**DIURETICS. DRUGS USED IN THE TREATMENT OF GOUT AND KIDNEY STONES. DRUGS EFFECTIVE IN RESTORING ACID-BASE AND/OR WATER-ELECTROLYTE BALANCE.**

**A. Actuality.** The retention of salts and water in the body is responsible for hydration of tissues with the formation of edema accompanying renal diseases, cardio-vascular insufficiency, some forms of liver pathology and emergency states (acute intoxication, hypertensive attacks, cerebral edema, etc.). To solve these situations, appropriate diuretic selection is required depending on their mechanism of action, pharmacodynamics and pharmacokinetics. Gout and urolithiasis require a long-term treatment to prevent access and the formation of kidney stones. Dysplasia of the hydro-electrolytic and acid-base balance, present in various pathologies and pathological conditions requires appropriate correction. Hypovolemic states accompany a wide range of pathologies (shock, hypotension, dehydration, intoxication, etc.) and are an emergency situation with the appropriate selection of plasma volume substitutes based on pharmacological effects and adverse reactions.

**B. The purpose of the training is** to study the pharmacology of diuretics, antigout preparations and it’s use in urolithiasis, disturbances of hydro-electrolytic and acid-base balance, plasma volume substitutes, as well as prescribing recipe and selecting medication according to pathology.

**C. Learning objectives:**

1) The student must **know:** definition, classification, mechanism of action, pharmacological effects, indications, contraindications, adverse reactions and pharmacokinetics of diuretics, antigout preparations used in urolithiasis, disturbances of hydro-electrolytic and acido-basic balance, plasma volume substitutes.

2) The student must **be able to:** prescribe the compulsory drugs of the respective groups in various forms of prescription and it’s administration depending on the pathological conditions.

#### D. Initial level of knowledge required for interdisciplinary integration:

**Human anatomy.** Anatomy of the kidneys.

**Histology.** Structure of nephron.

**Human physiology.** The main mechanisms of urine excretion. Acid-base state and hydro-electrolytic balance.

**Biochemistry.** Biochemistry of urine formation. The renal stones, their structure and the mechanism of formation.

**Pathophysiology.** Deregulation of hydro-electrolytic and acid-base balance. Pathogenesis of edema and hypovolemia.

**E. Self-training questions:**

1. Diuretics. The notion of diuretics and saluretic.

2. Classification of diuretics according to the mechanism of action, the place of action in the nephron, the rate of occurrence and the duration of the effect, the intensity of the action.

3. Diuretics with predominant influence on the glomerulus. Characterization of the diuretic action of cardiac glycosides, xanthines and vasodilators. Indications.

4. Diuretics with predominant influence on the proximal contour tube. Carboanhydrase inhibitors. The mechanism of action. Pharmacological effects, influence on water and electrolyte elimination. Indications. Contraindications. Adverse reactions.

5. Osmotic diuretics - acting throughout the nephron, but predominantly in proximal tubules. Mechanism of action. Pharmacological effects, influence on water and electrolyte elimination. Indications. Contraindications. Adverse reactions. Pharmacokinetics.

6. Diuretics with predominant influence on the ascending portion of the Henle (saluretic). Mechanism of action. Pharmacological effects, influence on water and electrolyte elimination. Indications. Contraindications. Adverse reactions. Pharmacokinetics.

7. Drugs influencing Henle's cortical segment and distal contour tube. Thiazide and related (non-thiazide) diuretics. The mechanism of action. Pharmacological effects, influence on water and electrolyte elimination. Indications. Contraindications. Adverse reactions. Pharmacokinetics.

8. Diuretics with predominant influence on the terminal segment of the distal contour tube and collector tube. Classification. Competitive and non-competitive aldosterone antagonists: mechanism of action, pharmacological effects, influence on the elimination of water and electrolytes. Indications. Contraindications. Adverse reactions. Pharmacokinetics.

9. Antigout preparations. Classification. The characteristic of the specific action drugs used in the gout crisis. Drugs used in gout prophylaxis (classification), mechanism of action, effects, indications and side effects of uric inhibitors, uricosuric and uricolytic agents.

10. Drugs used in urolithiasis: classification, characteristics of drugs that change the pH of urine and vegetal spasmolytics.

11. Classification of drugs used in disturbances of hydro-electrolytic balance. Crystalline solutions used in isotonic, hypotonic and hypertonic dehydration: pharmacological effects, indications, contraindications, side effects. Drugs used to correct hypokalemia, hypomagnesiemia and hypocalcemia.

12. Drugs used in acid-base disorders. Classification. Characteristics of drugs used in the treatment of acidosis and alkalosis.

13. Plasma volume expander. Classification.

14. Dextrans as plasma volume expander: classification, mechanism of action, effects, indications, contraindications, side effects.

15. Hydroxyethylamidone preparations as plasma volume expander: classification, mechanism of action, effects, indications, contraindications, adverse reactions.

16. Polypeptide polymer preparations as plasma volume substitutes: mechanism of action, effects, indications, contraindications, adverse reactions.

17. Blood preparations as plasma volume substitutes: mechanism of action, effects, indications, contraindications, adverse reactions.

**F. Independent work** (is done in written form while preparing for the lesson)

**1.) Brief characteristics of compulsory drugs:**

**Down:** Drug name. 1. Mannitol. 2. Furosemide. 3. Torasemid. 4. Hydrochlorothiazide. 5. Indapamide. 6. Spironolactone. 7. Triamterene. 8. Colchicine. 9. Etebenicide. 10. Allopurinol. 11. Cystenal. 12. Ammonium chloride. 13. Sodium hydrocarbonate. 14. Dextran-40. 15. Sodium chloride. 16. Potassium chloride. 17. Calcium chloride. 18. Rehydron. 19. Hydroxyethylamidon (refortan). 24. Dextran-70.

**Across:** 1. Medicinal form. 2. Way of administration. 3. Doses (therapeutic, maximal for one intake and for 24 hours). 4. Spectrum of action 5. Mechanism of action. 6. Indications and contraindications. 7. Side effects.

# 2.) Questions on medical prescriptions.

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

1. Mannitol. 2. Furosemide. 3. Torasemid. 4. Hydrochlorothiazide. 5. Indapamide. 6. Spironolactone. 7. Triamteren. 8. Colchicine. 9. Etebenicide. 10. Allopurinol. 11. Cystenal. 12. Ammonium chloride. 13. Sodium hydrocarbonate. 14. Dextran-40. 15. Polivinilpolividon (povidone). 16. Sodium chloride. 17. Potassium chloride. 18. Calcium chloride. 19. Rehydron. 20. Hydroxyethylamidone (refortan). 21. Trometamol. 23.Sulphinpirasone. 24. Dextran-70.

**Drugs used in (for):** cerebral edema, pulmonary edema, acute renal failure, chronic renal failure, acute intoxication, forced diuresis, essential arterial hypertension, arterial hypertension with hyperaldosteronism, glaucoma, acute heart failure, chronic congestive heart failure, gout access, gout prophylaxis, uricoinhibitors in gout, uricosurics in gout, alkalinisation of urine in urolithiasis, acidification of urine in urolithiasis, renal colic in urolithiasis, acidosis, alkalosis, isotonic dehydration, hypotonic dehydration, hypertonic dehydration, hypovolemic shock, detoxification of the body in peritonitis, detoxification of the body in food poisoning, acute arterial hypotension, prophylaxis and treatment of thrombosis, hypokalemia, hypocalcemia.

**3.) Tests** (Guidelines for Laboratory Work in Pharmacology).

**4.) Clinical case** (Guidelines for Laboratory Work in Pharmacology).

**5.) Virtual situations** (Guidelines for Laboratory Work in Pharmacology).

**6.) Virtual didactic movie.**

**7.) Tables**

*Table N1*

**Localization of the predominant action of diuretics and their clinical efficacy**

|  |  |  |
| --- | --- | --- |
| Localization of action | Drugs | Efficacy (high, medium, low) |
| Proximal convoluted tubules | a)… |  |
| In the thick ascending limb of Henle’s loop | a)…  b)…  c)… |  |
| [Cortical collecting ducts](https://en.wikipedia.org/wiki/Cortical_collecting_ducts) and  [distal convoluted tubules](https://en.wikipedia.org/wiki/Distal_convoluted_tubules) | a)…  b)…  c)…  d)…  e)… |  |
| At the distal segment of the distal tubule and collecting tubule | a)..  b)…  c)… |  |
| Throughout the nephron | a)…  b)… |  |

*Table N 2*

**Influence of diuretics on the elimination of ions and uric acid**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Group of diuretics | Na+ | K+ | Ca2+ | Mg2+ | Cl- | HCO3- | Uric acid |
| Thiazides and [thiazide-like diuretics](https://en.wikipedia.org/wiki/Thiazide-like_diuretic) |  |  |  |  |  |  |  |
| [Loop diuretics](https://en.wikipedia.org/wiki/Loop_diuretic) |  |  |  |  |  |  |  |
| [Carbonic anhydrase inhibitors](https://en.wikipedia.org/wiki/Carbonic_anhydrase_inhibitors) |  |  |  |  |  |  |  |
| [Competitive antagonist](https://en.wikipedia.org/wiki/Competitive_antagonist) of [aldosterone](https://en.wikipedia.org/wiki/Aldosterone) |  |  |  |  |  |  |  |
| Non-[competitive antagonist](https://en.wikipedia.org/wiki/Competitive_antagonist) of [aldosterone](https://en.wikipedia.org/wiki/Aldosterone) |  |  |  |  |  |  |  |
| Osmotic diuretics |  |  |  |  |  |  |  |

*Table N 3*

**Pharmacological characteristic of diuretic drugs**

|  |  |  |  |
| --- | --- | --- | --- |
| Drug | Way of administration | Beginning of action (min, hours) | Duration of action (min, hours) |
| Hydrochlorothiazide |  |  |  |
| Indapamide |  |  |  |
| Chlortalidon |  |  |  |
| Furosemide |  |  |  |
| Torasemid |  |  |  |
| Spironolactone |  |  |  |
| Triamteren |  |  |  |
| Mannitol |  |  |  |

*Table N 4*

**Select the principal indication of diuretics**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Indication | Thiazides and [thiazide-like diuretics](https://en.wikipedia.org/wiki/Thiazide-like_diuretic) | [Loop diuretics](https://en.wikipedia.org/wiki/Loop_diuretic) | Osmotic diuretics | [Carbonic anhydrase inhibitors](https://en.wikipedia.org/wiki/Carbonic_anhydrase_inhibitors) | [Competitive antagonist](https://en.wikipedia.org/wiki/Competitive_antagonist) of [aldosterone](https://en.wikipedia.org/wiki/Aldosterone) |
| Chronic heart failure |  |  |  |  |  |
| Arterial hypertension |  |  |  |  |  |
| Pulmonary edema |  |  |  |  |  |
| Cerebral edema |  |  |  |  |  |
| Acute renal failure |  |  |  |  |  |
| Acute heart failure |  |  |  |  |  |
| Secondary hyperaldosteronism |  |  |  |  |  |
| Glaucoma |  |  |  |  |  |
| Acute intoxication |  |  |  |  |  |

*Table N 5*

**Adverse reactions of diuretics**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Adverse reactions | Hydrochlorothiazide | Furose-mide | Acetazolami-de | Triamteren | Spironolac-tone |
| Hypokalemia |  |  |  |  |  |
| Hyperkalemia |  |  |  |  |  |
| Hyperuricemia |  |  |  |  |  |
| Hyperglycemia |  |  |  |  |  |
| Ototoxicity |  |  |  |  |  |
| Haematotoxicity |  |  |  |  |  |
| Gynecomastia |  |  |  |  |  |
| Hypotension |  |  |  |  |  |
| Hepatotoxicity |  |  |  |  |  |
| Acidosis |  |  |  |  |  |
| Alkalosis |  |  |  |  |  |

*Table N 6*

**Plasma volume substitutes: effects and mechanisms**

|  |  |  |
| --- | --- | --- |
| Substituent group | Pharmacological effect | Mechanism of effect |
| Isotonic sodium chloride solution |  |  |
| Dextran 40 |  |  |
| Hydroxyethylamidone (refortan) |  |  |
| Albumin |  |  |
| Poligeline preparations |  |  |

*Table N 7*

**Indication of plasma volume substitutes**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Indication | Dextran 40 | Dextran 70 | Polividon | Gelatinol | Trisol |
| Hypovolemic shock |  |  |  |  |  |
| Acute arterial hypotension |  |  |  |  |  |
| Acute intoxication |  |  |  |  |  |
| Pathologies with microcirculation disorder |  |  |  |  |  |
| Prophylaxis and treatment of thrombosis and thromboembolism |  |  |  |  |  |
| Dehydration of the body |  |  |  |  |  |

**8.) Solve the case:**

**Case 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.

**Case 2**

Which groups of drugs will use the doctor to correct the hypovolaemia conditions in case of: a) isotonic dehydration; b) hypotonic dehydration; c) haemorrhagic shock; d) endotoxic shock; e) cirrhosis with ascites.

Argument the group selection and usage principles.

**Case 3**

In experimental conditions was modeled the state of acidosis. For its correction, was administered the 4% sodium hydrocarbonate solution. Upon examination, the sanguine pH was normalized, but were detected a relative hypernatraemia and intracellular acidosis.

What was the cause of relative hypernatraemia and the persistence of intracellular acidosis?

What do you recommend for correcting intracellular acidosis?