CLINICAL FARMACOLOGY OF MEDICATIONS WITH INFLUENCE AFTER HEMOSTASIS AND FIBRINOLYSIS, HEMATOPOESIS.

A. Actuality

The dynamics of the coagulant, anticoagulant and fibrinolytic systems determine the state of tissue circulation and metabolic processes. In most diseases and pathological conditions, the ratio of these systems is disturbed. Moreover, platelet aggregation, hypercoagulability with the trombus formation causes serious complications, including deadly: pulmonary artery embolism, cerebral vessels embolism, etc. Medications with action on coagulant, anticoagulant and fibrinolytic systems are used to ensure adequate tissue circulation.

The disturbance of the hematopoietic process causes the appearance of various pathologies, which currently have scale, such as anemias, lymphomas, acute and chronic leukemia's, with a very high morbidity and mortality rate. To ensure a normal hematopoiesis, drugs with influence on erythropoiesis, leukopoiesis and influence on the megakaryocytic system are used.

B. Training aim

Acquiring and deepening of knowledge about the pharmacodynamic and pharmacokinetic properties of drugs with influence on hematopoiesis, blood coagulability, anticoagulant and fibrinolytic system.

C.Teaching objectives

The student should be able to:

a) Elucidate the mechanisms of action, indications, contraindications and adverse reactions of antithrombotic, hemostatic and drug substances used in hematopoietic disorders.

b) Estimate the usage and dosage principles of hemostatic and antithrombotic drugs depending on the disease and pathological states.

c) Establish the principles of drugs' interactions of hemostatic and antithrombotic agents with other drugs and predict the possible side effects.

d) Write down personal form (P-medicines).

D.Knowledge from previously studied disciplines and related subjects

Medico-biological subjects. Cellular components of the blood. The links of the blood clotting cascade. The blood anticoagulant and fibrinolytic system. The role of platelets in the coagulation process. Pathology of blood coagulation and fibrinolysis.

Clinical subjects: CID syndrome (disseminated intravascular coagulation), ethiopathogenesis, phases, forms and clinical manifestations. Coagulogram indices and their deviation within pathologies accompanied by hypo- or hypercoagulation. Physiological anticoagulants (antithrombin III, proteins C and S). Hemophilia.

Pharmacology. Classification of hemostatic and antithrombotic drugs. Pharmacodynamics of coagulants, antifibrinolytics, anticoagulants, fibrinolytics, antiaggregants.

E.Questions for self- training

I. Clinical-pharmacological characteristics of drug groups influencing on hemostasis and fibrinolysis, hematopoiesis.

1. Medicines with influence on hemostasis and fibrinolysis. Classification according to the mechanism of action, pharmacological effects and clinical use.
2. Direct acting anticoagulants: classification, pharmacodynamic and pharmacokinetic features of standard heparin and low molecular weight heparins, comparative characteristics, indications,

dosage regimen and principles of use, contraindications, adverse reactions and prophylaxis. Methods to verify the efficacy and safety of direct anticoagulants.
3. Anticoagulants with indirect action: classification, pharmacodynamic and pharmacokinetic features, dosage regimen and principles of use, indications, contraindications, adverse reactions and prophylaxis. Methods for verifying the efficacy and safety of indirect anticoagulants. Antagonists of indirect anticoagulants. Principles of rational selection and use in stationary and ambulatory. Comparative characterization of direct and indirect (oral) anticoagulants.
4. Fibrinolytics: classification, pharmacodynamic and pharmacokinetic peculiarities, indications, dosing regimen and principles of use, contraindications, adverse reactions, prophylaxis and their treatment.
5. Clinical pharmacology of antiaggregants (antiplatelets): classification, peculiarities of the mechanism of action, indications, contraindications and adverse reactions, principles of rational selection and use.
6. Classification of hemostatic drugs. Direct and indirect coagulants: peculiarities of the mechanism of action, indications, contraindications and adverse reactions. Principles of rational selection and use.
7. Synthetic antifibrinolytics and animal origin: features of the mechanism of action, indications, contraindications and adverse reactions, the principles of rational selection and use.
8. Aggregants: the particularities of the mechanism of action, indications, contraindications and adverse reactions, principles of selection and rational use.

9. Local hemostatics: characteristic of vasoconstrictors, astringent and thromboplastinic drugs, indications, contraindications and adverse reactions, principles of rational selection and use.
10. Systemic hemostatics: classification, pharmacodynamic and pharmacokinetic peculiarities, indications, contraindications and adverse reactions, principles of rational selection and use.
11. Drugs that improve blood rheology: classification, pharmacodynamic and pharmacokinetic peculiarities, indications and principles of use, contraindications, adverse reactions.
12. Antianemy. Classification. Drugs used in iron deficiency anemia, BI2-deficiency anemia, aplastic and hemolytic anemias. Principles of selection and rational use.
13. Drugs with influence on leukopoiesis. Classification, pharmacokinetics, mechanism of action, indications, contraindications, adverse reactions and principles of rational selection and use.
14.The peculiarities of the use of drugs with influence on hemostasis, fibrinolysis and hematopoiesis in various physiological states (pregnancy, lactation), in the elderly and children.

II. Clinical pharmacological selection and use of drugs in some pathological conditions and diseases:
• Principles for the selection and use of drugs in pulmonary artery thromboembolism, ischemic or hemorrhagic stroke, acute myocardial infarction.
• Principles of selection and use of drugs in CID syndrome depending on phases.
• Principles for the selection and use of medicines in hemophilia.
• Principles for the selection and use of medicinal products in anemias (iron deficiency anemia, megaloblastic, aplastic, etc.)
• Principles for the selection and use of drugs in leukopoiesis disorders.

F. Individual Work:

1. Brief characterization of the main drugs.

Vertically: International Nonproprietary Name (INN) of drug
Horizontally: synonyms, delivering forms, mode of administration, doses (therapeutic, maximal), mechanism of action, indications, contraindications, side effects.

Abciximab; tirofiban; rivaroxoban; phytomenadione; etamsilat; rutoside; bivaluridine; enoxaparin; warfarine; clopidogrel; raviset; argatroban; feroplex; ferum-lec; filgrastim; sargamostim; folic acid; coamid, diosmine; hesperidine; methyluracil; tiofosphamide.

2. Exercises on medical prescription (see year III):

Heparin, ethyl biscumacetate, menadione, streptokinase, acetylsalicylic acid, fercoven, ferrous sulphate, sodium nucleinate, fibrinogen, aminocapronic acid, cyanocobalamine, nadroparin, protamine sulfate, carbazocrom, acenocumarol, ticlopidin, alteplase, aprotinine.

3. Indicate drugs used in (for):

epistaxis, capillary hemorrhages, hemorrhages during otorinolaringological interventions, hypofibrinogenemia, hemophilia, hemorrhages by overdose of direct-acting anticoagulants, hemorrhages by overdose of indirect-action anticoagulants, hemorrhagic disease of the newborn, hemorrhages through capillary fragility, hemorrhages with hyperfibrinolysis, menorrages, hemorrhages by fibrinolytic overdose, pulmonary artery thromboembolism, deep vein thrombosis, acute myocardial infarction with hypercoagulability, thromboembolic myocardial infarction, acute coronary syndrome, thrombosis prophylaxis in surgery and obstetrics, diagnostic procedures on the heart and vessels, disseminated intravascular coagulopathy syndrome, atrial fibrillation in mitral and prosthetic valves, primary and secondary prophylaxis of cerebral and coronary heart strokes, obliterating endarteritis, transient cerebral ischemia, heparin-induced thrombocytopenia, iron deficiency anemia, megaloblastic anemia, acute leukemia, chronic leukemia, Hodgkin lymphoma, non-Hodgkin lymphoma.

4. Tests on clinical pharmacology (for faculty of medicine). Chisinau, 2014,

5. Clinical cases in clinical pharmacology. Chisinau, 2017,

6. Virtual situations.

7. Selection of Personal drugs (P- drugs) and Personal treatment (P- treatment) according to the criteria of efficacy, safety, acceptability and cost for inclusion in the personal form (P drugs).