

## **DIURETICS. DRUGS USED IN THE TREATMENT OF GOUT AND UROLYTHIASIS. DRUGS WITH INFLUENCE UPON ACID-BASE AND/OR WATER-ELECTROLYTE BALANCE. PLASMA VOLUME EXPANDERS.**

**A. Actuality.** The retention of salts and water in the body is responsible for tissue hydration, and in kidney diseases, cardiovascular insufficiency, liver pathologies and emergency situations (acute intoxications, hypertensive crises, cerebral edema, etc.) and the formation of edema.

In order to solve the respective situations, it is necessary to select the appropriate diuretics according to their place and mechanism of action, pharmacodynamic and pharmacokinetic properties.

Gout is a disease caused by the formation and excessive deposition of uric acid in the tissues and requires the use of drugs to control attacks and prophylaxis (treatment) of gout. Urolithiasis states, determined by the formation of various endogenous metabolites with precipitation in the form of stones, require systematic treatment to prevent the formation and/or dissolution of kidney stones. Disturbances of the hydro-electrolytic and acid-base balance, present in various diseases and pathological conditions, require appropriate correction. Hypovolemia states accompany a varied range of pathologies (shocks, arterial hypotension, dehydration, intoxication, etc.) and present emergency states with the appropriate selection of plasma volume substitutes depending on the pharmacological effects and adverse reactions.

**B. The aim of the training is** to familiarize students with the pharmacological properties of diuretics, anti-gout drugs and drugs used in urolithiasis, hydro-electrolytic and acid-base balance disorders, plasma volume substitutes, as well as prescribing recipe and selecting drugs according to pathology.

### **C. Learning objectives:**

1) The student must **know**: definition, classification, mechanisms of action, pharmacological effects, indications, contraindications, adverse reactions and pharmacokinetics of diuretics, antigout drugs, drugs used in urolithiasis, drugs used in hydro-electrolytic and acid-base balance disorders, plasma volume substitutes.

2) The student must **be able to**: prescribe the compulsory drugs from the respective groups in various medicinal forms and indicate them according to the disease and pathological conditions.

### **D. Knowledge from previous and related disciplines necessary for interdisciplinary integration.**

**Anatomy.** Functional anatomy of the urinary system.

**Histology.** The structure of nephron. The morphofunctional bases of regulation of the urine formation process. Development, structure, histophysiology of the urinary system.

**Physiology.** The main mechanisms of urine excretion (formation). Acid-base status and hydro-electrolyte balance.

**Biochemistry.** Disorders of glomerular filtration, tubular reabsorption and secretion. Biochemistry of urine formation. Kidney stones, their structure, and mechanism of formation.

**Pathophysiology.** Disorders of hydro-electrolytic and acid-base balance. Pathogenesis of edema and hypovolemia. Iso-, hypo- and hyperosmolar hyperhydration and dehydration. Dysmineraloses (hyper- and hyponatremia, hyper- and hypokalemia, hyper- and hypocalcemia, hyper- and hypochloremia, hyper- and hypophosphatemia). Manifestations of acid-base imbalance (acidosis and alkalosis (respiratory, metabolic, excretory, exogenous)).

### **E. Self-training questions:**

1. Diuretics. The notion of diuretics and saluretics.
2. Classification of diuretics according to the mechanism of action, place of action in the

- nephron, and duration of action.
3. Diuretics with predominant influence on the proximal convoluted tube. Carbonic anhydrase inhibitors: mechanism of action, pharmacological effects, indications, contraindications, adverse reactions.
  4. Diuretics with a predominant influence on the ascending portion of the loop of Henle (saluretics): mechanism of action, pharmacological effects, indications, contraindications, adverse reactions.
  5. Drugs with influence on the cortical segment of the loop of Henle and the distal convoluted tube. Thiazide and related (non-thiazide) diuretics: mechanism of action, pharmacological effects, indications, contraindications, adverse reactions.
  6. Diuretics with predominant influence on the terminal segment of the distal convoluted tube and the collecting tube. Competitive and non-competitive aldosterone antagonists: mechanisms of action, pharmacological effects, indications, contraindications, adverse reactions.
  7. Drugs with action throughout the entire nephron, but mainly in the proximal tubules. Osmotic diuretics: mechanism of action, pharmacological effects, indications, contraindications, adverse reactions.
  8. Drugs used in the treatment of gout. Classification. Drugs with specific action used in gout crisis: mechanism of action, pharmacological effects, indications, adverse reactions. Classification of drugs used in the prophylaxis (treatment) of gout. Mechanism of action, pharmacological effects, indications and adverse reactions of uricoinhibitors, uricosurics and uricolytics.
  9. Classification of drugs used in urolithiasis.
  10. Classification of drugs used in hydro-electrolytic balance disorders. Crystalloid solutions used in isotonic, hypotonic and hypertonic dehydrations: pharmacological properties, indications, contraindications, adverse reactions. Drugs used to correct hypokalemia, hypomagnesemia, hypocalcemia.
  11. Classification of drugs used in acid-base balance disorders and drugs used in the treatment of acidosis and alkalosis states.
  12. Classification of plasma volume substitutes (expanders).
  13. Dextrans as plasma volume substitutes: classification, pharmacological properties, indications, contraindications, adverse reactions.
  14. Hydroxyethylstarch drugs as plasma volume substitutes: pharmacological properties, indications, contraindications, adverse reactions.
  15. Polypeptide polymer drugs as plasma volume substitutes: pharmacological properties, indications, contraindications, adverse reactions.
  16. Blood preparations as plasma volume substitutes: pharmacological properties, indications, contraindications, adverse reactions.

**F. The student's individual work.** The student's individual work (points 1, 2, 3, 4 are done in written form during the preparation process)

**1) Medical prescription exercises**

**To prescribe the following drugs in all medicinal forms:**

1. Mannitol. 2. Furosemide. 3. Torasemide. 4. Hydrochlorothiazide. 5. Indapamide. 6. Spironolactone. 7. Triamteren. 8. Eplerenone. 9. Colchicine. 10. Allopurinol. 11. Cystenal. 12. Ammonium chloride. 13. Potassium chloride. 14. Sodium bicarbonate. 15. Dextran-40. 16. Polyvinylpyrrolidone (Neohemodes). 17. Sodium chloride. 18. Calcium chloride. 19. Rehydron. 20. Hydroxyethylstarch (refortan). 21. Albumin. 22. Succinylated gelatin (gelofusin).

	<i>Name of drug</i>	<i>Form of delivery, dose</i>
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<b>Nr.</b>		
1	<b>Mannitol</b>	Sol. in vials 20%-250ml and 500ml (intravenous)
2	<b>Furosemide</b>	Tablets 0,04 Sol. in ampoules 1%-2ml (intravenous, intramuscularly)
3	<b>Toraseamide</b>	Tablets 0,005 and 0,01 Sol. in ampoules 0,5% -2 ml (intravenous)
4	<b>Hydrochlorothiazide</b>	Tablets 0,025 and 0,05
5	<b>Indapamide</b>	Tablets 0,0025; 0,0015 Capsules 0,0025
6	<b>Spirolactone</b>	Tablets 0,025; 0,05 Capsules 0,025; 0,05
7	<b>Triamteren</b>	Capsules 0,05
8	<b>Eplerenone</b>	Tablets 0,025; 0,05
9	<b>Colchicine</b>	Tablets 0,001
10	<b>Allopurinol</b>	Tablets 0,1; 0,15; 0,2 and 0,3
11	<b>Cystenal</b>	Solution (oral drops) 10 ml in vials
12	<b>Ammonium chloride</b>	Sol. 5%-200ml in vials (internally)
13	<b>Potassium chloride</b>	Tablets 0,5; 1,0 Sol. 4%-10ml in ampoules (intravenous)
14	<b>Sodium bicarbonate</b>	Sol. 4%-200ml in vials (intravenous) Powder 50.0 (internal use)
15	<b>Dextran-40</b>	Sol. 10%-100 ml in vials (intravenous)
16	<b>Polyvinylpyrrolidone (Neohemodes)</b>	Sol. 6% -200ml; 400ml in vials (intravenous)
17	<b>Sodium chloride</b>	Sol. 0,9%-100; 500ml in vials (intravenous) Sol. in ampoules 0,9%-5; 10ml (intravenous)
18	<b>Calcium chloride</b>	Sol. 10%-5ml in ampoules Sol. 10%-100; 200 ml in vials (intravenous)
19	<b>Rehydron</b>	Powder for oral solution in packets 18.9
20	<b>Hydroxyethylstarch (Refortan)</b>	Sol. 10%-250ml in vials (intravenous)
21	<b>Albumin</b>	Sol. 20% -50 ml; 100 ml; 250 ml in vials (intravenous)
22	<b>Succinylated gelatin (gelofusin)</b>	Sol. 4% -100 ml in vials (intravenous)

**2) List the groups and drugs used in (for):** cerebral edema, pulmonary edema of toxic origin, diuretics in acute renal failure, diuretics in chronic renal failure, forced diuresis, diuretics in arterial hypertension, diuretics in arterial hypertension with hyperaldosteronism, diuretics in glaucoma, diuretics in acute heart failure, diuretics in chronic congestive heart failure, gout attack, prophylaxis (treatment) of gout, uricoinhibitor in gout, uricosuric in gout, alkalization of urine in urolithiasis, acidification of urine in urolithiasis, treatment of acidosis, treatment of alkalosis, treatment of isotonic dehydration, treatment of hypotonic dehydration, treatment of hypertonic dehydration, hypovolemic shock, detoxification of the body in peritonitis, detoxification of the body in food poisoning, hypokalemia, hypocalcemia.

### 3) Tables (recapitulation of knowledge)

*Table 1* Localization of the predominant action of diuretics and their mechanism of action

Location of action	Drugs	Mechanism of action
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Proximal convoluted tubules	a)...	
The ascending limb of the loop of Henle	a).. b).. c)...	
The cortical segment of the loop of Henle and the distal tubules	a).. b).. c).. d).. e)...	
The terminal segment of the distal tubules and collecting tubules	a).. b).. c)...	
Throughout the entire nephron	a).. b)...	

*Table 2* Select the main indications for administration of diuretics

<b>Indication</b>	<b>Thiazides and thiazid e-like diuretics</b>	<b>Loop diuretics</b>	<b>Osmotic diuretics</b>	<b>Carbonic anhydrase inhibitors</b>	<b>Competitive aldosterone antagonists</b>
Chronic heart failure					
Arterial hypertension					
Pulmonary edema					
Cerebral edema					
Acute renal failure					
Acute heart failure					
Secondary hyperaldosteronism					
Glaucoma					
Acute intoxication					

*Table 3* Adverse reactions of diuretics

<b>Adverse reactions</b>	<b>Hydrochlorothiazide</b>	<b>Furosemide</b>	<b>Acetazolamide</b>	<b>Triamteren</b>	<b>Spirolactone</b>
Hypokalemia					
Hyperkalemia					
Hyperuricemia					
Hyperglycemia					
Ototoxicity					
Haematotoxicity					
Gynecomastia					
Hypotension					
Hepatotoxicity					
Acidosis					
Alkalosis					

**Table 4 Plasma volume substitutes: effects and mechanisms**

Substituent group	Pharmacological effect	Mechanism of effect
Isotonic sodium chloride solution		
Dextran 40		
Hydroxyethylamidone (Refortan)		
Albumin		

**4) Situational problems:**

1. In experimental conditions was modeled cerebral edema. To remove edema in animal A, was administer mannitol, and for animal B-urea. Within one hour the cerebral edema was corrected. Upon 6-hour follow-up, there was a return of cerebral edema to animal B.

What is the cause of the observed effects?

Explain the mechanisms of observed phenomena.

2. Which group of drugs will the doctor use to correct hypovolemic states in case of:  
a) isotonic dehydration; b) hypotonic dehydration; c) hypertonic dehydration; d) endotoxic shock; e) hemorrhagic shock;

Argue the selection of groups and principles of use.

3. A doctor has the following diuretics available: acetazolamide, amiloride, mannitol, hydrochlorothiazide, spironolactone, triamterene. Make the rational choice of the drug for the following pathologies:

- a) treatment of heart failure in association with tonic-cardiac glycosides
- b) treatment of primary hyperaldosteronism
- c) prophylaxis of partial epileptic seizures
- d) treatment of poisoning with acidic medicinal preparations (e.g. barbiturates, salicylates)

Argue the selection of groups and the principles of use.

**5) Tests for self-training:** (Guidelines for Laboratory Work in Pharmacology).

**G. Interactive activity**

- 1. Experimental and virtual didactic movie (elaboration of protocol, conclusions).
- 2. Clinical cases. (Guide for laboratory work in pharmacology, Pharmacology book)
- 3. Virtual situations (Guide for laboratory work in pharmacology)