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PREFACE

The main objective of this book Pathophysiology is to help the students to understand the key notions of pathophysiology, its current concepts about the etiology of disease, its pathogenesis and manifestations, diagnostic methods, and therapeutic approaches to typical diseases of organs and organ systems. At the same time, in order to obtain maximum results during preparation for practical classes we recommend to study the lecture materials together with the appropriate chapter of the manual, and read additional literature recommended by the teacher.

This will enable to master the course successfully, as well as help to solve different medical problems, which may arise in your future practical work and thus reach the ultimate goal of learning pathophysiology as a subject.

The ultimate objective of studying clinical pathophysiology includes:

- mastering the skill of solving efficiently professional cases encountered by physicians;
- performing pathophysiological analysis, which requires knowledge and skills to define the proper mechanisms that caused the onset, development, and termination of pathological processes in cases of specific disorders and various diseases; to work out principles and methods of their detection, treatment, and prevention;
- formation of the methodological, methodical, and practical basis of the physician's clinical judgment and rational performance.

The objective of the collection of problems is to provide students with an educational material to develop skills, as well as to improve the obtained ability to resolve real clinical cases based on their pathophysiological analysis.

Performing pathophysiological analysis is a model of the physician's communication with a patient (making a scheme of diagnostical search for causes and risk factors of the disease, mechanisms of its development, substantiation of therapeutic and prophylactic measures).

The concept of pathophysiological analysis in the medical school implies:

- analysis and evaluation of particular information about a patient and, if required, additional clinical, laboratory and other data, which can be requested by a student;
- producing an analysis-based, tenable conclusion on the possible causes of onset, conditions and mechanisms of development, principles and methods of diagnostics and treatment of particular processes, reactions, conditions, and diseases.

The authors of the textbook wish students success in their studies of pathophysiology and are ready to help in learning this complex subject necessary for future medical professionals.

This textbook is prepared for medical students studying the course of pathophysiology in English.

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9. DISORDERS OF WATER AND ELECTROLYTE BALANCE. EDEMA

The general clinical terms for fluid volume abnormalities are hypohydration and hyperhydration. Both conditions are associated with a change in extracellular fluid volume.

Hypohydration

Hypohydration is a condition characterized by reduced volume of water in the extracellular compartment. Based on the osmolarity of the extracellular compartment, hypohydration is classified as isosmotic, hyperosmotic, or hyposmotic.

Isosmotic hypohydration is caused by hemorrhage, plasma exudation through burnt skin, and gastrointestinal fluid loss, i.e., through simultaneous loss of water and electrolytes. Initially, fluid is lost from blood plasma and then replenished from the interstitial space. No major change occurs in the osmolarity of extracellular fluid and therefore no water shifts into or out of the intracellular compartment.

Hyperosmotic hypohydration results from decreased water intake or loss of water exceeding the loss of electrolytes. The latter can be induced by excessive evaporation of water through the skin in severe sweating (sweat is hypotonic), renal diseases, or endocrine disorders such as diabetes mellitus or abnormal secretion of the antidiuretic hormone. Initially, fluid is lost from blood plasma, which becomes hyperosmotic, causing a fluid shift from the interstitial space to the plasma. The rise in the interstitial fluid osmolarity causes water to migrate from the intracellular to the extracellular compartment. Finally, the extracellular and intracellular fluid volumes both diminish, thus elevating the osmolarity of both fluid compartments.

Hyposmotic hypohydration is caused by renal loss of sodium chloride and other electrolytes exceeding the loss of water. It can result from adrenal insufficiency or therapy with aldosterone antagonists. Reduced mineralocorticoid activity results in potassium and sodium loss, with consequent hyperkalemia, hyponatremia, volume depletion, and hypotension. A reduction of extracellular osmotic pressure forces water to shift from the extracellular compartment into the intracellular one causing cell swelling with a drop in intracellular osmotic pressure.

Clinical manifestations of hypohydration include low skin turgor, soft and sunken eyeballs, dry mucous membranes, gray and cool skin. A reduction of plasma volume causes tachycardia, arterial hypotension, and flat neck veins.

Hyperhydration

Hyperhydration is a condition characterized by increased volume of water in the extracellular compartment. Similar to hypohydration, hyperhydration can be classified according to the osmolarity of the extracellular compartment as isosmotic, hyperosmotic, or hyposmotic.

Isosmotic hyperhydration is characterized by an overall expansion of the extracellular fluid volume with no change in the osmolarity of the intracellular and extracellular fluid compartments. It can result from oral or parenteral administration of a large volume of isotonic sodium chloride. Isosmotic hyperhydration may be seen in secondary aldosteronism because sodium retention is accompanied by water retention and water intake.

Hyperosmotic hyperhydration is caused by oral or parenteral administration of a large amount of hypertonic fluid. The rise in the plasma osmolarity causes water to shift from the interstitium into the plasma, thereby initially increasing the plasma volume. Concomitantly, an increase in the plasma salt concentration causes sodium chloride to diffuse into the interstitial space. The net result is an increase in the osmolarity of the extracellular fluid. An increase in osmolarity of the extracellular fluid causes water to flow out of the intracellular compartment, which eventually reduces the volume of the intracellular fluid and increases the volume of the extracellular fluid. The osmolality of both major fluid compartments is thus increased.

Hyposmotic hyperhydration is caused by drinking a large volume of water (psychogenic polydipsia) or renal retention of water due to the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Initially, water enters the plasma, causing a decline in the plasma osmolality, a shift of water into the interstitial space, and a decrease in the interstitial fluid osmolality. A decrease in the interstitial fluid osmolality causes water to shift from the extracellular fluid compartment to the intracellular fluid compartment. Finally, the extracellular and intracellular fluid volumes increase, and the osmolality of both major fluid compartments decreases.

Edema

Edema is accumulation of fluid in the interstitial tissue spaces. In addition, depending on the site, fluid build-up in different body cavities are variously designated as hydrothorax, hydropericardium, and ascites. Anasarca is a severe, generalized edema with a profound subcutaneous tissue swelling. Edema may be local or generalized.

Forces that regulate the distribution of fluid between the interstitial and vascular compartments are frequently referred to as the Starling forces. The hydrostatic pressure within the vascular system and the colloid-osmotic pressure in the interstitial fluid tend to promote the migration of fluid from the vascular to extravascular space.

The filtration pressure can be calculated according to the following equation:

$$FP = CHP + ICOP - (CCOP + IHP),$$

where: FP — filtration pressure;

CHP — capillary hydrostatic pressure;

ICOP — interstitial colloid-osmotic pressure;

CCOP — capillary colloid-osmotic pressure;

IHP — interstitial hydrostatic pressure.

In contrast, the colloid-osmotic pressure contributed by the plasma proteins and the hydrostatic pressure within the interstitial fluid, referred to as tissue tension, promote the movement of fluid into the vascular compartment.

The reabsorption pressure is calculated as following:

$$RP = CCOP + IHP - (CHP + ICOP).$$

Arterial hydrostatic pressure is three-fold venous hydrostatic pressure, whereas blood colloid osmotic pressure does not change. Interstitial colloid-osmotic pressure depends on capillary permeability and therefore it is varied in different tissues.

Consequently, there is a movement of water and diffusible solutes from the vascular space at the arterial end of the capillaries. Fluid returns from the interstitial space into the vessels at the venous end of the capillary. The lymphatic system controls the concentration of proteins in the interstitial fluid, the volume of the interstitial fluid and interstitial fluid pressure. The development of edema depends on one or more fluctuations in the Starling forces.

Classification of edema

Depending on its origin, edema can be classified as congestive, renal, inflammatory, hepatic, endocrine, toxic, neurogenic and so on.

According to the mechanisms of excessive fluid accumulation, edema can be classified as hydrostatic, oncotic, osmotic, vasogenic, and lymphatic.

Hydrostatic edema results from elevated intracapillary hydrostatic and filtration pressure. Elevated hydrostatic pressure within microvessels reduces the rate of fluid reabsorption leading to fluid accumulation in the interstitial compartment.

A generalized rise in venous pressure, with resulting systemic edema, occurs most commonly in congestive heart failure affecting the right ventricular function. Although elevated venous hydrostatic pressure is important, the pathogenesis of cardiac edema is more complex.

Mechanisms of realization of the hydrodynamic factor of edema are presented in **fig. 9.1**.

Oncotic edema results from reduced plasma colloid-osmotic pressure. It may be caused by protein malnutrition, malabsorption of amino acids, abnormal production of proteins in the liver (chronic liver failure), leakage of proteins, predominantly albumins, through the glomerular filter (nephrotic syndrome) or skin (extensive burn). In each case, reduced plasma colloid-osmotic pressure leads

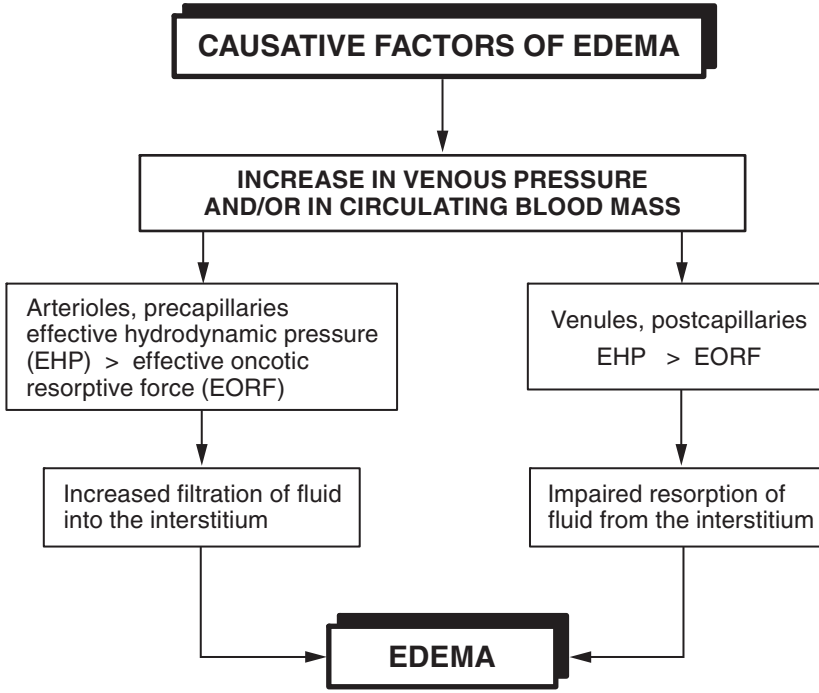

Fig. 9.1. Pathogenesis of edema

to a net movement of fluid into the interstitial tissues and a resultant reduction of plasma volume.

Osmotic edema results from sodium and water retention. Excessive salt retention, with the obligate water retention, causes both elevated hydrostatic pressure and diminished vascular colloid-osmotic pressure. Salt retention may occur upon any acute reduction of the renal function. Edema occurs in acute phases of glomerulonephritis. In most instances edema in this disease results from primary retention of sodium and water by the kidneys owing to renal insufficiency. In some forms of glomerulonephritis increased capillary permeability can be also responsible for the edema development.

Vasogenic edema results from increased permeability of vascular wall to proteins. Accumulation of proteins in the interstitial space enforces the rate of fluid filtration and diminishes the rate of fluid reabsorption. This variant of edema occurs in inflammation or allergic reactions.

Lymphatic edema results from impaired lymphatic drainage due to inflammatory or neoplastic obstruction. The parasitic infection filariasis is a common cause of massive lymphatic and lymph node fibrosis.

Case problems

N 1

Examination of a 32-year-old patient revealed various abnormal signs, including excess body weight: his height is 168 cm, and weight is 84.5 kg. The patient also has a pasty face, periorbital puffiness, pale skin; a slow rebound of tissue to its original contour after pressing the feet or shin with a fingertip. The patient told the physician that his ring and shoes felt tight in the evening. An assessment of the cardiovascular system revealed the following: minor arterial hypotension, areas of cardiac dullness are slightly increased; other parameters are unremarkable. The 24-hours urine volume is within the normal range.

Questions

- What is the possible cause of the patient's excess body weight?
- Can we assume that water balance is disturbed in this patient?
- What type of edema is observed in the patient?
- What additional data are required to specify the type of edema in this case?

N 2

A 42-year-old patient was admitted to hospital with a diagnosis of decompensated chronic heart failure due to valvular disease. The patient has a normal constitution with scarce subcutaneous tissue. His height is 165 cm, and body weight is 81 kg. On examination: the patient needs to sit in bed; he has dyspnea, acrocyanosis, marked edema of lower extremities, rales and wheezes during auscultation of the chest. An X-ray investigation of the abdominal area shows an accumulation of fluid; the liver is enlarged; stroke volume and cardiac output are decreased; hematocrit is 38%; the daily urine volume is decreased. Biochemical tests reveal excessive plasma activity of renin and an elevated sodium concentration.

Questions

- Are there signs of disturbed water balance in this patient?
- What type of water imbalance is observed in this case?
- Is there any association between the accumulation of fluid in the subcutaneous tissue, the abdomen, and the lungs?
- Explain the pathogenesis of elevated blood levels of renin and Na^+ in this patient.
- Explain the pathogenesis of edema in this patient.
- Explain the role of edema in the deterioration of the patient's condition.
- What therapeutic approaches can be used to treat edema in this case?

N 3

A 22-year-old patient who recovered from severe scarlet fever two weeks ago presented with headache, pain in the back, dyspnea, and palpitations. During

the last week, she gained 11.5 kg. On examination: her face is pale; periorbital puffiness and edema of the shins and feet; extended boundaries of cardiac dullness; blood pressure is 180/100 mm Hg; the 24-hours urine volume is reduced. Urine test shows the presence of erythrocytes and protein. An increased titer of antistreptolysin O antibodies is found in the blood.

Questions

- Is there evidence of kidney damage in this patient? What is the possible mechanism of this condition?
- What is the cause of hyperhydration in this case: diminished water excretion or excess water retention?
- Explain the mechanisms of edema in this patient.

N 4

A 7-year-old boy developed a progressive swelling of the soft palate with swallowing difficulty, and then asphyxia after he had drunk mango juice. The mucosal membrane in the swollen area is hyperemic without tenderness; a moderate increase in eosinophils is seen in the blood. The patient's body temperature is normal. His senior sister has periodic attacks of bronchial asthma.

Questions

- Is edema in this case the result of ordinary inflammation?
- What is the cause of edema in this patient?
- Explain the pathogenesis of the given condition.
- Does this type of edema lead to a life-threatening condition?

Tests

I. Water imbalance may be induced by such hormones as:

1) thyroxin;
2) epinephrine;
3) oxytocin;
4) antidiuretic hormone;
5) insulin;
6) aldosterone.

II. Events which may induce interstitial edema are:

1) greater permeability of the capillary membrane;
2) a drop in plasma colloid-osmotic pressure;
3) higher interstitial colloid-osmotic pressure;
4) higher hydrostatic pressure at the venous end of the capillary bed;
5) intense lymph outflow;
6) elevated hydrostatic pressure at the arterial end of pulmonary capillaries;
7) elevated plasma osmotic pressure.

III. Total hyposmolar hyperhydration can be caused by:
1) deficiency of antidiuretic hormone;
2) hypoaldosteronism;
3) diarrhea;
4) severe acute hemorrhage;
5) hyperaldosteronism;
6) excessive production of antidiuretic hormone;
7) severe sweating;
8) excessive water intake.

IV. Factors which initiate the development of edema in congestive heart failure are:
1) activation of osmoreceptors;
2) elevated tissue osmotic pressure;
3) activation of volume receptors;
4) hypoproteinemia;
5) a decrease in cardiac output;
6) accumulation of blood in venous circulation;
7) excessive production of antidiuretic hormone.

V. Factors which initiate the development of nephrotic edema are:
1) protein loss by the kidneys;
2) excess renin secretion;
3) excess water retention by the kidneys;
4) a drop in plasma osmotic pressure;
5) a drop in arterial blood pressure;
6) slower glomerular filtration rate.

VI. The order of events leading to the development of nephrotic edema is:
1) f, e, g, a, c, b, d;
2) f, e, g, c, a, b, d;
3) f, e, g, c, b, a, d;
4) f, e, c, g, a, b, d;

a) activation of the renin-angiotensin-aldosterone system;
b) activated ADH secretion;
c) greater sodium retention;
d) greater water retention;
e) a drop in plasma colloid osmotic pressure;
f) greater glomerular membrane permeability for plasma proteins;
g) a drop in effective arterial blood pressure.

VII. Conditions which may result in cerebral edema are:
1) greater permeability of the blood brain barrier;
2) greater outflow of the cerebrospinal fluid;
3) hypoxia;
4) a drop in blood osmotic pressure;
5) elevated blood colloid-osmotic pressure;

6) a drop in blood colloid-osmotic pressure;
7) hypoglycemia.

VIII. Starling forces include:
1) capillary hydrostatic pressure;
2) plasma colloid-osmotic pressure;
3) interstitial hydrostatic pressure;
4) interstitial colloid-osmotic pressure;
5) lymphatic hydrostatic pressure;
6) interstitial osmotic pressure;
7) plasma osmotic pressure.

IX. The main causes of hyperosmotic dehydration are:
1) excessive water evaporation through the skin;
2) diabetes mellitus;
3) hemorrhage;
4) plasma exudation through the burned skin;
5) diarrhea;
6) insufficiency of antidiuretic hormone;
7) adrenal insufficiency.

X. Factors which promote water absorption at the venous end of the capillary bed are:
1) interstitial colloid-osmotic pressure;
2) positive interstitial hydrostatic pressure;
3) hydrostatic pressure at the venous end of the capillary;
4) plasma colloid-osmotic pressure;
5) hydrostatic pressure at the arterial end of the capillary.

XI. Isosmolar hypohydration is observed in:
1) adrenal insufficiency;
2) osmotic diarrhea;
3) secretory diarrhea;
4) massive blood loss;
5) intractable vomiting;
6) extensive burns;
7) diabetes mellitus;
8) vasopressin deficiency.

XII. Factors which induce renin secretion from the kidneys in congestive heart failure are:
1) lesser Na^+ and Cl^- flux across the macula densa;
2) a drop in blood pressure in the glomerular vessels of kidneys;
3) stimulation of sodium reabsorption in the collecting tubules;
4) abnormal water retention in the collecting ducts.

Correct answers

I — 1, 4, 5, 6; **II** — 1, 2, 3, 4, 6; **III** — 6, 8; **IV** — 5, 6; **V** — 1; **VI** — 1; **VII** — 1, 3, 4, 6, 7; **VIII** — 1, 2, 3, 4; **IX** — 1, 2, 6; **X** — 2, 4; **XI** — 3, 4, 6; **XII** — 1, 2.