
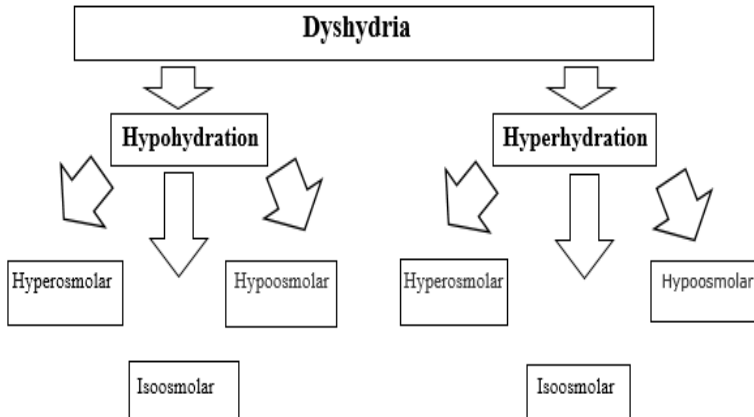

Figure 6 – **Classification of water balance disorders**

The human body is highly sensitive to dehydration and significantly more resistant to overhydration. Rapid loss of 20 % of the total liquid for a person is fatal, an increase in the volume of extracellular fluid by 2 times is usually quite tolerated, although it is accompanied by a serious condition.

Assessment and monitoring of fluid balance
Indications for fluid balance monitoring:

1. Increased fluid output:

− Diarrhea and vomiting – risk of dehydration, malnutrition and significant electrolyte disturbances including hyperkalaemia.

− High urine output – polyuria – ↑200 mls/hr – leads to dehydration if unmanaged. Common causes: diabetes, resolving AKI, excessive diuretics.

− High output stoma – increased frequency or ↑1 litre in 24 hrs.
Urinary catheter, convene, urostomy or irrigation – volumes must be measured. Incontinent patients may self-limit input in attempt to manage problem. Post-operative patients should be closely monitored:

• Large open wounds: output should be estimated if an accurate output is not possible.

• Drains: pleural, wound, ascetic.

• Increased 'insensible losses': sweating, sustained pyrexia of 38 °C or a sustained respiratory ↑rpm. Each example can lead to a fluid loss of ↑500 ml in any 24 hour period.

2. Reduced urine output:

− Oliguria – low urine output ↓0.5 ml per kilogram per hour. Oliguria can be an early sign of poor renal perfusion. Most common causes: hypotension or hypovolaemia. Anuria – absence of urine: ↓100 ml over 24 hours.

− Acute kidney injury (AKI) / chronic kidney disease. Patients with raised creatnine blood levels combined with a

low urine output may have an AKI: the kidneys are not effectively filtering blood, reabsorbing vital elements and excreting others. Prompt identification of an AKI is crucial as it can lead to serious complications if left untreated.

Medications which increase risk of AKI (patients on these need fluid balance monitoring):

1. Contrast medium – monitor fluid balance for 24 hours before and after procedure.

2. Chemotherapy – monitor fluid balance during therapy.

3. Antibiotic therapy – many antibiotics can cause renal impairment (Check BNF). High risk are: Gentamycin, Aciclovir and Vancomycin. Fluid balance should be monitored throughout therapy and for 24 hours post last dose.

4. ACE inhibitors and diuretics – often held in acute kidney injury.

The main parameters for monitoring and assessment are given in the Table 4.

Table 4 – **Medications which increase risk of AKI (patients on these need fluid balance monitoring):**

Assessment and monitoring of fluid balance

Parameter	Significance
History	Alerts to likelihood of fluid deficit (e. g. vomiting/ diarrhea / hemorrhage) or excess (e. g. from intraoperative fluids)
Autonomic responses	Pallor and sweating, particularly when combined with tachycardia, hypotension and oliguria are suggestive of intravascular volume deficit, but can also be caused by other complications, e. g. pulmonary embolus or myocardial

	infarction
Capillary refill	Slow refill compatible with, but not diagnostic of volume deficit. Can be influenced by temperature and peripheral vascular disease
Blood pressure	Cuff measurements may not always correlate with intraarterial monitoring. Does not necessarily correlate with flow. Affected by drugs (important to review medication charts). Nonetheless, a fall is compatible with intravascular hypovolemia, particularly when it correlates with other parameters such as pulse rate, urine output, etc. Systolic pressure does not usually fall until 30 % of blood volume has been lost
Skin turgor	Diminished in salt and water depletion, but this can also be caused by ageing, cold and cachexia
Sunken facies	May be due to starvation or wasting from disease, although compatible with salt and water depletion
Dry mouth	A poor indicator. Compatible with salt and water depletion, but usually due to mouth breathing
Edema	The presence of pulmonary edema should temporise further fluid administration. Peripheral edema (pedal and/or sacral) occurs in volume overload but can occur in patients with hypoalbuminemia who are

	intravascularly deplete (check serum albumin)
Urine output	Urine output < 30 ml/h (< 0.5 ml/kg/h) is commonly used as indication for fluid infusion, but in the absence of other features of intra – vascular hypovolemia suggesting a pathological cause, it is usually due to the physiological oliguric response to surgery. Urine quality (e. g. concentration, urine: plasma urea or osmolality ratio) is just as important, particularly in the complicated patient
Weighing	24-h change in weight (performed under similar conditions) – best measure of change in water balance. Takes account of insensible loss. Simple to carry out by bedside. May be difficult to measure in the critically ill
Fluid balance charts	Inherently inaccurate in measurement and recording. They do not measure insensible loss. Large cumulative error over several days. Good measure of changes in urine output, fistula loss, gastric aspirate, etc.
Serum biochemistry	Indicates ratio of electrolytes to water in the extracellular fluid. A poor indicator of whole body sodium status. Hyponatremia most commonly caused by water excess. If change in water balance over 24 h is known, then change in serum sodium concentration can

	guide sodium balance. Hypokalemia, on the other hand, nearly always indicates the need for potassium supplementation. Blood bicarbonate and chloride concentrations measured on point of care blood gas machines are useful in patients with acid-base problems including iatrogenic hyperchloremia. Serum creatinine reflects both muscle mass and renal function. Blood urea reflects renal function and protein catabolism
Urinary biochemistry	Urinary sodium concentration may reflect renal perfusion and a low value (< 20 mmol/l) is compatible with renal hypo – perfusion (pre renal acute kidney injury), although it is also a feature of the response to injury or sodium depletion. Urinary potassium measurement is helpful in assessing the cause of refractory hypokalemia. Urinary urea excretion increases several fold in catabolic states (e. g. sepsis) and is an indication for provision of additional free water to avoid hypernatremia and uremia. Urinary and blood creatinine are combined to measure creatine clearance to assess renal function

Dehydration

Dehydration is defined as the excessive loss of body water. The balance between fluid intake and fluid loss from the body becomes greatly disproportionate in dehydration.

Hypovolemia is another related term that means decreased circulatory volume due to the loss of blood or plasma.

Causes of dehydration:

Fluid deficiency can occur either as a result of insufficient fluid intake into the body, either as a result of increased body fluid loss, or as a result of pathological movement of fluids in organism. It is not uncommon for all three possible causes of dehydration to act simultaneously.

Insufficient fluid intake in the body may be associated with the impossibility of oral nutrition when the patient cannot or should not take food by mouth, with deficient oral intake, feeding through a tube (into the stomach, intestines) or parenteral administration of fluids. These situations can arise after operations and injuries, with various diseases of the gastrointestinal tract, psycho-neurological diseases, coma of the patient, etc.

Loss of significant amounts of fluid from the body occurs when frequent vomiting, constant removal of fluids from the gastrointestinal tract through a tube, profuse diarrhea and polyuria, discharge of large amounts of fluid from fistulas, wounds, vapors from an extensive wound (burn) surface, increased perspiration and the appearance of transpiration as a result of prolonged high fever, prolonged mechanical ventilation with unmoistened gas mixtures, excessive use of diuretics, etc.

Large losses of liquids occur during the formation of the third water compartment. The third body water compartment is an area of the body into which, as a result of

trauma, surgery or disease, it temporarily moves and is excluded from the active exchange of body fluids.

It was already indicated earlier, that the first water compartment is intracellular fluid, the second – extracellular. The third body water compartment does not normally occur, it is always pathological condition.

The third body of water is formed in two ways. First way it is the movement of body fluids into natural body cavities with the exclusion of fluids from active circulation. For example, the movement of fluids into the gastrointestinal tract with intestinal obstruction, into the abdominal cavity with peritonitis, into the pleural cavity with pleuritis, etc.

The loss from the active circulation of fluids when they move into the cavity is always combined with the second path of its functional losses – in edema, the essence of which is the sequestration of interstitial fluid in the foci and zones of disease, damage, surgery.

The third body of water can also form due to edema alone. For example, in diseases with local or generalized edema, injury or inflammation of tissues. Liquid exclusion volume from active metabolism in edema is proportional to the severity of the pathological conditions that caused them.

The formation of a third water space leads to dehydration of the body, since fluids that have moved into this space are excluded from active functioning.

Signs and Symptoms of dehydration:

Most patients with dehydration present with:

- Thirst.
- Headaches.
- Fatigue.

Symptoms of mild dehydration include: weight loss over short period of time, constipation, dry mouth, dizziness, and low urine volume (unless the cause of dehydration is polyuria).

Symptoms of more severe dehydration include: dry skin, sunken eyes, dry mucous membranes, confusion, hyperthermia, delirium, seizures, coma, and death.

Signs of hypovolemia may also be present, including: tachycardia, hypotension, decreased CVP, narrowed pulse pressure (systolic B/P minus diastolic B/P), oliguria and empty neck veins or shock.

**Classifications of dehydration**

There are three main types of dehydration: hypotonic (primarily a loss of electrolytes), hypertonic (primarily loss of water), and isotonic (equal loss of water and electrolytes).

Dehydration can be classified according to the ratio of fluid to electrolyte loss:

• Isotonic − characterized by isotonic loss of both water and solutes from the extracellular fluid (ECF) e. g., vomiting, diarrhea or through inadequate intake. No osmotic water shift from the intracellular fluid (ICF) to the ECF (mixed dehydration).

• Hypertonic − water loss exceeds salt loss e. g. − through inadequate water intake, excessive sweating, osmotic diuresis and diuretic drugs characterized by an osmotic shift of water from the ICF to the ECF (cellular dehydration).

• Hypotonic − Sodium loss is higher than water loss e. g. in some instances of high sweat or gastro-intestinal fluid losses or when fluid and electrolyte deficits are treated with water replacement only. Characterized by an osmotic shift of water from the ECF to the ICF (extracellular dehydration).
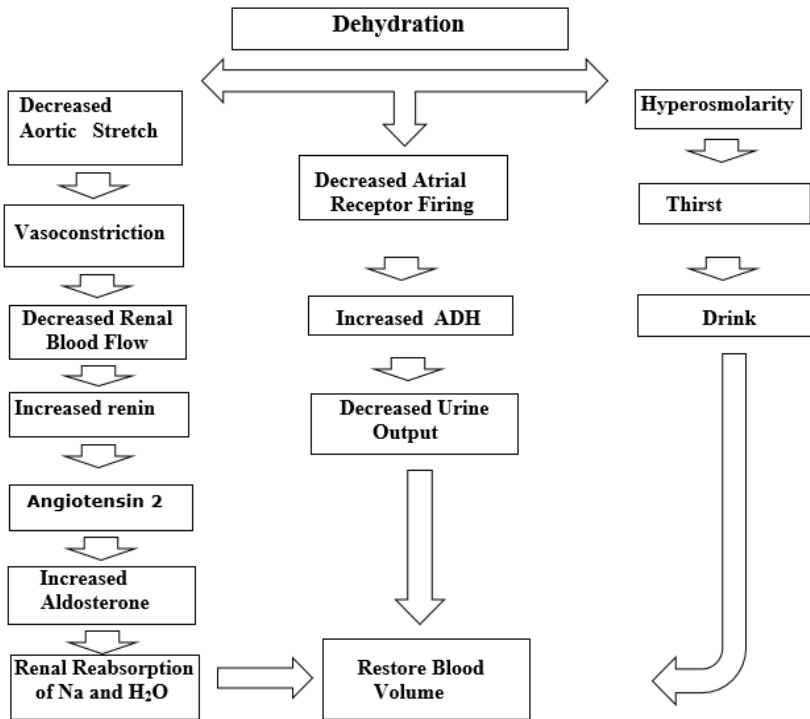
Figure 7 – **Compensation of dehydration**

The severity of dehydration ranges from mild to severe, and can be fatal when fluid losses exceed more than 15 % of total body water content.

Mild (loss: 4 % of body weight): decreased skin turgor, sunken eyes, dry mucous membranes.

Moderate (loss: 5–8 % of body weight): + oliguria, orthostatic hypotension, tachycardia.

Severe (loss: 8–10 % of body weight): + hypotension, decreased level of consciousness, stupor.

Isotonic dehydration

Isotonic dehydration is a condition in which both water and sodium are lost proportionally such that the serum sodium concentration maintains normal serum osmolality. So, no osmotic movement of water from the inside of cells to the outside.

Causes of isotonic dehydration:

• Vomiting and diarrhea**:** severe watery diarrhea and/or vomiting can be a life-threatening condition, especially in children. People with gastroenteritis may lose tremendous amounts of fluids and electrolytes in a short time and their oral replacement is limited due to recurrent vomiting, which can then result in severe dehydration.

• Excessive sweating**:** vigorous exercise, especially in humid weather, will increase sweating and lead to fluid and electrolyte loss.

• Inadequate intake of fluid.

• Haemorrhage and blood loss.

• Polyuria caused by diuretics.

• Internal loss: ileus, ascites, pleural effusion.

Signs and Symptoms:

The symptoms of hypovolemia prevails: decreased arterial, central venous pressure, circulating blood volume, tachycardia, oliguria (dehydration shock). Symptoms of cellular dehydration: dry skin, sunken eyes, dry mucous membranes, confusion, impaired consciousness (up to the development of coma) may also be present. Thirst with this type of dehydration is moderate.

Lab values in isotonic dehydration:

Isotonic dehydration will show normal serum laboratory values including normal osmolality of 285–295 mOsm/kg and normal serum sodium of 135–145 mmol/l. Urine volume will be decreased (oliguria) with low fractional sodium excretion and increased specific gravity.

Treatment

A fluid bolus should be given to restore the blood volume according to severity, followed by maintenance therapy with 0.9 % normal saline. 20 ml/kg of isotonic sodium solution or lactated Ringer's solution is given to restore hydration. Oral intake should be encouraged as early as possible.

To determine the existing fluid deficit and its further correction, a formula is used, which is based on the hematocrit indicator, since during isotonic dehydration, the Na^+ concentration changes little.

$$V = \frac{(Ht\ pat - 0{,}42)}{0{,}42} \ x\ 0.2\ x\ TBW,$$

where V is the volume of infusion in lite x rs; $Ht\ pat$ – patient's hematocrit (l / l); 0.42 – normal hematocrit (l / l); 0.2 – design factor (20 % content of extracellular fluid); TBW is the patient's body weight (kg).

Hypertonic dehydration

Hypertonic dehydration occurs with significant losses of hypotonic fluid (i. e., fluid free of electrolytes).

Since a large amount of water is lost, primarily from the extracellular space, an increased concentration of electrolytes (especially sodium) is created. According to the laws of osmosis, this causes the fluid to move from the cells into the extracellular space into the zone of increased osmotic pressure. Intracellular dehydration develops.

The main causes:
- Excessive fluid loss through the respiratory tract (hyperpnoea, mechanical ventilation).
- Excessive fluid loss through the skin (with fever, sweating).
- Diabetes insipidus (decreased ADH secretion).

- Tumors of the adrenal cortex (in which increased sodium reabsorption).
- Decreased water intake.
- Drinking seawater for survival.
- Osmotic diuresis (diabetes).
- Burn injuries.
- Iatrogenic hypertonic sodium administration.

Signs and Symptoms:

Symptoms of cellular dehydration: severe thirst, anxiety, impaired consciousness (up to coma as a result of osmotic dehydration of central nervous system cells), dry mucous membranes and skin (a skin fold does not straighten for a long time), and hyperthermia are typical for this type of water-electrolyte balance disorder.

With severe dehydration, the volume of circulating blood decreases, blood viscosity increases, diuresis decreases (oligoanuria). This is a sign of fluid deficiency not only in the extracellular, but also in the intracellular space (general dehydration).

Lab values in hypertonic dehydration:

Serum osmolality will exceed 300 mOsm/kg, while serum sodium will be greater than 150 mEq/l.

Urine volume will decrease, unless the cause of dehydration is polyuria or diuretic use.

The severity of hypertonic dehydration

There are three degrees of hypertonic dehydration:

- Mild, deficit water is 1–2 l; the main symptom is severe thirst.
- Moderate, water deficit from 3 to 5 liters; signs: severe thirst, oliguria, dry tongue, anxiety, fever.
- Severe, fluid deficiency 6–8 liters; signs: impaired consciousness (coma), decreased blood pressure, a picture of severe dehydration shock.

Treatment

Treatment for hypertensive dehydration involves the restoration of water deficiency in the body. The patient should drink a lot; if oral fluid intake is not possible, intravenous administration of a hypotonic (0.45 %) sodium chloride solution, 5 % dextrose in 0.9 % sodium chloride can be used with frequent monitoring of the serum sodium every 4 hours.

The volume of infusion in liters is calculated by the formula

$$V = \frac{(\text{Na } pat - 142)}{142} \text{ x } 0.6 \text{ x } TBW,$$

where V is the volume of infusion in liters; $\text{Na } pat$ – concentration of sodium ions in the blood plasma of the patient (mmol/l); 142 – normal concentration of sodium ions in blood plasma (mmol/l); 0.6 – calculated coefficient (60 % – water content relative to body weight); TBW – the patient's body weight (kg).

Dehydration and hypernatraemia should be corrected slowly; over a period of 48 hours at a rate of 10 mEq/L/24 hours. The more hypernatremic the patient, the more gradual is the correction. Excessively rapid rehydration may result in cerebral edema.

Hypotonic dehydration

Hypotonic dehydration occurs when sodium loss is greater than water loss, thereby resulting in a decrease in serum osmolality. This causes a shift of water from the extracellular space into the intracellular space. The cells will swell and cerebral edema may occur. Due to the predominant loss of extracellular fluid in hypotonic dehydration, vascular collapse is seen more often and earlier than in the other types of dehydration.

Causes of hypotonic dehydration:

• Addison's disease (associated with decreased reabsorption of Na^+ ions in the kidneys).

• Inadequate fluid replacement with hypotonic solution (the correction of isoosmolar hypohydration with dextrose solution).

• Diuretics, especially loop, thiazide.

• Improper dialysis procedures (dialysis with low osmolality of dialyzing solution).

• Renal tubular acidosis.

Symptoms:

Hypotonic dehydration symptoms are combination of hypovolemia symptoms and symptoms of cellular overhydration. Usually no thirst.

The severity of hypotonic dehydration

Lack of sodium in accordance with the degree of clinical hypotonic water will be divided into three degrees:

• Light lack of sodium: the patient has a sense of fatigue, dizziness, hand, foot numbness, no thirst. At serum sodium 135mmol/l below to reduce the urine sodium.

• Medium lacking sodium: in addition to the above symptoms, the often nausea, vomiting, rapid pulse of small, unstable blood pressure, blurred vision, less urine. At serum sodium 130 mmol/l following.

• Severe lack of sodium: patient unconsciousness, weakening or disappearance of tendon reflex, there stupor, and even coma. Shock often happen. At serum sodium 120 mmol/l following.

Lab values in hypotonic dehydration:

Serum sodium and serum osmolality will be less than the normal range. Urine specific gravity will be decreased under 1.010. Urine sodium excretion will be decreased.

Red blood cell count, hemoglobin volume, hematocrit, blood non-protein nitrogen and urea were increased.

Treatment

Patients may present with acute cerebral edema. Early steps should include stabilization of the patient, securing of the airway, and maintenance breathing and circulation.

As with hypernatremia, the treatment of hyponatremia is directed at correcting both the underlying disorder as well as the plasma [Na^+]. Isotonic saline is generally the treatment of choice for hyponatremic patients.

Acute symptomatic hyponatremia requires prompt treatment. In such instances, correction of plasma [Na^+] to > 125 mEq/l is usually sufficient to alleviate symptoms. The amount of NaCl necessary to raise plasma [Na^+] to the desired value, the Na^+ deficit, can be estimated by the following formula:

Na deficit = (Na desired − Na current) x 0.2 x body weight in kg.

Very rapid correction of hyponatremia has been associated with demyelinating lesions in the pons (central pontine myelinolysis), resulting in serious permanent neurological sequelae. Thus, the serum sodium should not increase by more than 15 mEq/l in a 24-hour period.

More rapid corrections can be achieved with intravenous hypertonic saline (3 % NaCl). Hypertonic saline may be indicated in markedly symptomatic patients with a plasma [Na^+] less than 110 mEq/l. Three percent NaCl should be given cautiously as it can precipitate pulmonary edema, hypokalemia, hyperchloremic metabolic acidosis, and transient hypotension.

Different diagnostic

Three types of dehydration different diagnostic are presented in Table 5.

Table 5 – **Different diagnostic of dehydration**

Parameters	Hypertonic dehydration	Hypotonic Dehydration	Isotonic dehydration
Se Na	+	-	N
Se osmolarity	+	-	N
Htk	+	+	+
Hb	+	+	+
Blood volume	-	-	-
Thirst	increased	no	mod. increased
Diuresis	-	N	-
CVP (central venous pressure)	-	-	-

Complications of dehydration:

- Hypovolemic shock: severe dehydration will lead to low blood volume and hypovolemic shock. It can lead to major end-organ damage through acidosis and can cause acute kidney injury, which can potentially be fatal.
- Seizures: sodium imbalance can cause abnormal neuronal excitability, resulting in confusion, seizures, delirium, and coma. Another cause of seizures in dehydrated patients is iatrogenic, caused by rapid correction of underlying serum sodium abnormalities. Hypotonic saline, if used in hypernatremic patients, will rapidly decrease the plasma

osmolality, and water will shift to the intracellular space, resulting in brain edema and seizures.

• Cardiac arrhythmias: potassium imbalances caused by dehydration may affect muscles and cause life-threatening cardiac arrhythmias, fatigue, weakness, and muscle breakdown.

• Heatstroke: during exercise or while working in a hot environment, fluid intake is recommended in order to avoid heat exhaustion, or even heat stroke.

• Kidney failure: possible causes of kidney injury include hypovolemic shock with low blood supply to the kidneys, acidosis due to hypovolemia, muscle breakdown, and electrolyte disturbances.

• Thrombosis: increased blood viscosity from dehydration will lead to venous thrombosis. Patients may present with DVT, portal vein thrombosis, or pancreatitis. Fever will also increase thrombosis risk and limit water intake.

• Coma and death: low blood pressure in severe dehydration will decrease the blood supply to the brain and could cause coma or death, particularly in elderly patients.

Overhydration

Overhydration is an excess of water in the body. People can develop overhydration if they have a disorder that decreases the body's ability to excrete water or increases the body's tendency to retain water. Drinking too much water rarely causes overhydration because normal kidneys easily excrete excess water. This condition is most common in patients whose kidney function is impaired.

Overhydration may also result from the syndrome of inappropriate antidiuretic hormone secretion. In this syndrome, the pituitary gland secretes too much vasopressin (antidiuretic hormone), stimulating the kidneys to conserve water when that is not needed.

Overhydration can be classified according to the ratio of fluid to electrolyte:

• Isotonic – as result forms excessive fluid in the extracellular fluid compartment.

No osmotic water shift from the intracellular fluid (ICF) to the ECF (mixed overhydration).

• Hypertonic – overhydration with increased sodium level and osmolarity.

Characterised by an osmotic shift of water from the ICF to the ECF (extracellular overhydration).

• Hypotonic – overhydration with decreased sodium level and osmolarity.

Characterised by an osmotic shift of water from the ECF to the ICF (cellular overhydration).

Signs and Symptoms of overhydration:
• Weight gain (primary symptom).
• Anorexia.
• Warm, moist skin.
• Vomiting and diarrhea.
• Peripheral edema.
• Effusions (pulmonary, pericardial, peritoneal).
• Pulmonary edema – increased respiratory rate, dyspnea, moist crackles on auscultation.
• Brain edema – headache, visual disturbances, skeletal muscle weakness, paresthesias, disorientation, lethargy and coma.

Symptoms of hypervolemia:
• Elevated Blood Pressure.
• Elevated CVP and JVP.
• Bounding pulses.
• Distended neck veins (JVP).
• Polyuria (if normal kidneys).

Isotonic Overhydration

Known as hypervolemia, isotonic overhydration as result forms excessive fluid in the extracellular fluid compartment. Only the extracellular fluid compartment is expanded, and fluid does not shift between extracellular and intracellular compartments.

Isotonic overhydration causes circulatory overload and interstitial edema; when sever or when it occurs in patients with poor cardiac function, congestive heart failure and pulmonary edema can result.

Causes:
- Renal Failure.
- Long-term corticosteroid therapy.
- Inadequately controlled IV therapy.
- Increase aldosterone.

Signs and Symptoms:
- Weight gain.
- Cardio – bounding, increased pulse rate, elevated BP, distended neck and hand veins, elevated central venous pressure.
- Respiratory – increased respiratory rate, dyspnea, moist crackles on auscultation.
- Neuromuscular – altered LOC, headache, visual disturbances, skeletal muscle weakness, paresthesias.
- Integumentary – pitting edema in dependent areas, skin pale and cool to touch.Increased motility in GI tract. Isotonic overhydration results in liver enlargement and ascites.

Lab values:
Normal serum osmolality and sodium level, decreased hematocrit, decreased BUN level, decreased serum sodium level.

Treatment:
- Restriction of fluid intake.

- Treatment of the cause of overhydration.
- Administration of diuretics.
- Some patients will need renal replacement therapies, such as dialysis or hemofiltration.

Hypotonic overhydration

Hypotonic overhydration is known as water intoxication. The excessive fluid moves into the intracellular space and all body fluid compartments expand. Electrolyte imbalances occur as a result of dilution.

Causes:
- Psychiatric disorder called psychogenic polydipsia.
- Early renal failure.
- Congestive heart failure.
- Syndrome of inappropriate antidiuretic hormone secretion.
- Inadequately controlled IV therapy.
- Replacement of isotonic fluid loss with hypotonic fluids.
- Irrigation of wounds and body cavities with hypotonic fluids.

Signs and Symptoms:

Water intoxication presents with symptoms that are largely neurologic due to the shifting of water into brain tissues and resultant dilution of sodium in the vascular space:
- Decreased mental alertness.
- Sleepiness.
- Anorexia.
- Poor motor coordination.
- Confusion.

In severe imbalances:
- Convulsions.
- Sudden weight gain.

- Hyperventilation.
- Warm, moist skin.

Signs of increased intracerebral pressure:
- Slow pulse.
- Increased SBP (more than 10 mm Hg).
- Decreased DBP (more than 10 mm Hg).
- Mild peripheral edema.

Lab values:

Decreased serum osmolality, decreased hematocrit, decreased BUN level, decreased serum sodium level, decreased urine specific gravity.

Treatment:

- Monitoring CVP, resp, neuromuscular, renal, integumentary, and GI status. Restriction fluid intake. Monitoring intake, output, and weight. Prevention further fluid overload, and restore normal fluid balance;
- Restriction of fluid intake.
- Treatment of the cause of overhydration.
- Administration diuretics; osmotic diuretics typically are prescribed first to prevent sever electrolyte imbalances.
- Monitor electrolyte values, and prepare to administer medication to treat imbalances, focusing on potassium and sodium.
- Hypertonic Saline solution that contains sodium chloride and is given to patients to treat severe hyponatremia (serum sodium levels below 120 mEq/l). These patients typically present with severe and potentially life-threatening symptoms such as: coma, seizures, and new focal neurological findings.

Hypertonic overhydration

Increased serum osmolarity leads to fluid shifting from the cells into the blood stream. Causes cell shrinkage and fluid

volume overload Fluid volume overload leads to increased blood pressure and increased cardiac workload. Can eventually lead to decrease cardiac output and congestive heart failure.

Causes:
- Administration of hypertonic IV.
- Over use of hypertonic enemas.
- Hypertonic tube feedings.
- Renal failure (Inability to excrete solutes and fluids).

Signs and Symptoms:
- Elevated Blood Pressure.
- Elevated CVP and JVP.
- Bounding pulses.
- Thirst - from cellular shrinkage.
- Disorientation, lethargy and coma.

Lab values:

High serum sodium, high serum osmolarity, decreased urine output – body retains water to dilute the sodium.

Treatment:

Fall precautions. Seizure precautions. Restrict foods and fluids high in Sodium. Oral administration of hypotonic fluids. May slowly administer hypotonic IV solution.

Table 6 **– Different diagnostic of overhydration**

Lab values	Hypotonic	Isotonic	Hypertonic
SeNa	–	n	+
Se osmolarity	–	n	+
Hb	–	–	–
Htk	(–)	–	–
Blood volume	+	+	+

Test tasks for checking the final level of knowledge:
1. Rapid loss of water by the body in a volume equal to the minimum of the total body water is deadly:
A. 10 %;
B. 20 %;
C. 30 %;
D. 40 %.
2. With any variants of acute isotonic dehydration, losses occur:
A. Water and electrolytes of the extracellular water space.
B. Cell electrolyte – free water.
C. Water and electrolytes in the gastrointestinal tract.
D. Blood cells.
3. Hypotonic dehydration is characterized by:
A. Thirst.
B. Anuria.
C. Hypernatremia.
D. Hypokalemia.
4. Hypertonic hyperhydration is characterized by:
A. Thirst.
B. Ease of correction of manifestations.
C. Intracellular edema.
D. High hematocrit.
5. What type of violation of the water balance is there no thirst:
A. hypoosmolar hypovolemia.
B. hyperosmolar hypovolemia.
C. isoosmolar hypovolemia.
D. hyperosmolar hypervolemia.
6. Hypotonic solutions are used to treat:
A. hypoosmolar hypovolemia.
B. hyperosmolar hypovolemia.
C. isoosmolar hypovolemia.

D. hyperosmolar hypervolemia.

6. Hypertonic solutions are used to treat:

A. hypoosmolar hypovolemia.

B. hyperosmolar hypovolemia.

C. isoosmolar hypovolemia.

D. hyperosmolar hypervolemia.

7. Patient age 56 years, body weight 90 kg. Diagnosis: coronary heart disease, atherosclerotic cardiosclerosis, obesity. The treatment includes drugs: Veroshpiron (100 mg per day) and Lasix (60 mg). After 3 days, despite treatment, the patient's condition worsened: blood pressure – 90/50 mm Hg, pulse – 108–120 min, CVP – 5 cm Hg, severe weakness, urine decreased to 850 ml per day, appetite and thirst are absent. Transferred to the intensive care unit with suspected myocardial infarction. No focal changes were detected on the ECG; the T wave became slightly lower. Potassium – 2.6 mmol/l; sodium – 120 mmol/l; chlorine – 86 mmol/l; calcium – 2.6 mmol/l; hematocrit – 0.49.

1. Determine the violation of the water – electrolyte state.

2. What is the cause of this condition?

3. Calculate plasma osmolarity.

4. What is the emergency care and treatment of this pathology?

THE MAIN ELECTROLYTES DISTURBANCES

Disorders of sodium balance
Hypernatremia

Hypernatremia is nearly always the result of either a loss of water in excess of sodium (hypotonic fluid loss) or the retention of large quantities of sodium. Even when renal concentrating ability is impaired, thirst is normally highly

effective in preventing hypernatremia. Hypernatremia is therefore most commonly seen in debilitated patients who are unable to drink, the very aged, the very young, and patients with altered consciousness. Patients with hypernatremia may have a low, normal, or high total body sodium content.

Net sodium balance is equal to total sodium intake (adults average 170 mmol/d) minus both renal sodium excretion and extrarenal sodium losses. One gram of sodium yields 43 mmol of Na^+ ions, whereas 1 g of sodium chloride yields 17 mmol of Na^+ ions. The kidneys' ability to vary urinary Na^+ excretion from less than 1 mmol/l to more than 100 mmol/l allows them to play a critical role in sodium balance.

Causes of hypernatremia:

1. Impaired thirst:
• Coma.
• Essential hypernatremia.
• Solute diuresis.
• Osmotic diuresis: diabetic ketoacidosis, nonketotic hyperosmolar coma, mannitol administration.

2. Excessive water losses:
• Renal:
− Neurogenic diabetes insipidus.
• Extra renal:
– Sweating.

3. Combined disorders:
• Coma plus hypertonic nasogastric feeding.

Hypernatremia with low total body sodium content

These patients have lost both sodium and water, but the water loss is in excess of the sodium loss. Hypotonic losses can be renal (osmotic diuresis) or extrarenal (diarrhea or sweat). In either case, patients usually manifest signs of hypovolemia. Urinary sodium concentration is generally greater than

20 mmol/l with renal losses and less than 10 mmol/l with extrarenal losses.

Hypernatremia with normal total body sodium content

This group of patients generally manifests signs of water loss without overt hypovolemia unless the water loss is massive. Total body sodium content is generally normal. Nearly pure water losses can occur via the skin, respiratory tract, or kidneys. Occasionally transient hypernatremia is observed with movement of water into cells following exercise, seizures, or rhabdomyolysis. The most common cause of hypernatremia with a normal total body sodium content is diabetes insipidus (in conscious individuals). Diabetes insipidus is characterized by marked impairment in renal concentrating ability that is due either to decreased ADH secretion (central diabetes insipidus) or failure of the renal tubules to respond normally to circulating ADH (nephrogenic diabetes insipidus). Rarely, "essential hypernatremia" may be encountered in patients with central nervous system disorders. These patients appear to have reset osmoreceptors that function at a higher baseline osmolality.

Hypernatremia with increased total body sodium content

This condition most commonly results from the administration of large quantities of hypertonic saline solutions (3 % NaCl or 7.5 % $NaHCO_3$). Patients with primary hyperaldosteronism and Cushing's syndrome may also have small elevations in serum sodium concentration along with signs of increased sodium retention.

Clinical manifestations of hypernatremia

Neurological manifestations predominate in patients with hypernatremia and are generally thought to result from cellular dehydration. Restlessness, lethargy, and hyperreflexia can progress to seizures, coma, and ultimately death.

Symptoms correlate more closely with the rate of movement of water out of brain cells than with the absolute level of hypernatremia. Rapid decreases in brain volume can rupture cerebral veins and result in focal intracerebral or subarachnoid hemorrhage. Seizures and serious neurological damage are common, particularly in children with acute hypernatremia when plasma [Na$^+$] exceeds 158 mmol/l.

Treatment of hypernatremia:

• The treatment of hypernatremia is aimed at restoring plasma osmolality to normal as well as correcting the underlying problem.

• Water deficits should generally be corrected over 48 h with a hypotonic solution such as 5 % dextrose in water. Abnormalities in extracellular volume must also be corrected.

• Hypernatremic patients with decreased total body sodium should be given isotonic fluids to restore plasma volume to normal prior to treatment with a hypotonic solution.

• Hypernatremic patients with increased total body sodium should be treated with a loop diuretic along with intravenous 5 % dextrose in water.

Hyponatremia

Hyponatremia invariably reflects water retention from either an absolute increase in TBW or a loss of sodium in excess of water.

Hyponatremia with low total body sodium

Progressive losses of both sodium and water eventually lead to extracellular volume depletion. As the intravascular volume deficit reaches 5–10 %, nonosmotic ADH secretion is activated. With further volume depletion, the stimuli for nonosmotic ADH release overcome any hyponatremia-induced suppression of ADH. Preservation of circulatory volume takes place at the expense of plasma osmolality.

Fluid losses resulting in hyponatremia may be renal or extrarenal in origin. Renal losses are most commonly related to thiazide diuretics and result in a urinary $[Na^+]$ greater than 20 mmol /L. Extrarenal losses are typically gastrointestinal and usually produce a urine $[Na^+]$ of less than 10 mmol/l. A major exception to the latter is hyponatremia due to vomiting, which can result in a urinary $[Na^+]$ greater than 20 mmol/l. In those instances, bicarbonaturia from the associated metabolic alkalosis obligates concomitant excretion of Na^+ with HCO_3 to maintain electrical neutrality in the urine; urinary chloride concentration, however, is usually less than 10 mmol/l.

Hyponatremia with increased total body sodium

Edematous disorders are characterized by an increase in both total body sodium and TBW. When the increase in water exceeds that in sodium, hyponatremia occurs. Edematous disorders include congestive heart failure, cirrhosis, renal failure, and nephrotic syndrome. Hyponatremia in these settings results from progressive impairment of renal free water excretion and generally parallels underlying disease severity. Pathophysiological mechanisms include nonosmotic ADH release and decreased delivery of fluid to the distal diluting segment in nephrons.

Hyponatremia with normal total body sodium

Hyponatremia in the absence of edema or hypovolemia may be seen with glucocorticoid insufficiency, hypothyroidism, drug therapy (chlorpropamide and cyclophosphamide), and the syndrome of inappropriate antidiuretic hormone secretion (SIADH). The hyponatremia associated with adrenal hypofunction may be due to cosecretion of ADH with corticotropin-releasing factor (CRF).

Clinical manifestations of hyponatremia

Symptoms of hyponatremia are primarily neurological and result from an increase in intracellular water. Their severity is generally related to the rapidity with which extracellular

hypoosmolality develops. Patients with mild to moderate hyponatremia ($[Na^+] > 125$ mmol/l) are frequently asymptomatic. Early symptoms are typically nonspecific and may include anorexia, nausea, and weakness. Progressive cerebral edema, however, results in lethargy, confusion, seizures, coma, and finally death. Serious manifestations of hyponatremia are generally associated with plasma sodium concentrations < 120 mmol/l.

Treatment of hyponatremia

As with hypernatremia, the treatment of hyponatremia is directed at correcting both the underlying disorder as well as the plasma $[Na^+]$. Isotonic saline is generally the treatment of choice for hyponatremic patients with decreased total body sodium content. Once the extracellular fluid deficit is corrected, spontaneous water diuresis returns plasma $[Na^+]$ to normal. Conversely, water restriction is the primary treatment for hyponatremic patients with normal or increased total body sodium. More specific treatments such as hormone replacement in patients with adrenal or thyroid hypofunction and measures aimed at improving cardiac output in patients with heart failure may also be indicated.

Acute symptomatic hyponatremia requires prompt treatment. In such instances, correction of plasma $[Na^+]$ to > 125 mEq/L is usually sufficient to alleviate symptoms. The amount of NaCl necessary to raise plasma $[Na^+]$ to the desired value, the Na^+ deficit, can be estimated by the following formula:

$$Na \text{ deficit} = TBW \ x \ (Na \text{ desired} - Na \text{ present}).$$

The following correction rates have been suggested: for mild symptoms, 0.5 mmol/l/h or less; for moderate symptoms, 1 mmol/l/h or less; and for severe symptoms, 1.5 mmol/l/h or less.

Disorders of potassium balance
Normal potassium balance

Potassium plays a major role in the electrophysiology of cell membranes as well as carbohydrate and protein synthesis. The resting cell membrane potential is normally dependent on the ratio of intracellular to extracellular potassium concentrations. Intracellular potassium concentration is estimated to be 140 mmol/l, whereas extracellular potassium concentration is normally about 4 mmol/l. Although the regulation of intracellular $[K^+]$ is poorly understood, extracellular $[K^+]$ generally reflects the balance between potassium intake and excretion.

Under some conditions, a redistribution of K^+ between the ECF and ICF compartments can result in marked changes in extracellular $[K^+]$ without a change in total body potassium content.

Renal excretion of potassium can vary from as little as 5 mmol/l to over 100 mmol/l. All the potassium filtered in glomeruli is normally reabsorbed in the proximal tubule and the loop of Henle. The potassium excreted in urine is the result of distal tubular secretion. Potassium secretion in the distal tubules is coupled to aldosterone-mediated reabsorption of sodium.

Extracellular potassium concentration is closely regulated by cell membrane Na^+–K^+ ATPase activity as well as plasma $[K^+]$. The former regulates the distribution of potassium between cells and ECF, whereas the latter is the major determinant of urinary potassium excretion.

Intercompartmental shifts of potassium

Intercompartmental shifts of potassium are known to occur following changes in extracellular pH, circulating insulin levels, circulating catechol-amine activity, plasma osmolality, and possibly hypothermia. Insulin and catecholamines are known to directly affect Na^+–K^+ ATPase activity and decrease

plasma [K$^+$]. Exercise can also transiently increase plasma [K$^+$] as a result of the release of K$^+$ by muscle cells; the increase in plasma [K$^+$] is proportionate to the intensity and duration of muscle activity.

Changes in extracellular hydrogen ion concentration (pH) directly affect extracellular [K$^+$] because the ICF may buffer up to 60 % of an acid load. During acidosis, extracellular hydrogen ions enter cells, displacing intracellular potassium ions; the movement of potassium ions out of cells maintains electrical balance but increases extracellular and plasma [K$^+$]. Conversely, during alkalosis, extracellular potassium ions move into cells to balance the movement of hydrogen ions out of cells; as a result, plasma [K$^+$] decreases.

Changes in circulating insulin levels can directly alter plasma [K$^+$] independent of glucose transport. Insulin enhances the activity of membrane-bound Na$^+$–K$^+$ ATPase, increasing cellular uptake of potassium in the liver and in skeletal muscle. In fact, insulin secretion may play an important role in the basal control of plasma potassium concentration and facilitates the handling of increased potassium loads.

Sympathetic stimulation also increases intracellular uptake of potassium by enhancing Na$^+$–K$^+$ ATPase activity. This effect is mediated through activation of β2-adrenergic receptors. In contrast, adrenergic activity may impair the intracellular movement of K$^+$. Plasma [K$^+$] often decreases following the administration of β2-adrenergic agonists as a result of uptake of potassium by muscle and the liver. Moreover, β2-adrenergic blockade can impair the handling of a potassium load in some patients.

Acute increases in plasma osmolality (hypernatremia, hyperglycemia, or mannitol administration) are reported to increase plasma [K$^+$] (about 0.6 mmol/l per 10 mOsm/L). In such instances, the movement of water out of cells (down its

osmotic gradient) is accompanied by movement of K^+ out of cells.

Hypothermia has been reported to lower plasma $[K^+]$ as a result of cellular uptake. Rewarming reverses this shift and may result in transient hyperkalemia if potassium was given during the hypothermia.

Urinary Excretion of Potassium

Urinary potassium excretion generally parallels its extracellular concentration. Potassium is secreted by tubular cells in the distal nephron. Extracellular $[K^+]$ is a major determinant of aldosterone secretion from the adrenal gland. Hyperkalemia stimulates aldosterone secretion, whereas hypokalemia suppresses aldosterone secretion. Renal tubular flow in the distal nephron may also be an important determinant of potassium secretion because high tubular flow rates (as during osmotic diuresis) increase potassium secretion by keeping the capillary to renal tubular gradient for potassium secretion high. Conversely, slow tubular flow rates increase $[K^+]$ in tubular fluid and decrease the gradient for K^+ secretion.

Hypokalemia

Hypokalemia is defined as plasma $[K^+]$ less than 3.5 mmol/l and can occur as a result of:

1. An intercompartmental shift of K^+ (see above).
2. Increased potassium loss.
3. An inadequate potassium intake.

Plasma potassium concentration typically correlates poorly with the total potassium deficit.

Causes of hypokalemia:

1. Excess renal loss:
- Mineralocorticoid excess.
- Primary hyperaldosteronism (Conn's syndrome).
- Glucocorticoid-remediable hyperaldosteronism.
- Renin excess.
- Renovascular hypertension.

- Diuresis.
- Chronic metabolic alkalosis.

2. Gastrointestinal losses:

- Vomiting.
- Diarrhea, particularly secretory diarrheas.

3. ECF – ICF shifts:

- Acute alkalosis.
- Insulin therapy.

4. Inadequate intake.

Hypokalemia due to the intracellular movement of potassium occurs with alkalosis, insulin therapy, β2-adrenergic agonists, and hypothermia and during attacks of hypokalemic periodic paralysis (see above). Hypokalemia may also be seen following transfusion of frozen red cells; these cells lose potassium in the preservation process and take up potassium following reinfusion.

Increased potassium losses are nearly always either renal or gastrointestinal. Renal wasting of potassium is most commonly the result of a diuresis or enhanced mineralocorticoid activity.

Increased gastrointestinal loss of potassium is most commonly due to vomiting, nasogastric suctioning, or diarrhea. Other gastrointestinal causes include losses from fistulae, laxative abuse, villous adenomas, and pancreatic tumors secreting vasoactive intestinal peptide.

Chronic increased sweat formation occasionally causes hypokalemia, particularly when potassium intake is limited. Dialysis with a low-potassium-containing dialysate solution can also cause hypokalemia.

A urinary $[K^+]$ less than 20 mmol/l is generally indicative of increased extrarenal losses, whereas concentrations greater than 20 mmol/l suggest renal wasting of K^+.

Clinical Manifestations of hypokalemia

Hypokalemia can produce widespread organ dysfunction. Most patients are asymptomatic until plasma $[K^+]$ falls below 3 mmol/l. Cardiovascular effects are most prominent and include an abnormal electrocardiogram (ECG), arrhythmias, decreased cardiac contractility, and a labile arterial blood pressure due to autonomic dysfunction. ECG manifestations are primarily due to delayed ventricular repolarization and include T-wave flattening and inversion, an increasingly prominent U wave, ST-segment depression, increased P-wave amplitude, and prolongation of the P–R interval. Increased myocardial cell automaticity and delayed repolarization promote both atrial and ventricular arrhythmias.
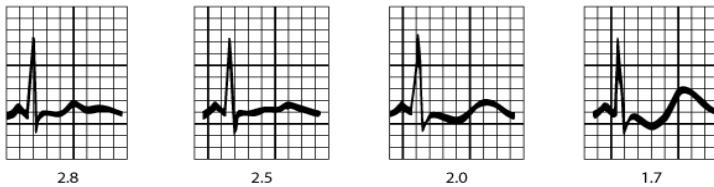

Figure 8 – **Hypokalemia. ECG changes**

Neuromuscular effects of hypokalemia include skeletal muscle weakness (particularly the quadriceps), ileus, muscle cramping, tetany, and, rarely, rhabdomyolysis.

The treatment of hypokalemia depends on the presence and severity of any associated organ dysfunction. Significant ECG changes such as ST-segment changes or arrhythmias mandate continuous ECG monitoring, particularly during intravenous K^+ replacement.

Treatment of Hypokalemia

Oral replacement with potassium chloride solutions is generally safest. Replacement of the potassium deficit usually requires several days. Intravenous replacement of potassium

chloride should usually be reserved for patients with or at risk for serious cardiac manifestations or muscle weakness. The goal of intravenous therapy is to remove the patient from immediate danger and not necessarily to correct the entire potassium deficit. Peripheral intravenous replacement should not exceed 8 mmol/h because of the irritative effect of potassium on peripheral veins. Dextrose – containing solutions should generally be avoided because the resulting hyperglycemia and secondary insulin secretion may actually lower plasma [K^+] even further. Faster intravenous replacement (10–20 mmol/h) requires a central venous catheter and close monitoring of the ECG.

Hyperkalemia

Hyperkalemia exists when plasma [K^+] exceeds 5.5 mEq/l. Hyperkalemia rarely occurs in normal individuals because of the kidney's tremendous capacity to excrete potassium. When potassium intake is increased slowly, the kidneys can excrete as much as 500 mmol of K^+ per day. The sympathetic system and insulin secretion also appear to play important roles in preventing acute increases in plasma [K^+] following potassium loads.

Hyperkalemia can result from:

1. An intercompartmental shift of potassium ions.
2. Decreased urinary excretion of potassium.
3. An increased potassium intake.

Causes of hyperkalemia:

1. Intercompartmental shifts:
- Acidosis.
- Hypertonicity.
- Rhabdomyolysis.
- Red cell hemolysis.
- Excessive exercise.
- Succinylcholine.

2. Decreased renal potassium excretion:

- Renal failure.
- Decreased mineralocorticoid activity and impaired Na^+ reabsorption.
- Competitive potassium-sparing diuretics.
- Nonsteroidal antiinflammatory drugs.

3. Increased potassium intake:

- Salt substitutes.

Hyperkalemia due to extracellular movement of potassium

Movement of K^+ out of cells can be seen with administration of succinylcholine, acidosis, cell lysis following chemotherapy, hemolysis, rhabdomyolysis, massive tissue trauma, hyperosmolality, digitalis overdoses, administration of arginine hydrochloride, and β2-adrenergic blockade.

Arginine hydrochloride, which is used to treat metabolic alkalosis, can cause hyperkalemia as the cationic arginine ions enter cells and potassium ions move out to maintain electroneutrality.

Hyperkalemia due to decreased renal excretion of potassium

Decreased renal excretion of potassium can result from:

1. Marked reductions in glomerular filtration.
2. Decreased aldosterone activity.
3. Defect in potassium secretion in the distal nephron.

Glomerular filtration rates less than 5 ml/min are nearly always associated with hyperkalemia. Patients with decreased degrees of renal impairment can also readily develop hyperkalemia when faced with increased potassium loads (dietary, catabolic, or iatrogenic).

Hypokalemia due to decreased aldosterone activity can result from a primary defect in adrenal hormone synthesis or a defect in the renin-aldosterone system. Patients with primary adrenal insufficiency (Addison's disease) and those with

isolated 21-hydroxylase adrenal enzyme deficiency have marked impairment of aldosterone synthesis.

Drugs interfering with the renin–aldosterone system have the potential to cause hyperkalemia, particularly in the presence of any degree of renal impairment. Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit prostaglandin-mediated renin release. Angiotensin-converting enzyme (ACE) inhibitors interfere with angiotensin II-mediated release of aldosterone. Large doses of heparin can interfere with aldosterone secretion.

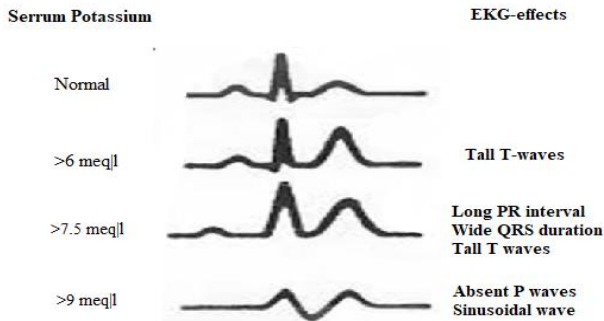### Hyperkalemia due to increased potassium intake

Increased potassium loads rarely cause hyperkalemia in normal individuals unless large amounts are given rapidly and intravenously. Hyperkalemia, however, may be seen when potassium intake is increased in patients receiving β2-blockers or those with renal impairment or insulin deficiency.

Clinical manifestations of hyperkalemia

The most important effects of hyperkalemia are on skeletal and cardiac muscle. Skeletal muscle weakness is generally not seen until plasma $[K^+]$ is greater than 8 mmol/l. The weakness is due to sustained spontaneous depolarization and inactivation of Na^+ channels of muscle membrane (similar to succinylcholine), eventually resulting in ascending paralysis.

Cardiac manifestations (Figure 10) are primarily due to delayed depolarization and consistently present when plasma $[K^+]$ is greater than 7 mmol/l.

ECG changes characteristically progress (in order) from symmetrically peaked T waves (often with a shortened QT interval) widening of the QRS complex prolongation of the P-R interval loss of the P wave loss of R-wave amplitude ST-segment depression (occasionally elevation) an ECG that resembles a sine wave – before progression to ventricular fibrillation and asystole. Contractility appears to be relatively well preserved. Hypocalcemia, hyponatremia, and acidosis accentuate the cardiac effects of hyperkalemia.

Serrum Potassium		EKG-effects
Normal		
>6 meq|l		Tall T-waves
>7.5 meq|l		Long PR interval Wide QRS duration Tall T waves
>9 meq|l		Absent P waves Sinusoidal wave

Figure 9 – **Hyperkalemia. ECG changes**
Treatment of hyperkalemia

Because of its lethal potential, hyperkalemia exceeding 6 mEq/l should always be treated. Treatment is directed at reversing cardiac manifestations, and skeletal muscle weakness, and restoring of plasma $[K^+]$ to normal. The number of treatment modalities employed (see below) depends on the severity of manifestations as well as the cause of hyperkalemia. Hyperkalemia associated with hypoaldosteronism can be treated with mineralocorticoid replacement. Drugs contributing to hyperkalemia should be discontinued and sources of increased potassium intake reduced or stopped.

Calcium (5–10 ml of 10 % calcium gluconate or 3–5 ml of 10 % calcium chloride) partially antagonizes the cardiac effects of hyperkalemia and is useful in patients with marked hyperkalemia. Its effects are rapid but unfortunately short lived. Care must be exercised in patients taking digoxin, as calcium potentiates digoxin toxicity.

When metabolic acidosis is present, intravenous sodium bicarbonate will promote cellular uptake of potassium and can decrease plasma $[K^+]$ within 15 min. β2-agonists promote cellular uptake of potassium and may be useful in acute hyperkalemia associated with massive transfusions; low doses

of epinephrine (0.5–2 mg/min) often rapidly decrease plasma [K^+] and provide inotropic support in this setting. An intravenous infusion of glucose and insulin (30–50 g of glucose with 10 units of insulin) is also effective in promoting cellular uptake of potassium and lowering plasma [K^+], but often takes up to 1 h for peak effect.

For patients with some renal function, furosemide is a useful adjunct in increasing urinary excretion of potassium. In the absence of renal function, elimination of excess potassium can be accomplished only with nonabsorbable cation-exchange resins such as oral or rectal sodium polystyrene sulfonate (Kayexalate).

Dialysis is indicated in symptomatic patients with severe or refractory hyperkalemia. Maximal potassium removal with hemodialysis approaches 50 mmol/h.

Disorders of calcium balance

Although 98 % of total body calcium is in bone, maintenance of a normal extracellular calcium concentration is critical to homeostasis. Calcium ions are involved in nearly all essential biological functions, including muscle contraction, the release of neurotransmitters and hormones, blood coagulation, and bone metabolism. It is not surprising that abnormalities in calcium balance can result in profound physiological derangements.

Normal calcium balance

Calcium intake in adults averages 600–800 mg/d. Intestinal absorption of calcium occurs primarily in the proximal small bowel but is quite variable. Calcium is also secreted into the intestinal tract; moreover, this secretion appears to be constant and independent of absorption. Up to 80 % of the daily calcium intake is normally lost in feces.

The kidneys are responsible for calcium excretion. Renal calcium excretion averages 100 mg/d but can be varied from as low as 50 mg/d to more than 300 mg/d. Normally, 98 % of the filterable calcium is reabsorbed. Calcium reabsorption parallels that of sodium in the proximal renal tubules and the ascending loop of Henle. In the distal tubules, however, calcium reabsorption is dependent on parathyroid hormone secretion, whereas sodium reabsorption is dependent on aldosterone secretion. Increased parathyroid hormone levels enhance distal calcium reabsorption and decrease urinary calcium excretion.

Plasma calcium concentration

The normal plasma calcium concentration is 2.1–2.6 mmol/l. Approximately 50 % is in the free ionized form, 40 % is protein bound (mainly to albumin), and 10 % is complexed with anions such as citrate and amino acids. It is the free ionized calcium concentration ($[Ca^{2+}]$) that is physiologically most important. Plasma $[Ca^{2+}]$ is normally 1.19–1.33 mmol/l.

Changes in plasma pH directly affect the degree of protein binding and thus ionized calcium concentration.

Regulation of extracellular ionized calcium concentration

Calcium normally enters extracellular fluid by either absorption from the intestinal tract or resorption of bone; only 0.5–1 % of calcium in bone is exchangeable with extracellular fluid. In contrast, calcium normally leaves the extracellular compartment by:

1. Deposition into bone.
2. Urinary excretion.
3. Secretion into the intestinal tract.
4. Sweat formation.

Extracellular $[Ca^{2+}]$ is closely regulated by three hormones: parathyroid hormone (PTH), vitamin D, and

calcitonin. These hormones act primarily on bone, the distal renal tubules, and the small bowel.

PTH is the most important regulator of plasma $[Ca^{2+}]$. Decreases in plasma $[Ca^{2+}]$ stimulate PTH secretion, while increases in plasma $[Ca^{2+}]$ inhibit PTH secretion. The calcemic effect of PTH is due to:

1. Mobilization of calcium from bone.

2. Enhancement of calcium reabsorption in the distal renal tubules.

3. An indirect increase in intestinal absorption of calcium via acceleration of 1.25-dihydroxycholecalciferol synthesis in the kidneys.

Vitamin D augments intestinal absorption of calcium, facilitates the action of PTH on bone, and appears to augment renal reabsorption of calcium in the distal tubules.

Calcitonin is a polypeptide hormone that is secreted by parafollicular cells in the thyroid gland. Its secretion is stimulated by hypercalcemia and inhibited by hypocalcemia. Calcitonin inhibits bone reabsorption and increases urinary calcium excretion.

Hypercalcemia

Hypercalcemia can occur as a result of a variety of disorders. In primary hyperparathyroidism, secretion of PTH is increased and is independent of $[Ca^{2+}]$. In contrast, in secondary hyperparathyroidism (chronic renal failure or malabsorption), the elevated PTH levels are in response to chronic hypocalcemia. Prolonged secondary hyperparathyroidism, however, can occasionally result in autonomous secretion of PTH, resulting in a normal or elevated $[Ca^{2+}]$ (tertiary hyperparathyroidism).

Patients with cancer can present with hypercalcemia whether or not bone metastases are present. Direct bony destruction or secretion of humoral mediators of hypercalcemia (PTH-like substances, cytokines, or prostaglandins) is probably

responsible in most patients. Hypercalcemia due to increased turnover of calcium from bone can also be encountered in patients with benign conditions such as Paget's disease and chronic immobilization. Increased gastrointestinal absorption of calcium can lead to hypercalcemia in patients with the milk-alkali syndrome (marked increase in calcium intake), hypervitaminosis D.

Treatment of hypercalcemia

Symptomatic hypercalcemia requires rapid treatment. The most effective initial treatment is rehydration followed by a brisk diuresis (urinary output 200–300 ml/h) with administration of intravenous saline infusion and a loop diuretic to accelerate calcium excretion. Premature diuretic therapy prior to rehydration may aggravate the hypercalcemia by additional volume depletion. Renal loss of potassium and magnesium usually occurs during diuresis, and laboratory monitoring and intravenous replacement should be performed as necessary. Although hydration and diuresis may remove the potential risk of cardiovascular and neurological complications of hypercalcemia, the serum calcium usually remains elevated above normal. Additional therapy with a bisphosphonate or calcitonin may be required to further lower the serum calcium. Severe hypercalcemia usually requires additional therapy after saline hydration and lasix calciuresis. Bisphosphonates (pamidronate 60–90 mg intravenously) or calcitonin (2–8 U/kg subcutaneously) are preferred agents. Dialysis may be necessary in the presence of renal or cardiac failure.

It is necessary to look for the underlying etiology and direct appropriate treatment toward the cause of the hypercalcemia once the initial threat of hypercalcemia has been removed. Approximately 90 % of all hypercalcemia is due to either malignancy or hyperparathyroidism. The best laboratory test for discriminating between these two main categories of hypercalcemia is the double-antibody PTH assay. The serum

PTH concentration will usually be suppressed in malignancy states and elevated in hyperparathyroidism.

Hypocalcemia

Hypocalcemia should be diagnosed only on the basis of the plasma ionized calcium concentration. When direct measurements of plasma $[Ca^{2+}]$ are not available, the total calcium concentration must be corrected for decreases in plasma albumin concentration.

The causes of hypocalcemia:

- Hypoparathyroidism.
- Vitamin D deficiency.
- Nutritional.
- Malabsorption.
- Postsurgical (gastrectomy, short bowel).
- Inflammatory bowel disease.
- Altered vitamin D metabolism.
- Magnesium deficiency.
- Chelation of calcium.
- Multiple rapid red blood transfusions or rapid infusion; of large amounts of albumin.

Hypocalcemia due to hypoparathyroidism is a relatively common cause of symptomatic hypocalcemia. Hypoparathyroidism may be surgical, idiopathic, or part of multiple endocrine defects (most often with adrenal insufficiency), or may be associated with hypomagnesemia. Magnesium deficiency is postulated to impair the secretion of PTH and antagonize its effects on bone. Hypocalcemia during sepsis is also thought to be due to suppression of PTH release.

Chelation of calcium ions with the citrate ions in blood preservatives is an important cause of perioperative hypocalcemia; similar transient decreases in $[Ca^{2+}]$ are also theoretically possible following rapid infusions of large volumes of albumin.

Clinical manifestations of hypocalcemia

Manifestations include paresthesias, confusion, laryngeal stridor (laryngospasm), carpopedal spasm (Trousseau's sign), masseter spasm, and seizures. Biliary colic and bronchospasm have also been described. Cardiac irritability can lead to arrhythmias. Decreased cardiac contractility may result in heart failure, hypotension, or both. ECG signs include prolongation of the QT interval. The severity of ECG manifestations is not necessarily correlated with the degree of hypocalcemia.

Symptomatic hypocalcemia is a medical emergency and should be treated immediately with intravenous calcium chloride (3–5 ml of a 10 % solution) or calcium gluconate (10–20 ml of a 10 % solution). (Ten milliliters of 10 % $CaCl_2$ contains 272 mg of Ca^{2+}, whereas 10 ml of 10 % calcium gluconate contains only 93 mg of Ca^{2+}.) To avoid precipitation, intravenous calcium should not be given with bicarbonate or phosphate-containing solutions. Serial ionized calcium measurements are mandatory. Repeat boluses or a continuous infusion (Ca^{2+} 1–2 mg/kg/h) may be necessary. Plasma magnesium concentration should be checked to exclude hypomagnesemia. In chronic hypocalcemia, oral calcium ($CaCO_3$) and vitamin D replacement are usually necessary.

Disorders of phosphorus balance

Phosphorus is an important intracellular constituent. Its presence is required for the synthesis of:

1. The phospholipids and phosphoproteins in cell membranes and intracellular organelles.

2. The phosphonucleotides involved in protein synthesis and reproduction.

3. ATP used for the storage of energy.

Only 0.1 % of total body phosphorus is in extracellular fluid, 85 % is in bone and 15 % is intracellular.

Normal phosphorus balance

Phosphorus intake averages 800–1 500 mg/d in adults. About 80% of that amount is normally absorbed in the proximal small bowel. Vitamin D increases intestinal absorption of phosphorus. The kidneys are the major route for phosphorus excretion and are responsible for regulating total body phosphorus content. Urinary excretion of phosphorus depends on both intake and plasma concentration. Secretion of PTH can augment urinary phosphorus excretion by inhibiting its proximal tubular reabsorption. The latter effect may be offset by PTH-induced release of phosphate from bone.

Plasma phosphorus concentration

Plasma phosphorus exists in both organic and inorganic forms. Organic phosphorus is mainly in the form of phospholipids. Of the inorganic phosphorus fraction, 80 % is filterable in the kidneys and 20 % is protein bound. The majority of inorganic phosphorus is in the form of $H_2PO_4^-$ and HPO_4^{2-} in a 1:4 ratio. By convention, plasma phosphorus is measured as milligrams of elemental phosphorus.

Normal plasma phosphorus concentration is 0.8–1.45 mmol/l in adults. Plasma phosphorus concentration is usually measured during fasting, because a recent carbohydrate intake transiently decreases the plasma phosphorus concentration. Hypophosphatemia increases vitamin D production, whereas hyperphosphatemia depresses it.

Hyperphosphatemia

Hyperphosphatemia may be seen with increased phosphorus intakes (abuse of phosphate laxatives or excessive potassium phosphate administration), decreased phosphorus excretion (renal insufficiency), or massive cell lysis (following chemotherapy for lymphoma or leukemia).

Clinical manifestations of hyperphosphatemia

Although hyperphosphatemia itself does not appear to be directly responsible for any functional disturbances, its

secondary effect on plasma $[Ca^{2+}]$ can be important. Marked hyperphosphatemia is thought to lower plasma $[Ca^{2+}]$ by precipitation and deposition of calcium phosphate in bone and soft tissues.

Treatment of hyperphosphatemia

Hyperphosphatemia is generally treated with phosphate-binding antacids such as aluminum hydroxide or aluminum carbonate.

Hypophosphatemia

Hypophosphatemia is usually the result of either a negative phosphorus balance or cellular uptake of extracellular phosphorus (an intercompartmental shift). Intercompartmental shifts of phosphorus can occur during alkalosis and following carbohydrate ingestion or insulin administration. Large doses of aluminum – or magnesium – containing antacids, severe burns, inadequate phosphorus supplementation during hyperalimentation, diabetic ketoacidosis, alcohol withdrawal, and prolonged respiratory alkalosis can all produce a negative phosphorus balance and lead to severe hypophosphatemia. In contrast to respiratory alkalosis, metabolic alkalosis rarely leads to severe hypophosphatemia.

Clinical manifestations of hypophosphatemia

Mild to moderate hypophosphatemia is generally asymptomatic. In contrast, severe hypophosphatemia is often associated with widespread organ dysfunction. Cardiomyopathy, impaired oxygen delivery (decreased 2.3-diphosphoglycerate levels), hemolysis, impaired leukocyte function, platelet dysfunction, encephalopathy, skeletal myopathy, respiratory failure, rhabdomyolysis, skeletal demineralization, metabolic acidosis, and hepatic dysfunction have all been associated with severe hypophosphatemia.

Treatment of hypophosphatemia

Oral phosphorus replacement is generally preferable to parenteral replacement because of the risk of hypocalcemia and

metastatic calcification. Potassium or sodium phosphate (2–5 mg of elemental phosphorus per kilogram, or 10–45 mmol slowly over 6–12 h) is generally used for intravenous correction of severe symptomatic hypophosphatemia.

Disorders of magnesium balance

Magnesium is an important intracellular cation that functions as a cofactor in many enzyme pathways. Only 1–2 % of total body magnesium stores is in the ECF compartment; 67 % is contained in bone whereas the remaining 31 % is intracellular.

Normal magnesium balance

Magnesium intake averages 240–370 mg/d in adults. Of that amount, only 30–40 % is absorbed, mainly in the distal small bowel. Renal excretion is the primary route for elimination, averaging 6–12 mmol/d. Magnesium reabsorption by the kidneys is very efficient. Twenty-five percent of filtered magnesium is reabsorbed in the proximal tubule, whereas 50–60 % is reabsorbed in the thick ascending limb of the loop of Henle. Factors known to increase magnesium reabsorption in the kidneys include hypomagnesemia, parathyroid hormone, hypocalcemia, ECF depletion, and metabolic alkalosis. Factors known to increase renal excretion include hypermagnesemia, acute volume expansion, hyperaldosteronism, hypercalcemia, ketoacidosis, diuretics, phosphate depletion, and alcohol ingestion.

Hypermagnesemia

Increases in plasma $[Mg^{2+}]$ are nearly always due to excessive intake (magnesium-containing antacids or laxatives), renal impairment (GFR < 30 ml/min), or both. Iatrogenic hypermagnesemia can also occur during magnesium sulfate therapy for gestational hypertension in the mother as well as the fetus. Less common causes include adrenal insufficiency, hypothyroidism, rhabdomyolysis, and lithium administration.

Clinical manifestations of hypermagnesemia

Symptomatic hypermagnesemia typically presents with neurological, neuromuscular, or cardiac manifestations. Hyporeflexia, sedation, and skeletal muscle weakness are characteristic features. Hypermagnesemia appears to impair the release of acetylcholine and decreases motor end-plate sensitivity to acetylcholine in muscle. Vasodilation, bradycardia, and myocardial depression can lead to hypotension at levels > 100 mmol/l. ECG signs are inconsistent but often include prolongation of the P–R interval and widening of the QRS complex. Marked hypermagnesemia can lead to respiratory arrest.

Treatment of hypermagnesemia

All sources of magnesium intake (most often antacids) should be stopped. Intravenous calcium (1 g calcium gluconate) can temporarily antagonize most of the effects of hypermagnesemia. A loop diuretic along with an infusion of ½-normal saline in 5 % dextrose enhances urinary magnesium excretion. Diuresis with normal saline is generally not recommended to decrease the likelihood of iatrogenic hypocalcemia, because the latter potentiates the effects of hypermagnesemia. Dialysis may be necessary in patients with marked renal impairment.

Hypomagnesemia

Hypomagnesemia is a common and frequently overlooked problem, particularly in critically ill patients. Associated deficiencies of other intracellular components such as potassium and phosphorus are common. Deficiencies of magnesium are generally the result of inadequate intake, reduced gastrointestinal absorption, or increased renal excretion. Drugs that cause renal wasting of magnesium include ethanol, theophylline, diuretics, cisplatin, aminoglycosides, cyclosporine, amphotericin B, pentamidine, and granulocyte colony-stimulating factor.

Causes of hypomagnesemia:
1. Inadequate intake:
• Nutritional.
2. Reduced gastrointestinal absorption:
•Malabsorption syndrome.
•Small bowel or biliary fistulas.
•Prolonged nasogastric suctioning.
•Severe diarrhea.
3. Increased renal losses:
•Diuresis.
•Diabetic ketoacidosis.
•Hyperparathyroidism.
•Hyperaldosteronism.
•Hypophosphatemia.
•Drugs.
•Postobstructive diuresis.

Clinical manifestations of hypomagnesemia

Most patients with hypomagnesemia are asymptomatic, but anorexia, weakness, fasciculation, paresthesias, confusion, ataxia, and seizures may be encountered. Hypomagnesemia is frequently associated with both hypocalcemia (impaired parathyroid hormone secretion) and hypokalemia (due to renal K^+ wasting). Cardiac manifestations include electrical irritability and potentiation of digoxin toxicity; both factors are aggravated by hypokalemia. Hypomagnesemia is associated with an increased incidence of atrial fibrillation. Prolongation of the P–R and Q–T intervals may also be present and usually reflects concomitant hypocalcemia.

Treatment of hypomagnesemia

Asymptomatic hypomagnesemia can be treated orally (magnesium sulfate heptahydrate or magnesium oxide) or intramuscularly (magnesium sulfate). Serious manifestations

such as seizures should be treated with intravenous magnesium sulfate, 1–2 g (4–8 mmol) given slowly over 15–60 min.

Test tasks for checking the final level of knowledge:

1. The normal content of electrolytes in the blood plasma is:

A. Potassium 3 mmol/l; sodium 110 mmol/l; chlorine 60 mmol/l.

B. Potassium 3.2 mmol/l; sodium 120 mmol/l; chlorine 80 mmol/l.

C. Potassium 4 mmol/l; sodium 140 mmol/l; chlorine 100 mmol/l.

D. Potassium 5.7 mmol/l; sodium 150 mmol/l; chlorine 120 mmol/l.

2. Indications for adjuvant renal therapy (hemodialysis) is the ion concentration:

A. Potassium in the blood plasma 5 mmol/l.

B. Potassium in the blood plasma 7 mmol/l.

C. Plasma calcium 1 mmol/l.

D. Plasma calcium 2 mmol/l.

3. Normal total sodium intake for adults in average:

A. 170mmol/d.

B. 70 mmol/d.

C. 120 mmol/d.

D. 250 mmol/d.

4. The amount of potassium in the body in cells:

A. 58 %.

B. 78 %.

C. 88 %.

D. 98 %.

5. According to the law of electroneutrality, hyperchloremia causes:

A. Metabolic alkalosis.

B. Metabolic acidosis.

C. Lactic acidosis.

D. Hyponatremia.

6. Hyperkalemia is characteristic of:

A. Exhausting vomiting.

B. Adrenocorticoid metabolic phase after operations and injuries.

C. Diabetic ketoacidosis.

D. Intestinal obstruction.

7. Potassium:

A. Is found mainly in extracellular fluids.

B. In cells is almost completely in mobile ionized condition.

C. Daily physiological requirement is 2 (1–3) mmol per 1 kg of body weight.

D. Daily requirement does not depend on physical activity.

8. With deep hypokalemia:

A. Possible cardiac arrest in diastole.

B. Spastic intestinal pains are natural.

C. Changes on the ECG occur late and the dynamics of the ECG pictures has no practical value.

D. There is a parallelism of ECG changes and the severity of hypokaliemissions.

9. Direct functional potassium antagonist is:

A. Carbon dioxide.

B. Insulin.

C. Glucose.

D. Calcium.

10. The patient was transferred to the intensive care unit from the operating room, where he underwent surgery for a traumatic rupture of the spleen, complicated by massive blood loss. Age 42 years, body weight 75 kg. During the operation, the infusion amounted to 6 500 ml, of which 2 100 ml – red blood cell mass. conscious, complains of weakness,

paresthesia, numbness of the extremities, muscle twitching, blood pressure of 90 and 60 mm Hg, pulse 48 in 1 min, arrhythmic; CVP = 8 cm water. Diuresis was 60 ml in 2 hours.

In the blood test: Er – 3.5 · 10^{12}/l, Hb – 100 g/l, Ht = 0.38; total protein = 60 g/l, albumin = 25 g/l, globulins = = 35 g/l. blood glucose – 5.4 mmol/l; Na^+ concentration = = 142 mmol/l; K^+ = 7.5 mmol/l; Cl^- = 104 mmol/l. The plasma creatinine concentration of 0.6 mmol/l, urea 6.0 mmol/l. In urine analysis: UV = 1004, the reaction is slightly acidic, hyaline and hemoglobin cylinders are determined, creatinine concentration = 0.4 mmol/l.

1. Your preliminary diagnosis, what is the cause of bradycardia and arrhythmias?

2. What is the cause of this condition?

3. What is the emergency care and treatment of this pathology?

4. Calculate plasma osmolarity.

ACID-BASE IMBALANCE

Acid-base imbalance (ABI) – relative constancy of concentration of hydrogen ions in internal environments of an organism that provides high-grade completeness of the metabolic processes proceeding in cells and tissues.

Hydrogen index (pH) – negative decimal logarithm of the activity, or concentration of hydrogen ions in solution (–lg[H]). It`s the main quantitative characteristic of the acidity of water solutions.

Value pH depends on the ratio between positively charged ions (forming an acidic environment) and negatively charged ions (forming an alkaline environment).

The human body constantly strives to balance this ratio, maintaining a strictly defined level pH. pH equal to 7.0 it`s

neutral environment. The lower the level pH – the more acidic the environment (from 6.9 to 0).

The alkaline environment has a high level pH (from 7.1 to 14.0).

The acid-base state is maintained by powerful homeostatic mechanisms.

They are based on the features of physicochemical properties of blood buffer systems and physiological processes in different systems (external respiration, kidneys, liver, gastrointestinal tract, etc.).

Buffers systems – are biological liquids organism. The role of buffer systems is in supporting normal pH blood.

Buffer system – it`s mixture of weak acid and salt, formed by strong base.

Strong acid getting into plasma causes a reaction of buffer systems, as a result of which a strong acid is converted into a weak one.

The same exactly happens and when strong base get into biological liquid which after interaction with buffer systems turns into weak basis. As a result of these processes pH changes either do not occur or are minimal.

All these systems are in the blood, where they maintain a pH = 7.4, despite the entry into the blood from the intestines and tissues of significant amounts of acids and small quantity basics.

Maintenance of stability pH of blood is provided by buffer systems:

1. Bicarbonate buffer system [carbonic acid – H_2CO_3, sodium bicarbonate – NaHCO3)] – the main buffer of intercellular fluid and blood, is formed in the kidneys and relieves the excretion of H^+.

2. Phosphate buffer system [monobasic (NaH_2PO4) and dibasic (Na_2HPO4) phosphate sodium] – relieves excretion H^+ in tubules of kidney. The main role is in regulation ABI inside

the cells (especially the kidneys), supports the "regeneration" of the bicarbonate system in the blood.

3. Plasma protein buffer system – the main intracellular buffer. In an acidic environment it binds hydrogen ions, in an alkaline environment – gives.

4. Hemoglobin buffer system [Hemoglobin – potassium salt of hemoglobin] – plays a major role in transport CO_2 from tissue to lungs, takes effect within minutes.

Participation of organs in regulation ABI

Respiratory system. The respiratory system is involved in regulation ABI, changing tension CO_2 in the blood. Closely connected with bicarbonate buffer.

Reduction frequencies of the breath (hypoventilation) leads to increase CO_2 concentration in the blood, which causes an increase the concentration of H_2CO_3 and developing acidosis. Increase frequencies of the breath (hyperventilation) decreases tension CO_2, reduce level of H_2CO_3 and alkalosis develops.

Kidneys regulate the acid-base state, eliminating or reducing violations by removal protons (H^+) and increasing or decreasing [$HCO3^-$] in liquid environment.

Secretion H^+ regulated CO_2 content in extracellular fluid: the higher the concentration of CO_2 – the more excretion H^+, which leads to increased acidity of urine.

When level H^+ in blood increases, the kidneys produce HCO_3^-, which helps maintain in the body correlation acids/bases at the level of 1:20. If HCO_3^- increases in the extracellular fluid or [H^+] decreases, the kidneys retain H+ and remove HCO_3^- in this case the urine becomes alkaline.

Acidosis increases the synthesis and excretion of ammonia in the kidneys, alkalosis has the reverse action.

Liver. It`s cells synthesize proteins of the buffer system; oxidized organic acids to CO_2 and water; lactate is

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converted to glucose and glycogen, together acidic and alkaline metabolic products are excreted from the body with bile.

Gastrointestinal tract. At alkalization of liquid environments of organism the release of hydrochloric acid in a stomach cavity is braked, at acidification – increases.

Secretion of HCO_3^- in the duct of the pancreas increases with alkalization of liquid environment, with acidification – decreases.

**Bone tissue**. Na^+, K^+, Ca^{2+}, Mg^{2+} contained in bone tissue can be exchanged for hydrogen ions, compensating the acidosis. In severe cases, this process can lead to decalcification of the skeleton.

Violation of the acid-base state of the body

In terms pathology acid-base balance can change both in the acid (acidosis) and in the alkaline (alkalosis) side.

Acidosis – acid-base imbalance, characterized by the appearance in the blood of an absolute or relative excess of acids and an increase in the concentration of hydrogen ions.

Alkalosis – acid-base imbalance, in which there is an absolute or relative increase quantity basics and reducing the concentration of hydrogen ions.

Level pH of the blood

6 **Death** 7 **Acidosis** 7.35 **Norm** 7.45 **Alkalosis** 7.8 **Death** 9
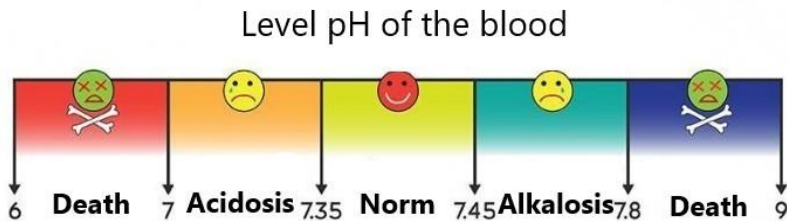
Classification of acid-base disorders:

1. For mechanism of development of acidosis and alkalosis are divided into:

• Respiratory.

- Metabolic.
- Mixed.

2. According to the degree of severity distinguish:

- Compensated acidosis and alkalosis. With compensated acidosis and alkalosis buffer and physiological systems of the body involved in the neutralization and excretion of acidic and alkaline products provide support pH within normal limits.

- Decompensated acidosis and alkalosis. With decompensated acidosis and alkalosis there is depletion and insufficiency protective mechanisms, pH shifts beyond the norm.

Respiratory acidosis develops with an excess of carbonic acid in the body.

Causes:

1. Insufficient function of external respiration system (depression of the respiratory center, severe disease of the lungs – pneumonia, atelectasis, pneumothorax, bronchospasm, asphyxia, etc.), in which due to reduced pulmonary ventilation CO_2 is retained in the body.

2. Insufficiency of blood circulation, when as a result of slowdown in blood flow reduces the removal of CO_2 from blood.

3. High concentration of CO_2 in the air.

Compensative mechanism of the respiratory acidosis:

1. The level of CO_2 in the blood increases significantly (hypercapnia). Because of this excitability of the respiratory center increases, dyspnea develops and excess of the carbonic acid removes from the body. This mechanism compensation is included quickly (2–3 min).

2. Later CO_2 enter to the erythrocytes, where the concentration of H^+ ions and $HCO3^-$ increases significantly. Excess of H^+ ions are contained in erythrocytes by hemoglobin,

and anions HCO3⁻ come in plasma in exchange for chlorine ions.

3. The role of kidneys is very important in compensative process. High level CO_2 in blood leads to the growth of reabsorption Na and consequently increase of $NaHCO_3$.

Metabolic acidosis. It is the most common and very severe form of acid-base imbalance in the blood. It is based on the accumulation in the body of non-volatile acidic products (acetoacetic, lactic acid, etc.).

Causes:

1. Excessive formation of acid products (ketone body, lactic acid and etc.) at metabolic disorders (diabetes mellitus, hypoxia, starvation and etc.).

2. Violation in excretion from organism acid substances at insufficiency secretory functions kidney (nephritis, uremia).

3. Loss in organism large quantity of bases with alkaline digestive juices (long diarrhea, fistula of intestines, pancreatic or biliary fistula).

4. Excessive introduction in organism mineral acids (poisoning acetic acid and etc.).

The role of the anion gap

The anion gap is defined as the concentration difference between the major measured cations (positively charged ions) and anions (negatively charged ions) within the plasma (normally from 12 to 18 mmol/l).
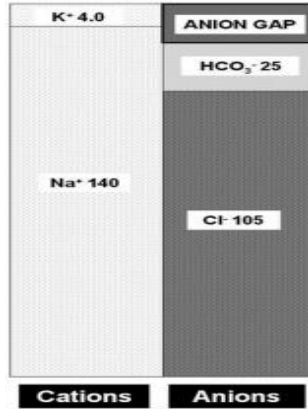
Figure 10 – **Illustration of the anion gap**
(all figures are mmol/l $^{-1}$)

Anionic proteins, phosphate, sulphate and low levels of organic acids, which are not measured, account for the difference (i. e. the – gap‖). When examining the cause of a metabolic acidosis it is useful to calculate the anion gap.

Anion gap

Anion gap = $[Na^+ + K^+] – [HCO_3^- + Cl^-] = 15(\pm 3)$ mmol/l^{-1}.

A normal anion gap implies that acidosis occurs due to primary bicarbonate loss:

• Plasma bicarbonate is low (the hallmark of acidosis) and chloride concentration is raised. This bicarbonate loss may be gastrointestinal (diarrhea, fistula) or renal (renal tubular acidosis, drug effect). Also occurs with rapid intravenous infusion of normal saline (excess chloride) or intravenous nutrition rich in cationic amino acids (e. g. arginine). An increased anion gap implies that fixed acids are being retained or an abnormal organic acid is present.

• Plasma bicarbonate is low and chloride concentration is normal.

• Fixed acids may be retained in:
– uremia;

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– ketoacidosis (diabetic, alcoholic);

– lactic acidosis.

If fixed acids are normal, exogenous acids should be considered:

– salicylate (aspirin) poisoning;

– methanol poisoning;

– ethylene glycol poisoning.

Compensative mechanism of metabolic acidosis:

1. Neutralization of excess acidic products occurs due to their dilution with extracellular fluids (fast mechanism).

2. Later these products are bound by bicarbonates and their concentration in the blood plasma falls, which is a characteristic indicator of metabolic acidosis.

3. A relative excess of carbonic acid is created, which is under the influence of the enzyme carbonic anhydrase decomposes into water and CO_2.

4. Carbon dioxide is removed from the body due to hyperventilation. This is a very important way to compensate, but decrease of the partial pressure of CO_2 can reduce the excitability of the respiratory and vascular centers.

5. The compensation includes protein buffer, which in excess of acidic products behaves as a weak base, combining with hydrogen ions.

6. H^+ ions often turn into erythrocytes, instead them K^+ ions are released in plasma.

7. In bone tissue, hydrogen ions are exchanged with ions Na^+ and Ca^{2+}.

Mixed acidosis

Causes:

Insufficient gas exchange in lungs leads to difficulty CO_2 releasing from the body (respiratory acidosis). It`s accompanied with decrease oxygenation of blood and, consequently, the development of oxygen starvation with the subsequent accumulation of under-oxidized products of

intermediate metabolism (mainly lactic acid). It causes development of metabolic acidosis. Such forms of acidosis are observed in pathology of the cardiovascular or respiratory systems.

Respiratory alkalosis. Respiratory alkalosis occurs in hyperventilation, when the excretion of CO_2 exceeds the rate of its formation in the body.

Causes:

1. With mountain sickness due to compensatory shortness of breath with a lack of oxygen.

2. Direct stimulation of the respiratory center (with encephalitis, hypothalamic tumors, severe crying in children, salicylate poisoning).

3. Reflex stimulation of the respiratory center (pneumonia, pneumosclerosis).

4. In addition, hyperventilation can occur with improperly performed artificial respiration.

Compensative mechanism respiratory alkalosis:

Due to hyperventilation decreases partial voltage of carbon dioxide in the alveolar air and blood (hypocapnia). It is caused that CO_2 at 20 times easier diffuses through alveolar-capillary membrane than oxygen.

1. The most important and fast gas compensation mechanism of alkalosis is a decrease in the excitability of the respiratory center. This leads to decrease frequencies of the breathing and delays CO_2 in the body.

2. At the deficiency of carbonic acid from erythrocytes chlorine ions arrive in plasma. They displace sodium from the bicarbonate. As a result content the latter decreases, and the concentration of H_2CO_3 increases.

3. In the renal tubules at low blood pressure CO_2 compensatory the secretion of hydrogen ions is reduced and the reverse absorption of bicarbonate is inhibited, which is intensively excreted in the urine (urine becomes alkaline).

Metabolic alkalosis. Metabolic (non-gas) alkalosis develops with an absolute or relative increase in the number of alkaline compounds in the body.

Causes:

1. Excretory non-gas alkalosis. It develops with an excessive loss of acids, chlorine (the main blood anion) and potassium from the extracellular fluid of the body, the so-called hypochloremic or hypokalemic:

• Hypochloremic alkalosis occurs during vomiting, when the body, together with acidic vomit, loses a significant amount of chlorine ions contained in the gastric juice (indomitable vomiting of pregnant women, pyloric stenosis, bowel obstruction, frequent gastric lavage after surgery).

• Hypokalemic alkalosis quite often accompanies hypochloremic, can occur with prolonged use of diuretics, diarrhea, hemolysis, in the postoperative period. Potassium loss occurs.

• With a delay in the body of alkalis (increased reabsorption of alkaline anions by the kidneys).

2. Exogenous non-gas alkalosis occurs with:

• Prolonged use of food and drink containing a large amount of alkali. It is observed in patients with gastric ulcer, taking in large quantities alkaline solutions and milk.

• Excessive administration of a solution of sodium bicarbonate or sodium lactate to correct metabolic acidosis.

• Administration large doses of desoxycorticosterone, contributing to the delay of sodium.

Compensative mechanism of metabolic alkalosis:

Compensation for metabolic alkalosis is aimed at removing excess bicarbonate and retaining carbon dioxide in the body.

1. When the concentration of hydrogen ions in the blood decreases, the respiratory center is inhibited.

2. As a result, pulmonary ventilation is reduced, and CO_2 accumulates in the blood and the ratio of H_2CO_3/ $NaHCO_3$ remains at 1/20.

3. In the process of compensation involved protein buffer (gives off hydrogen ions and binds sodium ions). A large amount is excreted in the urine: bicarbonate and dibasic phosphate.

4. However at a hypercapnia excitability of the respiratory center increases, excess of carbon dioxide is removed from an organism and the decompensated alkalosis can come.

5. As a result of reducing the content in the blood of ionized calcium, which passes into the bone tissue instead of H^+ ions, increases up to seizures neuromuscular excitability (for example, the so-called gastric tetany in unrestrained vomiting).

Mixed alkalosis – (combination of gas and non-gas alkalosis) can be observed in brain injuries accompanied by shortness of breath, hypocapnia and vomiting acidic gastric juice.

Indicators of acid-base imbalance

To such indicators belong the following:

• **pH** – it value pH arterial blood, measured without access air at 38 °C. Normal range 7.35–7.45.

• **Partial High-voltage carbon dioxide gas (pCO₂)** – it value pCO_2 arterial blood, measured without access air at 38 °C. Normal range 35–45 mmHg.

• **Standard bicarbonate (SB – «Standard Bicarbonate»)** – it contents bicarbonates in plasma blood (mmol/ l) at complete saturation her oxygen and pCO_2, equal 40 mm Hg, which is determined at 38 °C. Normal range 22–26 mmol/l.

• **Actual bicarbonate (AB – «Actual Bicarbonate»)** concentration bicarbonate in plasma blood (in mmol/ l) at true

pCO$_2$, which is determined at temperature 38 °C. Normal range 18.8–24 mmol/l.

•**Excess (deficit) buffer basics (BE - «Base Excess»)** – it difference between average normal content buffer foundations (whole blood at pH = 7.38 and pCO$_2$, equal 40 mm Hg) and found value concentration buffer basics (BB). Normal range –2.0 – 0 – +2.0 mmol/l.

Principles of correction of acid-base imbalance

The principles for the correction of acid-base balance are to eliminate the pH shift of the internal environment of the body by normalizing the composition of the buffer systems and eliminating the associated disturbances in water-electrolyte metabolism, eliminating complications, and treating pathological processes that cause acid-base balance or supporting them.

The main goal: reducing the degree or elimination of respiratory failure. The methods of elimination are different in acute and chronic forms of respiratory failure. In acute respiratory failure a complex of high priority measures is perform, aimed at ensuring the optimal volume of alveolar ventilation. Airway patency is restored (foreign bodies are removed, pumping out liquid, mucus or vomit, eliminate tongue retraction, etc.).

The intake of excess carbon dioxide stops (for example, normalize the gas composition of the air in space suits, aircraft, rooms, when performing mechanical ventilation).

The patient is transferred to mechanical ventilation in the absence or insufficiency of spontaneous breathing (after restoration of airway patency). For lung ventilation atmospheric air or oxygen-enriched gas mixtures are used. Moreover, the concentration of O$_2$ in the gas mixture should not be higher than the level that ensures the optimum pO$_2$ in this patient, since the body's hyperoxygenation is accompanied by increased formation of pathogenic reduced (reactive) forms

of oxygen and subsequent activation of lipid peroxidation processes. It is important to remember the inadmissibility of the use of hypoxic gas mixtures and mixtures with the addition of CO_2 in severe respiratory failure. Their use potentiates hypercapnia and exacerbates the patient's condition. In chronic respiratory failure, a set of measures is carried out based on the etiotropic, pathogenetic and symptomatic principles.

Etiotropic principle is aimed at eliminating the causes of acidosis: hypoventilation and / or hypoperfusion of the lungs, as well as reduced diffusion ability of aero-hematic barrier. The etiotropic principle of eliminating gas acidosis is implemented using a number of methods: restoration of adequate ventilation (e. g., using bronchodilators, expectorants, bronchial drainage, sputum aspiration) and normalization of lung ventilation. With decompensated gas acidosis, mechanical ventilation is performed. This is done under pH control to prevent hyperventilation and the development of post – hypercapnic gaseous alkalosis. Improvements pulmonary perfusion in blood (using cardiotropic drugs; drugs that regulate vascular tone and the state of aggregation of blood). Regulation of the activity of the respiratory center (restriction of the use of drugs that reduce its excitability, for example, sedatives or narcotic analgesics, and the appointment of stimulants of its function).

Pathogenetic principle. The implementation of this principle aims to eliminate the main pathogenic factor of respiratory acidosis – an increased level of CO_2 in the blood (hypercapnia) and other body fluids. This goal is achieved by taking measures to eliminate the cause of the violation of gas exchange in the lungs (etiotropic therapy). Intake of hydrogen carbonate-containing buffer solutions in order to eliminate chronic respiratory acidosis is ineffective. This is because exogenous HCO_3^- is quickly removed from the body by the

kidneys, and with violations of their excretory function (with renal failure), exogenic alkalosis can develop.

Symptomatic treatment aims to eliminate unpleasant and painful sensations that exacerbate the patient's condition: headache, severe and prolonged tachy- or bradycardia, psychomotor overexcitation, excessive sweating, etc.

Acid base calculation. Rules and practical application

An overview of the six sequential steps involved is outlined. A check of pH, pCO_2 and HCO_3^- against the Henderson-Hasselbalch equation is usually difficult without a calculator. However, a quick check of the logical consistency of the results is often possible. For example, pH must be less than 7.4 if PCO_2 is high and HCO_3^- is low. It is preferable to review the result print – out from the machine.

The six steps of systematic acid - base evaluation:

1. pH: assess the net deviation of pH from normal.

2. Pattern: check the pattern of bicarbonate and pCO_2 results.

3. Clues: check for additional clues in other investigations.

4. Compensation: assess the appropriateness of the compensatory response.

5. Formulation: bring the information together and make the acid base diagnosis.

6. Confirmation: consider if any additional tests to check or support the diagnosis are necessary or available and revise the diagnosis if necessary.

The first step is to look at the arterial pH (Tab. 7). A net acidemia means that acidosis must be present. A net alkalemia means that alkalosis must be present. A normal pH gives 2 possibilities: no acid-base disorder or a mixed disorder with alkalosis compensating acidosis.

Table 7 – **Systematic approach to blood gas analysis**

Steps	Principle	Guidelines
pH: check arterial pH	The net deviation in pH will indicate whether an acidosis or an alkalosis is present (but will not indicate mixed disorders)	If an acidemia is present then an acidosis must be present. If an alkalemia is present then an alkalosis must be present. If pH is normal pH then either (no acid-base disorder is present) or (compensating disorders are present i. e. a mixed disorder with an acidosis and an alkalosis)
Pattern: look for suggestive pattern in pCO_2 and [HCO_3]	Each of the simple disorders produces predictable changes in [HCO_3] and pCO_2	If both [HCO_3] and pCO_2 are low then suggests presence of either a metabolic acidosis or a respiratory alkalosis (but a mixed disorder cannot be excluded). If both [HCO_3] and pCO_2 are high then suggests presence of either a metabolic alkalosis or a respiratory acidosis (but a mixed disorder cannot be excluded). If [HCO_3] and pCO_2 move in opposite directions then a mixed disorder must be present. Which disorder is present is dependent on which change is primary and which is

		compensatory, and this requires an assessment based on the history, examination and other results
Clues: check for clues in the other biochemi-stry results	Certain disorders are associated with predictable changes in other biochemistry results	See separate list of – Aids to interpretation below
Compensa-tion: assess the compensato ry response	The 6 bedside rules are used to assess the appropriatenes s of the compensatory response	If the expected and actual values match => no evidence of mixed disorder If the expected and actual values differ => a mixed disorder is present
Formulation : formulate the acid-base diagnosis	Consider all the evidence from the history, examination and investigations and try to formulate a complete acid-base diagnosis	
Confirma-tion: check for specific	In some cases, further biochemical	Lactate, urinary ketones, salicylate level, aldosterone level, various tests for renal

biochemical evidence of particular disorders for confirmation.	evidence can confirm the presence of particular disorders. Changes in these results may be useful in assessing the magnitude of the disorder or the response to therapy.	tubular acidosis

The next step is to determine whether any disorder is of the respiratory or metabolic type by reviewing the pattern and magnitude of the bicarbonate and pCO2 results. If the disorder is minor (i. e. only one primary disorder present) then the acid-base disorder is diagnosed at this step. But the real problem is difficult to define, so a mixed disorder must always be checked. This is an important part of steps 2, 3 and 4.

Step 3 involves reviewing of other results looking for specific evidence of particular disorders. Some of these – clues are outlined in the table 8.

Table 8 **– Some aids to interpretation of acid-base disorders**

«Clue»	Significance
High anion gap	Always strongly suggests a metabolic acidosis.
Hyperglycaemia	If ketones also present in urine -> diabetic ketoacidosis
Hypokalaemia and/or hypochloraemia	Suggests metabolic alkalosis

Hyperchloraemia	Common with normal anion gap acidosis
Elevated creatinine and urea	Suggests uraemic acidosis or hypovolaemia (prerenal renal failure)
Elevated creatinine	Consider ketoacidosis: ketones interfere in the laboratory method (Jaffe reaction) used for creatinine measurement and gives a falsely elevated result; typically urea will be normal
Elevated glucose	Consider ketoacidosis or hyperosmolar non-ketotic syndrome
Urine dipstick tests for glucose and ketones	Glucose detected if hyperglycaemia; ketones detected in case of ketoacidosis

In most circumstances, these clues are confirmatory of the expected diagnosis but on occasion can alert to the presence of an unanticipated second disorder. An elevated anion gap can be particularly useful. Most of these – clues‖ are obtained from the biochemistry profile. An alert clinician can often correctly pick the diagnosis before the gas results are back.

The 4th step is to assess acid – based compensation. The approach discussed here involves the application of six rules. Much of the emphasis is made here to pick the presence of a second acid-base disorder.

Step 5: this stage is reached when overall acid-base assessment can be made.

Step 6: Sometimes the diagnosis suggests additional tests that can be used to confirm the diagnosis or at least allows

doctors to make a more precise diagnosis (e. g. measurement of the blood salicylate level in a child. In case it is high it can confirm a clinical suspicion of a salicylate over ingestion). If a diagnosis of renal tubular acidosis is suspected, then further specific tests should be done to specify further diagnosis.

The method of acid-base disorders assessment uses a set of six rules which are used primarily to check the magnitude of the patient`s compensatory response. The rules should always be kept in mind – with practice this is not difficult. A full assessment of blood – gas results must be based on a clinical assessment of each patient and understanding of the pathophysiology of the clinical conditions underlying the acid – base disorder.

Do not interpret the blood-gas results as an intellectual exercise in itself. It is only one part of the overall assessment and management process. Diagnosing a «metabolic acidosis», for example, by itself, is often of little clinical use. What is really required is a more specific diagnosis of the metabolic acidosis cause (e. g. diabetic ketoacidosis, acute renal failure, lactic acidosis) to initiate the appropriate management. The acid-base analysis must be interpreted and managed in the context of the overall clinical picture.

Test tasks for checking the final level of knowledge:
1. A patient with respiratory failure revealed a violation of the acid-base balance. What is the most likely mechanism for the identified changes in the acid-base balance?
A. Violation of the blood buffer systems.
B. Increased acid intake with drugs.
C. Enhanced CO_2 elimination for respiratory failure.
D. Decrease in CO_2 removal.
E. Decrease in O_2 income.
2. A patient with bilateral pneumonia revealed a violation of the acid-base balance – compensated gas acidosis.

What is the most likely protective and adaptive mechanism that supports the compensation of an acid-base balance in a patient?

A. Increased acidogenesis in the kidneys.

B. Development of hyperpnoea.

C. Reduction of hydrogen carbonate reabsorption in the kidneys.

D. Decreased acid secretion in tissues.

E. Enhanced elimination of acidic products through the gastrointestinal tract.

3. The miner as a result of an accident at the mine, was in an unventilated face for a day. After salvation, the hospital examined the acid-base balance. The following results were obtained: pH – less than normal, pCO_2 – more than normal, SB – normal. What is the violation of the acid-base balance detected in the patient?

A. Compensated gas acidosis.

B. Compensated metabolic acidosis.

C. Compensated gas alkalosis.

D. Decompensated gas acidosis.

E. Decompensated metabolic acidosis.

4. A patient with diabetes mellitus was admitted to the hospital in a severe precomatous state. In the study of the acid-base balance, acidosis was detected. The patient was prescribed complex therapy, including intramuscular insulin and intravenous sodium bicarbonate solution. What is the most likely mechanism for the identified changes in the acid-base balance?

A. Violation of the use of O_2 in cells.

B. Violation of the blood buffer systems.

C. Excretion of alkaline components in the urine.

D. Decrease in CO_2 removal.

E. Formation of insufficiently oxidized products.

5. The patient was admitted to the hospital three days after poisoning with poor-quality products. Throughout the

entire period of the illness, the patient was disturbed by abdominal pain and frequent diarrhea. In the study of the acid-base balance, acidosis was detected. What is the most likely mechanism for the identified changes in the acid-base balance?

A. Increased formation of insufficiently oxidized products in cells.

B. Violation of the blood buffer systems.

C. Excretion of alkaline components in the urine.

D. Excretion of hydrogen carbonate of the pancreas.

E. Hypoventilation and reduced CO_2 excretion.

6. After a trip to the mountains to a height of 4 000 m, lasting 10 days, a tourist determined the indicators of the acid-base balance and found compensated gas acidosis. What is the most likely protective and adaptive mechanism that supports the compensation of an acid-base balance in a patient?

A. Hyperventilation and increased CO_2 excretion.

B. Decrease in the production of alkaline components in the pancreas.

C. Reduction of hydrogen carbonate reabsorption in the kidneys.

D. Decreased acid secretion in tissues.

E. Enhanced elimination of acidic products through the gastrointestinal tract.

7. Patient O., 35 years old, was admitted to the emergency department of the hospital emergency and emergency care with complaints of nausea, vomiting, dizziness, headaches, severe shortness of breath. It is known that he had a car accident and was unconscious for 15 minutes. Examination revealed retrograde amnesia, slight stiff neck and a positive Kernig symptom, increased neuromuscular irritability. Body temperature – 37.5 °C, heart rate – 97 min^{-1}, blood pressure – 145/97 mm Hg. On the EEG, the delta rhythm is preserved, but its unevenness in amplitude and frequency is revealed. An analysis of rheoencephalography revealed a

decrease in pulse blood supply to the cerebral vessels. Acid-base blood condition: SB – 22 mmol/l, BB – 43 mmol/l, BE – +1,1 mmol/l, CO_2 – 30 mmHg, pH – 7.56.

Questions:

1. What condition did the patient develop? Argument the answer.

2. What are the main links in the pathogenesis of this condition?

3. What are the principles for removing patients from such conditions? Justify the answer.

BASIC CONCEPTS OF FLUID MANAGEMENT

Evaluation of Intravascular Volume

Clinical evaluation and assessment of intravascular volume must generally be relied upon, because measurements of fluid compartment volumes are not readily available. Intravascular volume can be assessed using physical or laboratory examinations or with the aid of sophisticated hemodynamic monitoring techniques. Regardless of the method employed, serial evaluations are necessary to confirm initial impressions and guide fluid therapy. Moreover, modalities should complement one another, because all parameters are indirect, nonspecific measures of volume; reliance on any one parameter may be erroneous and, therefore, hazardous.

Physical examination

Physical examination is most reliable preoperatively. Invaluable clues to hypovolemia (Tab. 9) include skin turgor, the hydration of mucous membranes, fullness of a peripheral pulse, the resting heart rate and blood pressure and the (orthostatic) changes from the supine to sitting or standing positions, and urinary flow rate. Unfortunately, many drugs

used during anesthesia, as well as the physiological effects of surgical stress, alter these signs and render them unreliable in the immediate postoperative period. Intraoperatively, the fullness of a peripheral pulse (radial or dorsalis pedis), urinary flow rate, and indirect signs, such as the response of blood pressure to positive-pressure ventilation and the vasodilating or negative inotropic effects of anesthetics, are most often used.

Pitting edema – presacral in the bedridden patient or pretibial in the ambulatory patient – and increased urinary flow are signs of hypervolemia in patients with normal cardiac, hepatic, and renal function. Late signs of hypervolemia include tachycardia, pulmonary crackles, wheezing, cyanosis, and pink, frothy pulmonary secretions.

Table 9 – **Fluid Loss (Expressed as percentage of body weight)**

Sign	5 %	10 %	15 %
Mucous membranes	Dry	Very dry	Parched
Sensorium	Normal	Lethargic	Obtunded
Orthostatic changes	None	Present	Marked. In heart rate > 15 bpm. In blood pressure > 10 mm Hg
Urinary flow rate	Mildly decreased	Decreased	Markedly decreased
Pulse rate	Normal or increased	Increased > 100 bpm	Markedly increased > 120 bpm
Blood pressure	Normal	Mildly decreased with respiratory variation	Decreased

Laboratory evaluation

Several laboratory measurements may be used as surrogates of intravascular volume and adequacy of tissue perfusion. These measurements include serial hematocrits, arterial blood pH, urinary specific gravity or osmolality, urinary sodium or chloride concentration, serum sodium, and the serum creatinine to blood urea nitrogen (BUN) ratio. These measurements are only indirect indices of intravascular volume and often cannot be relied upon intraoperatively because they are affected by many other variables and results are often delayed. Laboratory signs of dehydration include a rising hematocrit, a progressive metabolic acidosis, a urinary specific gravity greater than 1.010, a urinary sodium less than 10 mmol/l, a urinary osmolality greater than 450 mOsm/l, hypernatremia, and a BUN-to-creatinine ratio greater than 10:1. Only radiographic signs of increased pulmonary vascular and interstitial markings (Kerly "B" lines) or diffuse alveolar infiltrates are reliable measures of volume overload.

Hemodynamic measurements

Central venous pressure monitoring is indicated in patients with normal cardiac and pulmonary function when volume status is difficult to assess by other means or when rapid or major alterations are expected. Central venous pressure readings must be interpreted in view of the clinical setting. Low values (< 5 mm Hg) may be normal unless associated with other signs of hypovolemia. Moreover, the response to a fluid bolus (250 ml) is equally as important: a small elevation (1–2 mm Hg) may indicate the need for more fluid, whereas a large increase (> 5 mm Hg) suggests the need for a slower rate of administration and a reevaluation of volume status. Central venous pressure readings greater than 12 mm Hg are considered elevated and imply hypervolemia in the absence of right ventricular dysfunction, increased intrathoracic pressure, or restrictive pericardial disease.

Pulmonary artery pressure monitoring is necessary if central venous pressures do not correlate with the clinical assessment or if the patient has primary or secondary right ventricular dysfunction; the latter is usually due to pulmonary or left ventricular disease, respectively. Pulmonary artery occlusion pressure (PAOP) readings of less than 8 mm Hg indicate hypovolemia in the presence of confirmatory clinical signs; however, values less than 15 mm Hg may be associated with relative hypovolemia in patients with poor ventricular compliance. PAOP measurements greater than 18 mm Hg are elevated and generally imply left ventricular volume overload. The presence of mitral valve disease (particularly stenosis), severe aortic stenosis, or a left atrial myxoma or thrombus alters the normal relationship between PAOP and left ventricular end-diastolic volume. Increased thoracic and pulmonary airway pressures also introduce errors; consequently, all pressure measurements should always be obtained at end expiration and interpreted in the context of the clinical setting. Newer techniques of measuring ventricular volumes with transesophageal echocardiography or by radioisotopes are more accurate but are not as widely available.

Properties of intravenous crystalloids and colloids

Intravenous fluid therapy may consist of infusions of crystalloids, colloids, or a combination of both. Crystalloid solutions are aqueous solutions of low-molecular-weight ions (salts) with or without glucose, whereas colloid solutions also contain high-molecular-weight substances such as proteins or large glucose polymers. Colloid solutions maintain plasma colloid oncotic pressure and for the most part remain intravascular, whereas crystalloid solutions rapidly equilibrate with and distribute throughout the entire extracellular fluid space.

Controversy exists regarding the use of colloid versus crystalloid fluids for surgical patients. Proponents of colloids

justifiably argue that by maintaining plasma oncotic pressure, colloids are more effective in restoring normal intravascular volume and cardiac output. Crystalloid proponents, on the other hand, maintain that the crystalloid solutions are equally as effective when given in sufficient amounts. Concerns that colloids may enhance the formation of pulmonary edema fluid in patients with increased pulmonary capillary permeability appear to be unfounded, because pulmonary interstitial oncotic pressure parallels that of plasma. Several generalizations can be made:

1. Crystalloids, when given in sufficient amounts, are just as effective as colloids in restoring intravascular volume.

2. Replacing an intravascular volume deficit with crystalloids generally requires three to four times the volume needed when using colloids.

3. Most surgical patients have an extracellular fluid deficit that exceeds the intravascular deficit.

4. Severe intravascular fluid deficits can be more rapidly corrected using colloid solutions.

5. The rapid administration of large amounts of crystalloids (> 4–5 l) is more frequently associated with significant tissue edema.

Some evidence suggests – but does not prove – that marked tissue edema can impair oxygen transport, tissue healing, and return of bowel function following major surgery.

Crystalloid solutions

Crystalloids should be considered as the initial resuscitation fluid in patients with hemorrhagic and septic shock, in burn patients, in patients with head injury to maintain cerebral perfusion pressure, and in patients undergoing plasmapheresis and hepatic resection. If 3–4 l of crystalloid has been given, and the hemodynamic response is inadequate, colloids may be added.

A wide variety of solutions is available (Tab. 10). Solutions are chosen according to the type of fluid loss being replaced. For losses primarily involving water, replacement is with hypotonic solutions, also called maintenance-type solutions. If losses involve both water and electrolytes, replacement is with isotonic electrolyte solutions, also called replacement-type.

Glucose is provided in some solutions to maintain tonicity or to prevent ketosis and hypoglycemia due to fasting. Dextrose is metabolized, dextrose containing solutions are distributed through the total body water and hence have a limited and transient blood volume expanding capacity. Solutions like 5 % dextrose and dextrose saline are not meant for resuscitation, but are a means of providing free water when this is appropriate.

Because most intraoperative fluid losses are isotonic, replacement-type solutions are generally used. The most commonly used fluid is lactated Ringer's solution. Although it is slightly hypotonic, providing approximately 100 ml of free water per liter and tending to lower serum sodium to 130 mmol/l, lactated Ringer's generally has the least effect on extracellular fluid composition and appears to be the most physiological solution when large volumes are necessary. The lactate in this solution is converted by the liver into bicarbonate.

Normal saline is the preferred solution for hypochloremic metabolic alkalosis and for diluting packed red blood cells prior to transfusion. Five percent dextrose in water (D_5W) is used for replacement of pure water deficits and as a maintenance fluid for patients on sodium restriction. Hypertonic 3 % saline is employed in therapy of severe symptomatic hyponatremia. Three to 7.5 % saline solutions have been advocated for the resuscitation of patients in hypovolemic shock. These solutions must be administered

slowly (preferably through a central venous catheter) because they readily cause hemolysis.

Table 10 – **Electrolyte composition of the crystalloid solutions**

Solution	pH	Na$^+$	Cl$^-$	K$^+$	Ca^{2+}	Lactate	Glucose	Osmolality
0.9 % Normal Saline	5.0	154	154	0	0	0	0	308
Lactated Ringers	6.5	130	109	4	3	28	0	275
5 % Dextrose in Water (D5W)	4.0	0	0	0	0	0	50 g/l	252
0.45 % Normal Saline with Dextrose (D51/2 NS)	4.5	77	77	0	0	0	50 g/l	06
0.45 % Normal Saline (1/2 NS)	0	7	7				0	55

Colloid solutions

The osmotic activity of the high-molecular-weight substances in colloids tends to maintain these solutions intravascularly. Although the intravascular half-life of a crystalloid solution is 20–30 min, most colloid solutions have intravascular half-lives between 3 and 6 h. The substantial cost

and occasional complications associated with colloids tend to limit their use. Generally accepted indications for colloids include:

• Fluid resuscitation in patients with severe intravascular fluid deficits (e. g. hemorrhagic shock) prior to the arrival of blood for transfusion, and

• Fluid resuscitation in the presence of severe hypoalbuminemia or conditions associated with large protein losses such as burns. In burn patient`s colloids should also be considered if the injury involves more than 30 % of the body surface area or if more than 3–4 l of crystalloid has been given over 18–24 h post injury.

Many clinicians also use colloid solutions in conjunction with crystalloids when fluid replacement needs exceed 3–4 l prior to transfusion. It should be noted that these solutions are prepared in normal saline (Cl – 145–154 mmol/l) and can also cause hyperchloremic metabolic acidosis (above).

Several colloid solutions are generally available. All are derived from either plasma proteins or synthetic glucose polymers and are supplied in isotonic electrolyte solutions.

Blood-derived colloids include albumin (5 % and 25 % solutions) and plasma protein fraction (5 %). Both are heated to 60 °C for at least 10 h to minimize the risk of transmitting hepatitis and other virally transmitted diseases. Plasma protein fraction contains and globulins in addition to albumin and has occasionally resulted in hypotensive reactions. These reactions are allergic in nature and may involve activators of prekallikrein.

Synthetic colloids include dextrose starches and gelatins. Dextran is available as dextran 70 (Macrodex) and dextran 40 (Rheomacrodex), which have average molecular weights of 70 000 and 40 000, respectively. Although dextran 70 is a better volume expander than dextran 40, the latter also improves blood flow through the microcirculation, presumably

by decreasing blood viscosity. Antiplatelet effects are also described for dextrans. Infusions exceeding 20 ml/kg per day can interfere with blood typing, may prolong bleeding time (dextran 40), and have been associated with renal failure. Dextrans can also be antigenic, and both mild and severe anaphylactoid and anaphylactic reactions are described. Dextran 1 (Promit) may be administered prior to dextran 40 or dextran 70 to prevent severe anaphylactic reactions; it acts as a hapten and binds any circulating dextran antibodies.

Hetastarch (hydroxyethyl starch) is available as a 6 % solution with an average molecular weight of 450 000. Small molecules are eliminated by the kidneys, whereas large molecules must be first broken down by amylase. Hetastarch is highly effective as a plasma expander and is less expensive than albumin. Moreover, hetastarch is nonantigenic, and anaphylactoid reactions are rare. Coagulation studies and bleeding times are generally not significantly affected following infusions of up to 0.5–1.0 l. Whether kidney transplant patients do worse following hetastarch infusions is controversial. Similarly, controversy exists as to an association between using hetastarch for patients undergoing cardiopulmonary bypass. Pentastarch, a lower molecular weight starch solution, is less likely to cause adverse effects and may replace hetastarch.

Fluid prescription and administration

Appropriate fluid and electrolyte prescriptions may be administered orally, enterally, subcutaneously, or intravenously, depending on the clinical situation. Before any prescription is written it is important to ask a number of questions:

1. Does the patient need any prescription at all today?

2. If so, does the patient need this for resuscitation, replacement of losses or merely for maintenance?

3. What is the patient's current fluid and electrolyte status and what is the best estimate of any current abnormality?

4. Which is the simplest, safest, and most effective route of administration?

5. What is the most appropriate fluid to use and how is that fluid distributed in the body?

If the patient is eating and drinking, the answer is usually no. In the case of a post-operative patient, for example, any intravenous fluids should be discontinued as soon as possible. Intravenous fluids are often continued unnecessarily, leading to fluid overload as well as increased risk of cannula-site sepsis. Nasogastric tubes are only indicated for drainage in the presence of true ileus or gastric dysfunction (e. g. delayed gastric emptying after pancreatic surgery). In the majority of cases, morbidity from nasogastric tubes exceeds any benefit. Gastrointestinal function returns more rapidly post-operatively than previously assumed. The absence of bowel sounds per se does not mean that food and drink will not be tolerated. In the past, a combination of nasogastric tubes and excess intravenous fluids has frequently caused unnecessary delay in reestablishing oral intake, thereby prolonging the length of stay. Patients receiving artificial nutrition (parenteral or enteral) usually receive an adequate amount of water and electrolytes via the feed and most do not require additional intravenous fluids. It is a common mistake to prescribe intravenous maintenance requirements in addition to the water and electrolyte content of the feed, leading to avoidable fluid overload.

Many patients are fluid overloaded because prescriptions based on resuscitation are continued thoughtlessly when maintenance fluids are all that is required. For example, 1 liter of 0.9 % saline contains enough salt to meet 2 days' normal maintenance requirements. Intravenous fluid therapy

may be needed for resuscitation, replacement or maintenance, depending on the stage of the illness.

Resuscitation

In the event of blood loss from injury or surgery, plasma loss e. g. from burns or acute pancreatitis, or gastrointestinal or renal losses of salt and water, a resuscitation regimen is needed to restore and maintain the circulation and the function of vital organs. In this situation, the recommendation is to infuse 500 ml (250 ml if cardiac failure) of a balanced crystalloid stat (e. g. Hartmann's solution or Ringer's lactate) rapidly. If hyperkalemia is present ($K^+ > 0.5$ mmol/l) or suspected oliguric AKI or rhabdomyolysis 0.9 % saline is preferred initially (no potassium in crystalloid).

However, there is no evidence that administration of crystalloids containing 3–5 mmol/l of K^+ worsen the hyperkalemia. The clinical response should be assessed immediately following administration of the fluid bolus in terms of improved peripheral perfusion, decreased pulse rate, rise in blood pressure, rise in JVP and increase in urine output. Further administration will depend on response. If 0.9 % saline has been used initially conversion to a balanced crystalloid can be considered once potassium concentrations are known and good urine output established. In the case of intravascular fluid losses, colloids or a combination of colloids and crystalloids are appropriate to avoid causing excessive rises in oncotic pressure and potential osmotic nephrosis (renal tubular injury). Large volumes of 0.9 % saline are best avoided, except after gastric losses, because of the risk of producing hyperchloremic metabolic acidosis and its undesirable sequelae. In the case of major blood loss it is also necessary to cross match and to give packed cells.

Early and adequate treatment of the underlying cause of fluid loss, e. g. control of bleeding, is vital. In the severely

injured patient, resuscitation of blood loss with packed cells, fresh frozen plasma and platelets in a ratio of 1:1:1 has been shown to be more beneficial than packed cells alone, as this helps correct the associated coagulation defects.

Once resuscitation has been achieved as judged by normalisation of vital signs and urine output or of parameters from more invasive measurements, the prescriber should switch to a maintenance regimen with accurate replacement of any on-going losses. Exceeding such requirements, on the unwarranted assumption that the patient will excrete any excess, is deleterious to the outcome and delays recovery.

Replacement

Any fluid prescription should incorporate not only daily maintenance requirements, but replacement of any ongoing abnormal losses. In the case of a patient with losses from the gastrointestinal tract, e. g. from a fistula or from nasogastric aspiration, the fluid prescription should include the daily maintenance requirements plus like-for-like water and electrolyte replacement of any losses. In order to achieve this, the prescriber should be aware of the approximate electrolyte content of fluid from various parts of the gastrointestinal tract

Maintenance

Maintenance prescriptions should aim to restore insensible loss (500–1 000 ml), provide sufficient water and electrolytes to maintain normal status of body fluid compartments, and sufficient water to enable the kidney to excrete waste products 500–1 500 ml. The average person requires 25–35 ml/kg water, 1 mmol/kg Na^+ and 1 mmol/kg K^+ per day.

Decision making should be informed by all the information available, including history, examination, vital signs, measurements and tests including urine output and concentration and serum biochemistry, fluid balance charts, weight changes, and an understanding of the likely patho-

physiological changes. It should not be based just on casual bedside assessment of unreliable and nonspecific signs such as dry mouth or diminished skin turgor. Remember, serial weighing is the most accurate measure of external water balance.

The most appropriate method of administration should be the simplest and safest that is effective. The oral route should be used whenever possible. In acute situations and in the presence of gastrointestinal dysfunction or large deficits, the intravenous route is the most appropriate. This, however, should be discontinued at the earliest opportunity. Enteral tube administration may be appropriate where swallowing is the major problem. Subcutaneous infusions should be considered, particularly in the elderly, for the management of chronic or recurrent problems.

The most appropriate fluid to use is that which most closely matches any previous or ongoing losses. Recent published data favors the use of balanced electrolyte solutions rather than 0.9 % saline to replace salt and water deficits, except in the case of losses of gastric juice with its high chloride content. Following intravascular fluid losses, current thinking favors a combination of artificial colloid and balanced electrolyte solutions, supported by packed cells after significant blood loss.

Methods of fluid administration
Oral or enteral

The use of oral rehydration solutions to treat diarrheal disease in both children and adults is one of the most commonly used treatments worldwide, particularly in developing countries. They can also be useful in the management of short bowel or inflammatory bowel disease in hospital or at home. These preparations are based on the principle that salt absorption in the small bowel is linked to that of carbohydrate and is, therefore, enhanced by glucose, glucose

polymers and starch (e. g. rice water). Some preparations also contain K^+ and an alkalising agent to counter acidosis. In developing countries, they can be made using locally available materials, with simple measuring devices to ensure the correct proportions of salt, sugar or rice starch, and boiled water. These solutions may also be administered via enteral tubes where oral administration is difficult. One of the advantages of oral and enteral administration is that it is difficult to give excess fluid owing to limited tolerance. With intravenous fluids it is only too easy to give excess salt and water with deleterious consequences. On the other hand, when fluid losses are very great, the intravenous route may be necessary for resuscitation, replacement and to maintain balance.

Intravenous

• Peripheral. Most fluids are infused via a peripheral venous cannula. Such cannulas should be inserted and maintained using   meticulous care, technique and protocols, since their potential for causing morbidity and even mortality from infection is often underestimated. Each hospital should have clear guidelines, as part of clinical governance, to ensure optimal care of peripheral cannulas. Insertion sites should be inspected daily and cannula removed or resited at the earliest sign of any inflammation. In any case, it is good policy to resite cannula at least every 72 h.

• Central. Modern single or multi lumen polyurethane or silastic cannulas inserted via the internal jugular or subclavian vein have even greater potential than peripheral cannulas to cause morbidity and mortality unless inserted and maintained by skilled staff observing strict protocols.

Sub-cutaneous route (hypodermoclysis)

This method has been used in pediatrics and geriatrics for many years, but it is so effective for replacing small or medium fluid and electrolyte losses in patients unable to maintain balance by the oral route, that it deserves wider use.

One of its virtues is that patients or their carers can be taught to manage it at home. We have found it particularly useful for domiciliary use in adult and elderly patients with salt and water losses from gastrointestinal diseases. 0.9 % saline (500–2 000 ml daily) or 5 % dextrose (500 ml) containing up to 20 mmol K^+ and/or 4 mmol Mg^{2+} per liter may be infused over 3–4 hours via a fine butterfly cannula inserted into the subcutaneous fat, usually over the torso.

Infusion pumps

When fluid is delivered by either the enteral or parenteral route, what is prescribed is not necessarily what is delivered and patients may receive either too much or too little as a result of inaccuracies in delivery rates. It is now recommended that fluids should be delivered with infusion pumps at predetermined rates, which can be up to 999 ml/h. This increases the accuracy of fluid delivery. Nevertheless, delays in changing fluid bags once they are empty may still lead to inaccuracies.

Test tasks for checking the final level of knowledge:

1. To prevent transcapillary migration, it is advisable to supplement the infusion of crystalloid solutions:

A. Whole blood.

B. Gelofusin.

C. Corticosteroids.

D. Dopamine.

2. Crystaloids have all the properties, except:

A. Eliminate the deficiency of extracellular fluid.

B. Their composition is in congruence with the composition of the plasma.

C. Have a hemodynamic effect.

D. cause the development of hemodilution.

3. The administering 0.45 % sodium chloride in 5 % dextrose in water understands that this solution will hydrate the

intravascular and intracellular spaces based on which of the following transport mechanisms?

A. Diffusion.

B. Osmosis.

C. Filtration.

D. Sodium–potassium pump.

4. You have just completed a physical assessment of a 68-year-old man. He knows who he is but is unsure of where he is (previous orientation normal). His eyes are sunken, his mouth is coated with an extra longitudinal furrow, and his lips are cracked. Hand vein filling takes more than 5 seconds, and tenting of the skin appears over the sternum. His vital signs are BP 128/60 mm Hg, pulse 78, and respiratory rate 16 (previously 150/78, 76, 16, respectively). Your assessment would lead you to suspect:

A. Fluid volume deficit.

B. Hyponatremia.

C. Fluid volume excess.

D. Hypernatremia.

5. A patient admitted to the emergency department with intractable vomiting was started on 5 % dextrose and 0.9 % sodium chloride to support which of the following objectives of infusion therapy?

A. Maintenance of daily requirements.

B. Replacement of current losses.

C. Restore ongoing losses.

6. What is the most commonly used balanced electrolyte solution?

A. 5 % Dextrose in water.

B. 0.9 % Sodium chloride.

C. Lactated Ringer's solution.

D. 5 % Dextrose and sodium chloride.

7. Which of the following is the most common complication of the colloid dextran?

A. Fluid overload.

B. Hypersensitivity reactions.

C. Hyponatremia.

D. Hyperkalemia.

8. What is the purpose of a colloid solution?

A. To expand the interstitial compartment.

B. To replace electrolytes.

C. To expand the intravascular compartment.

D. To correct acidosis.

9. Dextrose and hypotonic sodium chloride solutions are considered hydrating fluids because they:

A. Provide more water than is required for excretion of sodium.

B. Provide fluid to determine renal filtration.

C. Maximize retention of potassium in the cell.

D. Maximize the retention of sodium.

10. The expected outcome of administering a hypertonic solution is to:

A. Shift ECF from the intracellular space to plasma.

B. Hydrate cells.

C. Supply free water to the vascular space.

11. A patient with acute enterocolitis is ill for the third day. Diarrhea does not stop, sharp weakness. Received massive infusion therapy. In connection with the appearance of signs of threatening pulmonary edema, the resumption of vomiting, and an increasing headache, he was transferred to the intensive care unit. Body weight – 80 kg, blood pressure – 170/115 mm Hg, CVP – 15.6 cm Hg, hourly diuresis – 20 ml; potassium – 3.0 mmol/l; sodium – 122 mmol/l; chlorine – 93 mmol/l; calcium – 5.0 mmol/l; hemoglobin – 100 g/l; pH 7.26; BE (–16 mmol/l); pCO_2 – 28 mmHg.

1. Determine the type of violation of the water-electrolyte and acid-base state.

2. What is the cause of this condition?

3. How is water moving between water sectors?

4. What is the emergency care and treatment of this pathology?

CLINICAL TRANSFUSION PRACTICE

Blood transfusion is an important part of day- to- day clinical practice. Blood and blood products provide unique and life- saving therapeutic benefits to patients. Standard practices should be in place to include appropriate testing, careful selection of donors, screening of donations, compatibility testing, storage of donations for clinical use, issue of blood units for either routine or emergency use.

Principles of clinical transfusion practice

• The patient with acute blood loss should receive effective resuscitation (intravenous replacement fluids, oxygen and other medication) immediately and the need for transfusion is estimated thereafter.

• The patient's hemoglobin (Hb) value, although important, should not be the sole deciding factor in the decision to transfuse blood. This decision should be supported by the need to relieve clinical signs and symptoms and to prevent significant morbidity or mortality.

• Clinicians should be aware of the risk of transfusion transmissible infections in blood products prescribed for patients.

• Transfusion should be prescribed only when the benefits to the patient are likely to outweigh the risks.

• Clinicians should clearly record the reason for ordering a transfusion (clinical diagnosis).

• Trained staff should monitor a patient undergoing transfusion and respond immediately there are signs of an adverse effect.

Blood components

A blood component is a constituent of blood, separated from whole blood, such as:

•Red cell concentrate.

•Plasma.

•Platelet concentrate.

•Cryoprecipitate (prepared from fresh frozen plasma; rich in Factor VIII and fibrinogen).

A plasma derivatives are made from human plasma proteins prepared under pharmaceutical manufacturing conditions, such as:

•Albumin.

•Coagulation factor concentrates.

•Immunoglobulin.

Red blood cells

Approved name: Red Blood Cells. Also referred to as Packed Cells, Red Cells, Packed Red, Blood Cells, RBCs.

Description of Components: Red Blood Cells consist of erythrocytes concentrated from whole blood donations by centrifugation or collected by apheresis method. RBC units are prepared by removing 200 to 250 ml of plasma from a whole blood unit (500 ml). The remaining packed red blood cells concentrate has a volume of approximately 250 to 350 ml. The component is anticoagulated with citrate and may have had one or more preservative solutions added. Depending on the preservative-anticoagulant system used, the hematocrit of Red Blood Cells ranges from 50–65 % to 65–80 %. Each unit contains approximately 42.5–80 g of hemoglobin or 128–240 ml of pure red cells, depending on the hemoglobin level of the donor, the starting whole blood collection volume, and the collection methodology or further processing. Each unit of Red Blood Cells contains approximately 147–278 mg of iron, most in the form of hemoglobin. In a normal adult patient, 1 unit of

RBCs should raise the Hb level approximately 10 g/L and the Hct level 3 %.

Dosing: A dose of one unit of compatible Red Blood Cells will increase the hemoglobin level in an average sized adult who is not bleeding or hemolyzing by approximately 10g/L. In neonates, a dose of 10–15 ml/kg is generally given. The updated guidelines recommend: for hospitalized adult patients who are hemodynamically stable, including critically ill patients, transfusion is not recommended until the hemoglobin concentration is 70 g/L. For patients undergoing orthopaedic surgery, cardiac surgery, and those with preexisting cardiovascular disease, a restrictive transfusion threshold of 80 g/L is recommended.

Infection risk: Capable of transmitting an agent present in cells or plasma which was undetected during routine screening for TTIs, i. e. HIV, hepatitis B and C, syphilis and malaria.

Red blood cells are indicated:

•For patients with a symptomatic deficiency of oxygen-carrying capacity or tissue hypoxia due to an inadequate circulating red cell mass.

•For exchange transfusion (e. g., for hemolytic disease of the newborn) and red cell exchange (e. g., for acute chest syndrome in sickle cell disease).

Patients must be evaluated individually to determine the proper transfusion therapy, taking care to avoid inappropriate over- or under- transfusion. Transfusion decisions should be based on clinical assessment and not on laboratory values alone. Red blood cells should not be used to treat anemia that can be corrected with a non-transfusion therapy (e. g. iron therapy). They also should not be used as a source of blood volume, or oncotic pressure or to improve wound healing, or sense of well being. Blood loss of greater than 30 % of blood volume causes significant clinical symptoms but resuscitation

with crystalloid alone is usually successful in young healthy patients with blood loss of up to 40 % of blood volume (e. g., 2-liter blood loss in an average adult male). Beyond that level of acute blood loss after adequate volume resuscitation, acute normovolemic anemia will exist. However, oxygen delivery in healthy adults is maintained even with hemoglobin levels as low as 60–70 g/l. Thus up to 40 % of the blood volume in a bleeding, otherwise healthy young adult can be replaced with crystalloid without the need for red cell transfusion.

Storage: Between +2 °C and +6 °C in an approved blood bank refrigerator, fitted with a temperature monitor and alarm.

Administration:
- Must be ABO and RhD compatible with the recipient.
- Never add medication to a unit of blood.
- Complete transfusion within 4 hours of commencement.

Frozen plasma

Approved name: Fresh frozen plasm (FFP), Fresh frozen plasma donor retested, Plasma cryoprecipitate reduced.

Fresh frozen plasma can be used as a source of stable coagulation factors for up to 5 days. Plasma cryoprecipitate reduced is indicated in the treatment of Thrombotic Thrombocytopenic Purpura (TTP).

Description of Components: Plasma consists of the noncellular portion of blood that is separated and frozen after donation. It may be prepared from whole blood or collected by apheresis. The anticoagulant solution used and the volume are indicated on the label. The volume of the unit is approximately 250 ml but variation may be expected. FFP is frozen at −18 °C or colder within 6–8h of collection (depending upon the anticoagulant). FFP contains normal levels of the stable clotting factors, albumin and immunoglobulins. It contains at

least 70 % of the original coagulant factor VIII and at least similar quantities of the other labile clotting factors and natural inhibitors of coagulation. FFP for clinical use must not contain clinically significant irregular anti-erythrocyte antibodies. In order to increase its safety, FFP can be quarantined for a minimum period of 4 months.

Plasma, cryoprecipitate reduced contains 20–30 % reduced levels of Factor VIII, von Willebrands' factor, fibrinogen, fibronectin and Factor XIII. By convention, 1 Unit of a coagulation factor is defined as that activity present in each milliliter of a standard pool of plasma units.

Dosing: The dose of plasma is determined by the patient size and clinical condition. When used to correct multiple coagulation factor deficiencies, plasma transfusion should be guided by coagulation testing. A prothrombin time (PT) greater than 1.5 times the mid-range of normal, an activated partial thromboplastin time (APTT) greater than 1.5 times the top of the normal range, or factor assay less than 25 %, can be used as thresholds at which therapeutic or prophylactic replacement may be indicated in an appropriate clinical setting. When such testing is not readily available, clinical evidence of bleeding may be used to direct transfusion decisions. Plasma should be administered in doses calculated to achieve a minimum of 30 % of plasma factor concentration. This is usually achieved with the administration of 10–20 ml/kg, though more may be required depending upon the clinical situation.

Infection risk: Same as for Red blood cells.

Indications:

• Active bleeding due to deficiency of multiple coagulation factors, or risk of bleeding due to deficiency of multiple coagulation factors.

• Severe bleeding due to warfarin therapy, or urgent reversal of warfarin effect.

- Massive transfusion with coagulopathic bleeding.
- Bleeding or prophylaxis of bleeding for a known single coagulation factor deficiency for which no concentrate is available.
- Thrombotic thrombocytopenic purpura.
- Rare specific plasma protein deficiencies, such as C1-inhibitor.

Frozen plasma should not be used for:
- Increasing blood volume or albumin concentration.
- Coagulopathy that can be corrected with Vitamin K.
- Normalizing abnormal coagulation screen results, in the absence of bleeding.

Storage: FFP is stored at –25 °C or colder for up to 1 year. Before use, it should be thawed in the blood transfusion center between +30 °C and +37 °C.

Administration:
- Should be ABO compatible.
- Infuse as soon as possible after thawing.
- Labile coagulation factors rapidly degrade; use within 6 hours of thawing.
- FFP may be beneficial if PT and/or partial thromboplastin time (PTT) > 1.5 times normal.
- FFP for volume expansion carries a risk of infectious disease transmission and other transfusion reactions (e. g. allergic) that can be avoided by using crystalloid or colloid solutions.

Platelet concentrates (PC)
Description: PCs are prepared from units of whole blood   that have not been allowed to cool below +20 °C. A single donor unit consists of 50–60 ml plasma that should contain ≥ 55×109 platelets.

Unit of issue: PCs may be supplied as a pooled unit, i. e. platelets prepared from 4- 6 donor units containing at least 240x109 platelets.

Dosing: 1 unit of platelet concentrate/10 kg; for an adult of 60–70 kg, 4–6 single donor units containing at least 240x109 platelets should raise the platelet count by 20–40x109/L. Increment will be less if there is splenomegaly, disseminated intravascular coagulation (DIC) or septicemia.

Infection risk: Bacterial contamination affects about 1 % of pooled units.

Indications: Treatment of bleeding due to:

• Thrombocytopenia.

• Platelet function defects.

• Prevention of bleeding due to thrombocytopenia as in bone marrow failure.

Contraindications:

• Idiopathic autoimmune thrombocytopenic purpura (ITP).

• Thrombotic thrombocytopenic purpura (TTP).

• Untreated DIC.

• Thrombocytopenia associated with septicemia, or in cases of hypersplenism.

Storage: PCs may be stored for up to 5 days at +20 °C to +24 °C (with agitation). PCs require continuous agitation during storage, on a platelet shaker and in an incubator that maintains the required storage temperature.

Administration: Platelet concentrates after pooling should be infused as soon as possible because of the risk of bacterial proliferation. Depending on the condition of the recipient, a unit should be infused over a period of not more than 30 minutes. Do not give platelet concentrates prepared from RhD positive donors to an RhD negative female with childbearing potential. Give platelet concentrates that are ABO compatible, whenever possible.

Cryoprecipitated anti-haemophilic factor (cryo-ahf)

Description: Cryo-AHF is prepared from FFP by collecting the precipitate formed during controlled thawing at +4 °C and resuspending in 10–20 ml plasma. It is stored at –25 °C or colder for up to 1 year after the date of phlebotomy. Cryo-AHF contains about half the Factor VIII and fibrinogen as a pack of fresh whole blood: e. g. Factor VIII: 80–100 iu/pack; fibrinogen: 150–300 mg/ pack.

Infection risk: As for plasma, but a normal adult dose involves at least 6 donor exposures.

Indications: As an alternative to Factor VIII concentrate in the treatment of inherited deficiencies of:

• von Willebrand Factor (von Willebrand's disease).

• Factor VIII (hemophilia A).

• As a source of fibrinogen in acquired coagulopathies; e. g. DIC.

• Can be used in isolated Factor XIII deficiency.

• Ameliorate platelet dysfunction associated with uraemia.

• Used topically as a fibrin sealant.

Storage: At –25 °C or colder for up to 1 year.

Administration:

• ABO compatible product should be used.

• After thawing, infuse as soon as possible.

• Must be transfused within 6 hours of thawing.

Blood groups and compatibilities

There are many blood groups in the human population including ABO, Rh, Kidd, Kell, Duffy, MNS and Lewis. The ABO blood types were discovered by Karl Landsteiner in 1901; he received the Nobel Prize in Physiology or Medicine in

1930 for this discovery. Routine blood typing involves determining the ABO and RhD (Rh factor) type. In human blood transfusions they are the most important of the 38 different blood groups currently recognized. A mismatch in these, or any other serotype, can cause a potentially fatal adverse reaction after a transfusion, or an unwanted immune response to an organ transplant.

ABO antigens and antibodies

The ABO blood group is the most important of all the blood group systems. There are four different ABO blood groups (see Table 11), determined by whether or not an individual's red cells carry the A antigen, the B antigen, both A and B antigens or neither. Normal healthy individuals, from early in childhood, make red cell antibodies against A or B antigens that are not expressed on their own cells. These naturally occurring antibodies are mainly IgM immunoglobulins. They attack and rapidly destroy red cells carrying the corresponding antigen. For example, anti-A attacks red cells of group A or AB. Anti-B attacks red cells of group B or AB.

Table 11 – **ABO antigens and antibodies**

Name of Blood group	Antigens present on the red cell surface	ABO antibodies present in the plasma
Type O	nil	anti-A and anti-B
Type A	A antigen	anti-B
Type B	B antigen	anti-A
Type AB	A and B antigens	nil

If ABO incompatible red cells are transfused, red cell hemolysis can occur. For example, if group A red cells are

infused into a recipient who is group O, the recipient's anti-A antibodies bind to the transfused cells. An ABO incompatible transfusion reaction may result in overwhelming hemostatic and complement activation, resulting in shock, renal failure and death.

Rhesus D (RhD) antigen

The Rh blood group system is the second most important blood group system, after the ABO blood group system. The Rh blood group system consists of 49 defined blood group antigens, among which the five antigens D, C, c, E, and e are the most important. There is no d antigen. The presence of RhD antigen in individual is normally described with a «Rh-positive» status. The term «Rh negative» refer to the lack of RhD antigen. Among Europeans, the frequency of rhesus-positive people reaches 85 %, Rh-negative – 15 %. The mongoloid race has about 1 % Rh-negative individuals.

Antibodies to RhD develop only after an individual is exposed to RhD antigens via transfusion, pregnancy or organ transplantation. Anti RhD (or anti-D) antibodies destroy RhD positive red cells and can lead to hemolytic transfusion reactions. This is of particular importance in pregnancy where anti-D antibodies can cross the placenta from mother to unborn child and lead to hemolytic disease of the newborn.

As a general rule, RhD negative individuals should not be transfused with RhD positive red cells, especially RhD negative girls and women of childbearing age. If transfusion of an RhD positive product to RhD negative recipient is unavoidable a hematologist should be consulted and administration of anti-D immunoglobulin considered.

When a transfusion is given, it is preferable for patients to receive blood and plasma of the same ABO and RhD group. However, if the required blood type is unavailable, a patient may be given a product of an alternative but compatible group as shown below (see Table 12).

Table 12 – **Blood Compatibility**

Patient Type	Compatible Red Cell Types	Compatible Plasma Types (FFP and Cryoprecipitate)
A	A, O	A, AB
B	B, O	B, AB
O	O	O, A, B, AB
AB	AB, A, B, O	AB
RhD Positive	RhD Positive RhD Negative	RhD Positive RhD Negative
RhD Negative	RhD Negative	RhD Positive RhD Negative

Note that Group O RhD negative (O negative) red cells have neither ABO nor RhD antigens on their surface. O RhD negative red cells are issued in emergency situations where life saving transfusion is required prior to completion of a crossmatch. Both RCH and RWH blood banks maintain a reserve of 5 emergency O RhD Negative red cells. Group O is often referred to as the universal red cell donor.

Group AB individuals have neither anti-A nor anti-B antibodies in their plasma. Group AB plasma can therefore be given to patients of any ABO blood group and is often referred to as the universal plasma donor.

Avoiding ABO incompatible transfusions.

Most ABO incompatible transfusions occur as a result of improper patient identification at the time of collection of the pre-transfusion sample or administration of the blood product. The pre-transfusion check is carried out at the bedside by 2 members of clinical staff to ensure the right blood is transfused to the right patient. Positive patient identification

prior to blood sample collection and labelling the specimen tube at the bedside is critical for accurate sample collection.

Other blood cell antigen-antibody systems

There are many other antigen systems expressed on red cells, white cells and platelets. Transfusion can cause antibodies to develop in the recipient. Some of these antibodies can cause transfusion reactions or damage the fetus. The purpose of pretransfusion testing (or crossmatching) is to detect potentially harmful antibodies in a patient before transfusion and where possible select red cell units that will not react with them.

Red cell compatibility testing includes:

• ABO and RhD grouping on patient and donors.

• Antibody screening on patient:

1. For patients who have "no red cell antibodies detected", compatible units are selected and issued electronically.

2. For patients who have "red cell antibodies detected", further laboratory work is required to identify the specificity of the antibody, to type the patient and donor units in order to provide specific antigen negative blood and to perform a full serological crossmatch. For patients with multiple antibodies this work can take several hours to complete.

• Crossmatching between serum of patient and red cells of donor. These procedures normally take about an hour or more to complete. Shortened procedures are possible in case of emergency, but may fail to detect some incompatibilities.

• Correlating with previous transfusion and blood group records. The patient's current blood group must agree with any previous record of the patients group. Patient's, who have previously had clinically significant red cell antibodies detected require antigen negative blood and full serological crossmatching.

Testing for ABO group

Procedure:

Necessary equipment:

1. Blood sample.
2. Anti-A and anti-B reagents.
3. Standard serums AB0 of 2 series.
4. Testing plate.
5. Glass stick for blood missing.
6. Normal saline.

One end of a slide is labelled Anti-A, and the other Anti-B. A drop of Anti-A test serum is added to the end marked Anti-A, and a drop of Anti-B serum is added to the end marked Anti-B. One drop of blood is added to each end of the slide, and mixed well, using separate glass sticks.

The results are read directly from the slide. The subject is blood group A if agglutination occurred with the Anti-A test serum; group B if agglutination occurred with the Anti-B test serum; group AB if agglutination occurred with both test serums, and O if there was no agglutination in either case.

Identification of RH blood group

In order to identify RH blood group standard anti-RH-antiserums with Rh-antigens are used. Those serums are produced in bottles signed Rh-anti-D, Rh-anti-C, Rh-anti-E. During Rh-test of the recipient only Rh-anti-D serum is used. However, in case of blood donors all 3 are needed.

Procedure:

Apply on the special testing plate drops of anti-D standard serum and patient's blood. Mix them with a special glass stick until they become one homogenic drop. Evaluate results in 5 minutes: agglutination means that patient`s blood contains the Rh-D-antigen. Another method of Rh-blood group system testing is agglutination with the usage of 10 % gelatin solution (48 ^{0}C, water bath).

Antibody screening

Antibody screening is done to look for unexpected antibodies to other blood groups, such as certain Rh (e. g. E, e, C, c), Duffy, MNS, Kell, Kidd, and P system antigens. The recipient's serum is mixed with screening reagent red blood cells. The screening reagent red blood cells are cells with known antigens. This test is sometimes called an indirect antiglobulin or Coombs test. If an antibody to an antigen is present, the mixture will cause agglutination (clumping) of the red blood cells or cause hemolysis (breaking of the red cell membrane). If an antibody to one of these antigens is found, only blood without that antigen will be compatible in a cross-match. This sequence must be repeated before each transfusion a person receives.

Crossmatching

Crossmatching is the final step in pretransfusion testing. It is commonly referred to as compatibility testing, or "type and cross." Before blood from a donor and the recipient are cross-matched, both are ABO and Rh typed. To begin the cross-match, a unit of blood from a donor with the same ABO and Rh type as the recipient is selected. Serum from the patient is mixed with red blood cells from the donor. The cross-match can be performed either as a short (5–10 min) incubation intended only to verify ABO compatibility or as a long (45 min) incubation with an antihuman globulin test intended to verify compatibility for all other red cell antigens. If clumping occurs, the blood is not compatible; if clumping does not occur, the blood is compatible. If an unexpected antibody is found in either the patient or the donor, the blood bank does further testing to ensure that the blood is compatible.

In an emergency, when there is not enough time for blood typing and cross-matching, O red blood cells may be given, preferably Rh-negative. O-type blood is called the universal donor because it has no ABO antigens for a patient's

antibodies to combine with. In contrast, AB blood type is called the universal recipient because it has no ABO antibodies to combine with the antigens on transfused red blood cells. If there is time for blood typing, red blood cells of the recipient type (type-specific cells) are given. In either case, the cross-match is continued even though the transfusion has begun.

Purpose of compatibility testing:
• To select blood components that will cause no harm to the recipient and will have acceptable survival rates when transfused.

• When correctly performed, compatibility tests will confirm ABO compatibility between component and recipient and will detect the most clinically significant unexpected antibodies.

• Compatibility (cross-match) must be performed before blood is transfused. The cross match is incompatible if there is a reaction between the patient's serum and donor's red cells.

Monitoring the transfusion
• It is essential to take baseline observations and to ensure that the patient is monitored during the transfusion in order to detect any adverse event as early as possible. Before commencing the transfusion, it is essential to encourage the patient to notify a nurse or doctor immediately if he or she becomes aware of any discomfort such as shivering, flushing, pain or shortness of breath or begins to feel anxious.

• Ensure that the patient is in a setting where he or she can be directly observed.

• For each unit of blood transfused monitor the patient:
1. Before starting the transfusion (baseline observation).
2. 15 minutes after starting the transfusion.
3. At least every hour during transfusion.

4. Carry out a final set of observations 15 minutes after each unit has been transfused.

Adverse effects of transfusion

- The very first step is to stop the transfusion immediately. If the reaction is severe, the needle should be removed to prevent any further transfusion of blood.
- All suspected acute transfusion reactions should be reported immediately to the blood transfusion center and to the doctor responsible for the patient. With the exception of urticarial allergic reactions and febrile non- hemolytic reactions, all are potentially fatal and require urgent treatment.
- Acute reactions may occur in 1 % to 2 % of transfused patients. Rapid recognition and management of the reaction may save the patient's life. Once immediate action has been taken, careful and repeated clinical assessment is essential to identify and treat the patient's problems.
- Errors and failure to adhere to correct procedures are the common causes of life- threatening acute hemolytic transfusion reactions.
- Bacterial contamination in red cells or platelet concentrates is an under- recognized cause of acute transfusion reaction.
- Patients who receive regular transfusions are particularly at risk of acute febrile reactions. These should be recognized so that transfusion is not delayed or stopped unnecessarily.
- Transfusion transmitted infections are the serious delayed complications of transfusion. Since a delayed transfusion reaction may occur days, weeks or months after the transfusion, the association with the transfusion may not be recognized.

- The transfusion of a large volume of blood and intravenous fluids may cause hemostatic defects or metabolic disturbances.

Acute or Immediate Transfusion Reactions:

1. Acute Hemolytic Transfusion Reactions

The most serious and potentially life-threatening reaction is acute hemolytic transfusion reaction (AHTR), which occurs when the donor's red cells are incompatible with the patient's plasma as a result of identification errors during the transfusion process. As few as 10 ml of the wrong blood can produce AHTR symptoms. Death from AHTR is estimated to occur in 1:1.8 million transfusions.

Signs and symptoms:

- Typically begin with fever and tachycardia.
- Mild: Abdominal, chest, flank/back pain.
- Severe: Fever, chills, hypotension, dyspnea, flank pain, shock.
- Oliguria or anuria, abnormal bleeding.
- Red/dark urine may be first sign in an anesthetized patient.
- If infusion is allowed to continue, symptoms progress to shock and DIC.

Interventions:

Prompt recognition of AHTR is critical to successful outcome.

- Stop the transfusion immediately.
- Disconnect the tubing from the I.V. catheter and prepare/infuse fresh administration set primed with fresh 0.9 % sodium chloride.
- Notify the LIP and blood bank or transfusion service immediately.
- Monitor vital signs.
- Anticipate the following interventions:

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1. Intravascular volume may be maintained with fluids to improve hypotension and promote renal circulation.

2. The patient's respiratory status may have to be supported.

3. Low-dose dopamine may be administered to increase renal function (controversial).

4. Furosemide may be ordered to maintain urine output greater than 100 ml/hr to decrease the risk of renal damage.

5. Therapies, such as heparin to prevent DIC or mannitol to produce an osmotic diuresis, are controversial but are sometimes used cautiously.

Extreme care during the entire identification process is the first step in prevention. Clerical and human errors involving proper patient, sample, and blood unit identification are the most common causes of AHTR. The transfusion must be started slowly, and evaluation of the patient for reactions during the first 15 minutes is needed to monitor for initial AHTR.

2. Nonhemolytic febrile reactions

The nonhemolytic febrile reaction is manifested by a rise in temperature of 1 °C or more occurring in association with transfusion and not having any other explanation. It usually occurs as a result of reactions to antibodies directed against leukocytes or platelets. Febrile reactions occur in only 1% of transfusions; repeat reactions are uncommon. Such reactions can occur immediately or within 1 to 2 hours after transfusion is completed.

Signs and symptoms:
- Fever, increase greater than 1 °C.
- Chills.
- Headache.
- Vomiting.

Interventions:

• Stop transfusion and initiate transfusion reaction workup.

• Change administration set and administer 0.9 % sodium chloride to keep the vein open.

• Notify LIP and blood bank, and institute transfusion reaction protocol.

• Monitor vital signs.

• Administer antipyretic agents as ordered.

Another transfusion unit may be safely infused once symptoms subside. The remainder of the implicated component should not be transfused.

3. Allergic Reactions

In its mild form, allergic reactions are a common type of reaction. They are probably caused by allergens in the component or less often by antibodies from an allergic donor. The patient may experience mild localized urticaria, pruritus, and flushing. Allergic reactions usually occur within seconds to minutes of starting the transfusion. Most reactions respond to antihistamines. Severe anaphylactic reactions include symptoms of urticaria and angiedema but progress to severe hypotension, shock, and loss of consciousness.

Signs and symptoms:

• Mild: Itching, hives, urticaria, angiedema (deep swelling around eyes/lips).

• Severe: Anxiety, bronchospasm, wheezing, hypotension, shock, loss of consciousness.

Interventions:

• Stop the transfusion.

• Keep the vein open with normal saline.

• Monitor vital signs.

• For a mild reaction, administer antihistamines and resume transfusion after symptoms have resolved.

Anaphylactic reaction: give fluids, place patient in Trendelenberg position, administer epinephrine, antihistamines, steroids.

Prevention

For mild reactions, premedicate with diphenhydramine 30 minutes before the transfusion. For patients whose reactions are severe, washing red cells or platelets may be considered. Administration of deglycerolized rejuvenated RBCs has met with some success. For patients with anaphylactic reactions, IgA-deficient components are required. There should be an availability of various treatments including oxygen, adrenaline, corticosteroids, bronchodilators, diuretics and an emergency team.

Test tasks for checking the final level of knowledge:

1. Antibodies in the blood system are called:

A. HLA.

B. Agglutinogens.

C. Agglutinins.

D. Antigens.

2. Which of the following diseases is donor blood screened for?

A. Hepatitis B.

B. West Nile Virus.

C. Crohn's Disease.

D. Epstein – Barr Virus (Ebv).

3. The initial nursing intervention for an acute hemolytic transfusion reaction would be to:

A. Slow the transfusion and call the lip.

B. Stop the transfusion and turn the saline side of the administration set on at a slow keep open rate.

C. Stop the transfusion, disconnect the tubing from the i.v. catheter, and initiate new saline and tubing to keep the vein open.

D. Stop the transfusion and turn the saline side of the administration set on at a rapid rate.

4. The component albumin 25 % is hypertonic. Caution should be used by nurses when infusing 25 % albumin because this product can:

A. Cause circulatory overload.

B. Cause clotting disorders.

C. Increase rbc hemoglobin.

D. Lower the blood pressure.

5. Which of the following must an RN check with another nurse before initiating a unit of blood? (Select all that apply.)

A. ABO and Rh.

B. Patient name.

C. Unit number.

D. Expiration date.

E. Preservative.

6. The universal recipient is a person with blood type:

A. A-positive.

B. Ab-positive.

C. O-negative.

D. AB-negative.

6. If a patient receives 2 units of packed red blood cells for an Hct of 24 %, what would the anticipated Hct be 24 hours postinfusion?

A. 26 %.

B. 28 %.

C. 30 %.

D. 32 %.

7. A patient with group O blood type may receive which of the following RBCs?

A. Group A only.

B. Group 0 only.

C. Group AB and 0.

D. Any blood group.

8. In order to identify blood group you need:

A. To mix the drop of patient`s blood and recipient serum 1/7 respectively.

B. To mix the drop of patient`s blood with all standard serums.

C. To mix drops of standard serums of 2 series with drops of patient`s blood.

D. To perform the actions described in B with water bath.

9. Patient S., 24 years old, was admitted to the surgical department with the clinic of gastrointestinal bleeding. When examining the blood group O (I), er-2.6×10^{12}/l, HB-60 g/l. In order to correct anemia, 500 ml of erythrocyte mass O (I) was transfused. The patient's condition improved, but within a few day renal failure began to grow. Urine in the first 2 days was the color of meat slops. What is the possible cause of this complication?

10. The patient, 15 minutes after the start of the transfusion, developed shortness of breath, chills, headache, abdominal pain, a sharp decrease in blood pressure, tachycardia. What complication is observed in the patient?

8. PARENTERAL NUTRITION

The main goal in initiating nutritional therapy is to prevent or treat malnutrition/undernutrition among patients unable to sustain sufficient oral intake.

Patients should be considered malnourished or at risk for malnutrition under the following conditions:

• Inadequate nutrient intake for 7 or more days.

• Involuntary weight loss of 5 % or greater of usual body weight in 1 month.

• Involuntary weight loss of 10 % or greater of usual body weight over 6 months.

Three types of malnutrition have been defined and classified by an International Classification of Diseases (ICD) diagnostic code: marasmus, kwashiorkor, and mixed malnutrition.

Marasmus, or simple starvation, is caused by a decrease in the intake of calories with adequate protein–calorie ratio. In this type of malnutrition, a gradual wasting of body fat and skeletal muscle takes place with preservation of visceral proteins. The individual appears emaciated and has decreased anthropometric measurements (e. g., history of weight loss) and anergy to common skin test antigens.

Kwashiorkor is characterized by an adequate intake of calories but with a poor protein intake. This condition causes visceral protein wasting with preservation of fat and somatic muscle. It is seen during a period of decreased protein intake, as seen in patients on liquid diets, fad diets, and long-term use of I.V. fluids containing dextrose. Loss of body protein is caused by depleted circulating proteins in the plasma. Individuals may appear well nourished or obese and have adequate anthropometric measurements but decreased visceral proteins and depressed immune function.

Mixed malnutrition is characterized by aspects of both marasmus and kwashiorkor. The person presents with skeletal muscle and visceral protein wasting, depleted fat stores, and immune incompetence. The affected person appears cachectic and usually is in acute catabolic stress. This mixed protein–calorie disorder is associated with the highest risk of morbidity and mortality.

For some conditions, there are disease specific formulae to optimize the patient`s nutritional status by managing nutrients, fluid and electrolytes, adjusted to the specific pathophysiological processes. Historically, serum proteins such as albumin and prealbumin have been widely used by physicians to determine patient nutritional status. However,

recent focus has been on an appropriate nutrition-focused physical examination for diagnosing malnutrition due to laboratory markers are not reliable by themselves but could be used as a complement to a thorough physical examination.

A careful balance of macronutrients (protein, lipid and carbohydrate) provides energy requirements, while micronutrients (vitamins and minerals) are required in very small amounts to maintain health but not to provide energy.

The variability in resting energy expenditure makes it very difficult to predict caloric requirements. Both underfeeding and overfeeding can be harmful.

Resting energy expenditure (REE) can be measured using indirect calorimetry and calculated using the Oxford equation, which has now largely replaced the abbreviated Weir equation and the Harris Benedict equation.

These equations estimate Basal metabolic rate (BMR) in afebrile healthy individuals and therefore need to be modified in the following circumstances:

• Fever increase by 10 % for each 1 °C above 37 °C (up to max of 40 °C).

• Sepsis increase by 9 % regardless of temperature.

• Surgery increase by 6 % if patient has had surgery or trauma.

• Burns increase by 100 % if any size over 30 % (or use Toronto formula).

These factors are additive, so the energy requirements for a 33-year old man (height 1.80 m, weight 75 kg), admitted after a laparotomy for a ruptured appendix and sepsis (temperature 39 °C), work out to approximately 2 460 kcal/kg^{-1} / day^{-1} as follows: 25 kcal/kg^{-1}/ day^{-1} is generally recommended for most acutely ill patients.

BMR = (13.75 × 75 kg) + (5 × 180 cm) − (6.78 × 33 years) + 66 = 1 773.5 kcal/day^{-1}.

REE = 1 773.5 × 1.2 (add 20 % for temperature) × 1.09 (for sepsis) × 1.06 (surgery) = 2 458.9 kcal/day^{-1} (i. e. roughly 2 460 kcal/day^{-1}). The Harris–Benedict equation is an empirically derived equation with variables that reflect the relative contributions to overall heat production per square meter body surface area of activity, age, sex, and body size:

For males: BEE = 66.47 + 13.75 × BW (kg) + 5 × H (cm) – 6.74 × Age (years).

For females: BEE = 655 + 9.6 × BW (kg) + 1.85 × H (cm) – 4.68 × Age (years).

Basal energy expenditure (BEE) equals basal energy expenditure in kilocalories per day.

To apply this equation to nutritional requirements the BEE is multiplied by time activity and injury factors to arrive at a daily nutrition requirement in kilocalories per day, or TEE.

Activity factors vary from 1 for bed rest to 1.3 for ambulatory patient. Injury factors vary from 1 to 1.2 for minor surgery to 1.8 for major sepsis. For each degree above 37.2 °C the daily nutrition requirement is multiplied by 1.07.

Protein requirements are determined and the remaining calories are divided between glucose and lipid (Tab. 13). During recovery the aim should be to provide values of 25–30 kcal/kg^{-1} / day^{-1} to support the process of anabolic reconstitution.

Table 13 – **Protein, glucose and lipid requirements**

Protein	Protein Provides 4 kcal/g $^{-1}$ Around **1.5 g/kg^{-1}/day^{-1}** (range 1.2 to 2 g/kg–1 /day^{-1} for ICU patients) Use **2 g/kg^{-1}/day^{-1}** if severely catabolic e. g. severe sepsis, burns or trauma Should be a mixture of essential and non-essential amino acids
Lipid	Provides 9.3 kcal/g $^{-1}$ Calories from lipid should be limited to 40 % of total calories
Carbohydrate	Provides 3.75 kcal/g $^{-1}$ in vivo **3 to 4 g/kg^{-1}** /day^{-1} Give the remaining energy requirements as carbohydrate

Failure to deliver at least 25 % of calculated requirements is associated with worse outcome, however it is better to underfeed rather than attempt to match a calculated energy requirement, particular in sepsis and trauma.

The National Institute for Clinical Excellence (UK) has recommended that parenteral nutrition should be limited to a maximum of 50 % or the calculated requirements for the first 48 hours after initiation.

Predictive equations should be used with caution, as they provide a less accurate measure of energy requirement then indirect calorimetry.

They are even more problematic in the obese patients. For all classes of obesity (BMI above 30), the goal of an enteral nutrition regime should not exceed 60–70 % of target energy requirement or 11–14 kcal/kg^{-1} actual body weight per day (or 22–25 % kcal/kg^{-1} ideal body weight per day).

The proportion of a feed made up by protein is sometimes expressed as a calorie: nitrogen ratio. 6.25 g of protein contains 1 g of nitrogen. Then calories (kcal) are divided by nitrogen (g). Recommended calorie: nitrogen ratios are around 100:1 which will be achieved using the above figures. The optimal ratio for lipid/carbohydrate is not known.

Oral feeding is the optimal route of nutritional support. However, most ICU patients are incapable or intolerant of oral diet and are therefore fed enterally or parenterally.

Enteral nutrition is recommended over parenteral nutrition by practice guidelines in Europe and North America. This is based on numerous trials involving a variety of critically ill patients, including trauma, burns, head injury, major surgery and acute pancreatitis.

Parenteral nutrition is indicated where enteral nutrition is not recommended, for example in intestinal obstruction/perforation, non-functioning gut, gastrointestinal fistula, prolonged ileus, esophageal/gastric surgery, perforation or malignancy.

Micronutrients. Vitamins are organic compounds that usually act as cofactors for enzymes involved in metabolic pathways. Trace elements are ions that act as cofactors for enzymes or as structurally integral parts of enzymes and are often involved in electron transfer.

Types of nutritional support:

1. Food fortification. This is the process of adding micronutrients to food.

2. Enteral nutrition can be either oral or tube feeding (nasogastric, orogastric, enterostomy (gastrostomy or jejunostomy), post-pyloric feeding (nasojejunal or jejunostomy)).

3. Parenteral nutrition (via either peripheral or central vein):

– Peripheral access: low osmolarity fluids only (< 850 mOsm/l^{-1}). Limited by large volumes needed to provide calories.

– Central access: solutions usually hypertonic.

Enteral nutrition

Enteral nutrition should be started within the first 24–48 hours of admission. It is also important to achieve the estimated caloric target within 48–72 hours. The use of enteral feeding protocols increases the overall percentage of provided goal calories, since they allow doctors to avoid slow initiation and premature cessation of feed.

If caloric and protein needs cannot be met by enteral feeding alone, parenteral feeding or a combination of both needs to be considered. The important steps to ensure adequate enteral nutrition:

1. Confirm the tube position (clinically and radiographically).

2. Secure the tube well and check the site regularly for potential tube dislodgment.

3. Start feeding early.

4. Aspirate regularly (4 hourly) and accept gastric residual volumes of 200–250 ml. Adjust feeding rates accordingly. Once feeding is established this can be stopped.

5. Minimize aspiration risk via the following:

• Patient should be head-up tilt at least 30 °C.

• Avoid bolus feeds.

• Use prokinetics early: metoclopramide 10 mg IV 8 hourly.

• Consider switch to post-pyloric tube feed.

6. Diarrhea associated with tube feeding, needs further evaluation.

Enteral nutrition (i. e., tube feeding) is indicated for patients with a functional GI tract when oral nutrient intake is insufficient to meet needs. Options for enteral access devices

include nasoenteric tubes for short-term use and long-term devices such as gastrostomy, jejunostomy, and gastrojejunostomy tubes. In addition to anticipated duration of need, access device selection is also based on the patient's disease state, GI anatomy and function, and ability to safely access the GI tract via radiological, surgical, or endoscopic techniques.

Advantages of enteral access include the following:

1. Maintenance of the functional integrity of the GI tract.
2. Efficient utilization of nutrients.
3. Ease and safety of administration.
4. Lower cost compared to PN.

Disadvantages / risks include:

1. Contraindications, which include severe short gut syndrome, severe GI malabsorption, severe GI bleed, high-output fistulas, intractable vomiting and/or diarrhea, paralytic ileus.
2. Gastric feedings that require adequate gastric emptying; gastric residuals are used to monitor the safety and effectiveness of tube feedings.
3. Risk for aspiration.
4. Tube placement issues.

PARENTERAL NUTRITION

Parenteral feeding is the intravenous administration of nutrients. This may be supplemental to oral or tube feeding, or it may provide the only the source of nutrition as total parenteral nutrition (TPN). The only absolute indication for parenteral nutrition (PN) is gastrointestinal failure. All efforts to improve tolerance of enteral feeding such as use of prokinetic agents and/or a post-pyloric feeding tube should be used before starting PN.

The goals of PN are:

1. To provide all essential nutrients in adequate amounts to sustain nutritional balance during periods when oral or enteral routes of feedings are not possible or are insufficient to meet the patient's caloric needs.

2. To preserve or restore the body's protein metabolism and prevent the development of protein or caloric malnutrition;

3. To diminish the rate of weight loss and to maintain or increase body weight.

4. To promote wound healing.

5. To replace nutritional deficits.

Patients receiving less than 25 % of their predicted needs are at the increased risk of sepsis and those who are intolerant of enteral nutrition, despite all attempts to improve this, should be considered for parenteral supplementation.

During acute illness, the aim is to provide energy as close as possible to estimated or measured energy expenditure in order to decrease the negative energy balance. In the absence of indirect calorimetry, ICU patients should receive 25 kcal/kg^{-1} /day^{-1} increasing to target levels over the next 2–3 days.

PN can be given as separate components but is more commonly given as a sterile emulsion of water, protein, lipid, carbohydrate, electrolytes, vitamins and trace elements according to the recommendations discussed earlier regarding nutritional requirements.

Standard formulations require thorough mixing before infusion. The electrolyte concentration can be altered for each patient and additional trace elements and vitamins may be added.

Protein is given as amino acids and includes essential amino acids. It should also ideally include most of the non-essential amino acids. Amino acids are the basic units of protein. There are eight essential amino acids needed by adults

that must be supplied in the diet: isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine. There are also nonessential amino acids; these amino acids can be synthesized by the body and include alanine, aspartic acid, asparagine, glutamic acid, glycine, proline, and serine. Conditionally essential amino acids required in the diet during certain disease states include histidine, cysteine, tyrosine, arginine, and glutamine.

Protein in PN is provided as synthetic crystalline amino acids. They are available in concentrations of 3 % to 20 %, with and without electrolytes. There are also specialty amino acid formulations that may be used with certain disease states, such as hepatic encephalopathy and renal failure.

Lipid is commonly given as Intralipid®; it is emulsion made of soya with chylomicron-sized particles. It provides a source of essential fatty acids, (linolenic acid, an omega-3 fatty acid and linoleic acid, an omega-6 fatty acid) and is a vehicle to deliver fat-soluble vitamins.

Because lipid preparations are expensive, it is possible to give parenteral nutrition with low levels of lipid thus giving 6 % of total energy requirement as lipid is enough to avoid essential fatty acid deficiency.

Fat emulsions provide 1.1 kcal/ml (10 % solution) or 2.0 kcal/ml (20 % solution). Lipids may be administered as a separate infusion, concurrently with the aminoacid/dextrose solution via a Y tubing, or as part of a total nutrient admixture. All fat emulsion products are isotonic, have a pH between 6 and 9, and can be administered via a peripheral vein.

Carbohydrate mostly is given as glucose. The minimal amount of carbohydrate required is about 2 g/kg^{-1} glucose per day. Carbohydrates are the major source for energy and provide approximately 60 % of nonprotein calories.

Carbohydrate types include dextrose (glucose), fructose, sorbitol and xylitol, and glycerol. Dextrose is the most

commonly used source of carbohydrate in PN solutions and is commercially available in concentrations from 5 % to 70 %. In addition to caloric need, considerations in the amount and concentration of glucose are based on respiratory, cardiac, renal, and fluid volume status.

Dextrose may be administered with amino acids as the only nonprotein source of calories or administered in conjunction with lipids. When PN is administered peripherally, the final concentration of dextrose must be 10 % or less to prevent vein irritation, damage to the vein, and thrombosis. Hypertonic concentrations of 10 % and above must be administered through a central vascular access device (CVAD).

Electrolytes and micronutrients. Critically ill patients are prone to fluid and sodium overload, and renal dysfunction is frequent. The exact electrolyte requirement needs to be determined by close plasma electrolyte monitoring and should not be a fixed element of parenteral nutrition prescription. Patients with sepsis may have large amount of vitamin A losses in their urine, burn patients lose selenium, zinc and copper via their exudates and trauma patients lose selenium and zinc through their drains. Selenium impairs the role of glutathione peroxidase as a free radical scavenger and selenium supplementation may be helpful in general ICU patients.

Peripheral parenteral nutrition (PPN) is used to nourish patients who either already are malnourished or have the potential for developing malnutrition and who are not candidates for enteral nutrition. Patients who are candidates for PPN must meet the criteria of good peripheral I.V. access and able to tolerate large volumes of fluid, up to 3 l/day. PPN is considered a controversial therapy; some believe that the risks of PPN outweigh the benefits because candidates for this therapy have minor nutritional deficits.

Advantages of PPN:

1. Avoids insertion and maintenance of a CVAD.

2. Has reduced risk of metabolic complications compared to PN.

Disadvantages / limitations of PPN:

1. Contraindications include significant malnutrition, compromised renal/hepatic status.

2. Cannot be used in volume-restricted patients because higher volumes of solution are needed to provide adequate calories.

3. May cause phlebitis because of high solution osmolarity.

Parenteral nutrition via a central vein (often called total parenteral nutrition [TPN]) is used to provide nutrients at greater concentrations and fluid volumes than is possible with PPN. Central vascular access can be maintained for prolonged periods (weeks to years) with a variety of catheters. The PN formula may be administered with the lipids mixed together with dextrose/aminoacid components (total nutrient admixture; addressed in next section), or the lipids may be administered as a separate intermittent infusion. PN solutions infused through a central vein are highly concentrated. Final concentrations of standard PN solutions include 4.25 % amino acids, 25 % dextrose along with electrolytes, trace elements, and vitamins. PN is usually administered at rates of no more than 200 ml/hr. The delivery of centrally delivered PN involves both advantages and disadvantages.

Advantages:

1. Dextrose solution of 20 % to 70 % can be administered as a calorie source.

2. Is beneficial for long-term use (usually longer than 2 weeks).

3. Large caloric and nutrient needs can be met.

4. Provides calories, restores nitrogen balance and replaces essential vitamins, electrolytes, and minerals.

5. Promotes tissue synthesis, wound healing, and normal metabolic function.

6. Improves tolerance to surgery.

7. Is nutritionally complete.

Disadvantages:

1. Requires placement of a CVAD.

2. May cause metabolic complications, including glucose intolerance and electrolyte imbalances.

3. Fat emulsions may not be used effectively in some severely stressed patients (especially burn patients).

4. Potential complications related to CVADs.

Total Nutrient Admixtures (Three-in-One Admixtures)

Total nutrient admixtures (TNAs) are PN solutions containing dextrose, amino acids, and fat emulsions in one large solution container. TNAs are often referred to as "all-in-one solutions" or "three-in-one solutions" (3-in-1 solutions). The solution is compounded in the pharmacy and is usually milky white and opaque, although a faint yellow hue may be evident with the addition of vitamins. "Multichamber bags" are often used in home infusion. This is defined as a container designed to promote extended stability of the PN formulation by separating some components (e. g., intravenous fat emulsion) from the rest of the formulation. It consists of two or more chambers separated by a seal or tubing that is clamped.

Figure 11 – **Multichamber PN solution container**

At the time of administration, the seal or clamp is opened to allow the contents of the chambers to mix and create an admixture. TNA solutions offer some important **advantages**, including the following:

1. All components compounded aseptically in the pharmacy.

2. Less manipulation during administration and less risk of contamination (compared to administering lipids as a separate infusion).

3. Less nursing time required.

4. Less supply and equipment expense (e. g., one infusion pump and administration set).

5. Dextrose and venous access tolerance in some cases.

6. May be more cost effective.

7.Improved fat clearance when administered over more than 12 hours.

Disadvantages may include less solution stability and risk for separation of lipids, difficulty in visualizing precipitate or particulate matter in the solution, more risk for drug-nutrient

incompatibilities, and increased risk for catheter occlusion over time.

Total nutrient admixtures must be administered through a 1.2 – micron filter because of the risk of particulate matter. Although bacterial contaminants such as Staphylococcus epidermidis and Escherichia coli will not be filtered out, large organisms such as Candida albicans will be trapped by the 1.2 – micron filter. The stability of TNA is affected by many factors, including admixture contents, storage time and conditions, addition of non-nutrient drugs, pH of the solution, and variability in temperature.

Cyclic Parenteral Nutrition

For patients requiring long-term PN support, cyclic PN is widely used. This therapy delivers the PN solution over a reduced time frame between 8 and 16 hours, versus a 24 – hour continuous infusion. Cyclic parenteral nutrition is indicated for patients who have been stable on continuous PN and require long-term PN; for those receiving home PN for patients who can handle total infusion volume in a shortened time period; and for patients who require PN for only a portion of their nutritional needs. Patients are transitioned to cyclic parenteral nutrition once they are stable on a 24 – hour continuous infusion. The hourly rate of PN infusion is increased as the number of infusion hours is decreased. Because of the increased fluid volume and increased glucose delivery over less time, the patient is monitored carefully for signs of fluid volume excess and hyperglycemia. Symptoms of excess fluid administration should be monitored, such as weight gain resulting in edema or infusion-related shortness of breath. If too much fluid is administered during the cyclic period, the time frame should be extended. Cyclic PN administration requires twice as many central line manipulations as continuous PN because of the initiation of the infusion and the discontinuation of the infusion every 24 hours. This increases

the risk of introducing bacteria via the internal catheter lumen and thus the risk for bloodstream infection.

Advantages:

1. Allows for more physiological hormonal response and appetite stimulation because of periods of time without infusion.

2. Prevents or treats hepatotoxicity induced by continuous PN; reverses fatty liver and liver enzyme elevations; faster albumin level recovery.

3. For patients on long – term PN, improved quality of life by encouraging normal daytime activities and enhances psychological wellbeing; patient does not need to carry around an infusion pump 24 hours/day; usually run over nighttime hours for home care patients.

Disadvantages:

1. Patients must be observed for symptoms of hypoglycemia, hyperglycemia, dehydration, excessive fluid administration, and sepsis associated with central-line manipulation.

2. Patients require monitoring for hyperglycemia, which can develop during the peak flow rate (> 250 mg/dl). Inability to control BG levels may require a change back to continuous PN.

3. There is also a risk for hypoglycemia generally during the first hour after cyclic PN discontinuation. BG levels should be checked whenever the patient displays symptoms of nausea, tremors, sweating, anxiety, or lethargy. Tapering the infusion rate for 1 to 2 hours at the end of the infusion may be needed.

Complications associated with parenteral nutrition:

1. Altered glucose metabolism: rebound hypoglycemia.

Rebound hypoglycemia may occur with the discontinuation of cyclic PN or if continuous PN is interrupted

because of continued secretion of insulin by the pancreas in response to the high-dextrose solution. Hypoglycemia is defined as BG less than 7 g/l. Symptoms include diaphoresis, irritability, nervousness, and shaking and may result in a decrease in level of consciousness.

2. Altered glucose metabolism: hyperglycemia. Hyperglycemia is a common and significant complication associated with PN and is caused by poor tolerance of the high dextrose concentrations. Other factors that put the patient at risk for hyperglycemia are the presence of overt or latent diabetes mellitus, older age, sepsis, hypokalemia, and hypophosphatemia. Hyperglycemia is associated with increased risk for complications such as pneumonia and acute renal failure and with an increased mortality rate. Close attention to BG monitoring and management are critical.

3. Electrolyte imbalances: Major electrolyte imbalances associated with PN can occur if excessive or deficient amounts of electrolytes are supplied in the daily fluid allowance. The most common imbalances associated with PN include imbalances of potassium, magnesium, and phosphate. Interventions include frequent monitoring of serum electrolytes and adjustments in the PN solution.

• Potassium: Hypokalemia. Potassium is also driven into the intracellular space during PN. Serum potassium can become depleted with an inadequate supply of this electrolyte. Insulin administration further intensifies intracellular potassium.

• Potassium: Hyperkalemia. A high potassium blood level can occur with renal impairment, can be iatrogenic induced, or can occur with metabolic and respiratory acidosis when potassium shifts out of the cells. Interventions include reducing the amount of potassium ion in the PN solution.

• Magnesium: Hypomagnesemia. The magnesium electrolyte also is driven into the intracellular space during PN administration.

• Phosphate: Hypophosphatemia. Adenosine triphosphate (ATP) is required for all cell energy production. Protein synthesis begins when PN is administered and phosphate is driven into the intracellular space as a component of ATP. Therefore, a deficiency of phosphate can occur.

4. Refeeding syndrome. Cardiac and pulmonary failure can occur when aggressive nutritional support is initiated in a severely malnourished patient. Refeeding syndrome is a rare complication. This occurs when the body, during its bout with starvation, adapts to nutritional deprivation and compensates by decreasing basal energy requirements and diminishing cardiac reserves. This initiation of nutritional support, especially if it is undertaken too aggressively, can lead to an electrolyte shift from the plasma to the intracellular fluid and can result in hypophosphatemia in particular.

Cardiorespiratory complications can occur. The result of refeeding syndrome is manifested by dyspnea, tachycardia advancing to heart failure, and cardiac arrest.

5. Essential fatty acid deficiency essential fatty acid deficiency is a risk when the PN formula is lipid free. Clinical signs and symptoms include:

• Alopecia.
• Impaired wound healing.
• Thrombocytopenia.
• Dry and scaly skin.

The condition is corrected when an IVFE (Intravenous fat emulsion) is added to the formula. Fats may be administered in amounts that supply 30 % to 50 % of the calories.

6. Altered vitamin and trace element balance because of the addition of vitamins and trace elements to the formula,

deficiencies are not common. Twice yearly serum levels are recommended for long-term PN, and patients should be monitored for signs and symptoms of deficiencies. It is important that multivitamins be added to the solution just prior to infusion because vitamin degradation can occur when vitamins are present in the PN admixture for extended periods of time.

Test tasks for checking the final level of knowledge:

1. The type of malnutrition that most commonly occurs in the acutely ill hospitalized patient is:

A. Kwashiorkor.

B. Marasmus.

C. Mixed malnutrition.

D. Anorexia nervosa.

2. How many kilocalories/ml does a 20 % lipid emulsion provide?

A. 1.0.

B. 1.1.

C. 2.0.

D. 2.2.

3. Which of the following are the three essential substrates included in PN required for anabolism and tissue synthesis?

A. Trace elements, protein, and fats.

B. Protein, carbohydrates, and fats.

C. Fats, electrolytes, and carbohydrates.

D. Vitamins, electrolytes, and protein.

4. Which of the following filters should be used with TNA solutions?

A. 0.22-micron filter.

B. 0.45-micron filter.

C. 1.2-micron filter.

D. 170-micron filter.

5. To treat or prevent essential fatty acid deficiency, which of the following should be included in PN?

A. Trace elements.

B. Transferrin.

C. Crystalline amino acids.

D. Lipids.

6. Due to its' short half-life, which of the following visceral proteins is most useful in monitoring protein malnutrition during refeeding?

A. Albumin.

B. Transferrin.

C. Prealbumin.

D. Total protein.

7. Refeeding syndrome is associated with which of the following electrolyte abnormalities?

A. Hyponatremia.

B. Hypercalcemia.

C. Hypophosphatemia.

D. Hypermagnesemia.

8. Which of the following are points of care in delivery of PPN?

A. PPN is mildly hypertonic and should be delivered into a large peripheral vein.

B. A 20 % dextrose solution can be delivered via PPN.

C. Phlebitis is a complication of PPN; the catheter site should be observed with frequent documentation of the condition of the vein and site.

D. PPN is most commonly used for short-term therapy for fairly stable patients whose normal GI functioning will resume within 3 to 4 weeks.

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Навчальне видання

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ВСТУП ДО ІНФУЗІЙНОЇ ТЕРАПІЇ

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Навчальний посібник присвячений питанням інфузійної терапії, яка стала невід'ємним компонентом інтенсивної терапії тяжкохворих пацієнтів. Детально обгрунтований підхід до діагностики і лікування основних типів порушень електролітного обміну та кислотно-лужного балансу. Використані положення міжнародних протоколів із питань, присвячених парентеральному живленню.

Навчальний посібник відповідає Навчальній програмі, затвердженій Міністерством охорони здоров'я України, Міністерством освіти і науки України, та призначений для студентів медичних (фармацевтичних) закладів вищої України ІІІ–IV рівнів акредитації.