DRUGS AFFECTING BLOOD AND HEMATOPOIETIC ORGANS

A. Actuality. Coagulation disorders, fibrinolysis and haematopoiesis are frequent, sometimes severe (acute hemorrhage, surgical interventions) or lethal (thrombosis of pulmonary artery, of cerebral vessels, intravascular coagulation, leucosis).

B. The purpose of the training is to familiarize the students with pharmacological properties of drugs used in fibrinolysis and hematopoietic disorder.

C. Learning objectives:

1.)The students must **know:** definition, classification, mechanism of action, indications, contraindications and side effects of antithrombotic drugs, haemostatic drugs used in disturbances of haematopoiesis.
2.) The students must **be able to:** prescribe drugs influencing on the blood system in different medicinal forms, to order drugs of this group in different forms of blood system pathology.

D. Initial level of knowledge required for interdisciplinary integration:

Human physiology. Blood coagulation. Modern scheme of blood coagulation. Origin and physiological role of heparin.

Biochemistry. Cascade mechanism of action of enzymes, which lead to blood coagulation. Metabolic functions of cyanocobolamin and folic acid.

Physiopathology. Blood anticoagulant system. Pathology of blood coagulation and fibrinolysis. Anemias, leucopenias, thrombocytopenias. Forms, causes and mechanisms of their development. Leukemia, thrombocytopenia. Causes and development mechanism.

E. Self-training questions:

1. Definition and classification of antithrombotic drugs.
2. Clasification of direct anticoagulants.
3. Standard heparin preparations (unfractionated heparin): mechanism of action, effects, indications, contraindications, side effects and pharmacokinetics. Heparin antagonists.
4. Low molecular weight heparins. Pharmacokinetic and pharmacodynamics features, comparative characteristics with standard heparin.
5. Heparinoids: pharmacodynamics properties. Indications, contraindications, side effects.
6. Direct antagonists of thrombine: classification, characteristic, indications.
7. Indirect anticoagulants. Classification according to duration of action, to mechanism of action. Indications, contraindications, side effects. Comparative characteristics with direct anticoagulants. Antagonists of indirect anticoagulants.
8. Antiaggregant (antiplatelet) drugs: classification, mechanism of action, indications, contraindications, side effects.
9. Fibrinolytic drugs: classification, mechanism of action, indications, contraindications, side effects.
10. Definition and classification of haemostatic drugs.

11. Classification of local haemostatics. Characteristic of vasoconstrictors, astringents, with thromboplastinic and thrombinic action.
12. Classification of systemic hemostatic drugs.
13. Direct action coagulants: pharmacodynamics propierties and indications.
14. Indirect action coagulants: mechanism of action, indications, side effects.
15. Antifibrinolytic drugs: classification, mechanism of action, indications, side effects.
16. Aggregant drugs: classification, mechanism of action, indications, side effects.
17. Classification of antianemic drugs.
18. Drugs used in iron deficient anemias: classification, pharmacokinetic, indications, side effects.
19. Drugs used in megaloblastic anemia B-12 deficitary: pharmacodynamics and pharmacokinetic properties, indications.
20. Drugs used in megaloblastic anemia folic acid deficiency: pharmacodynamics and pharmacokinetic properties, indications.
21. Drugs used in hemolytic, hypo or aplastic anemia: pharmacodynamics and pharmacokinetic properties.
22. Erythropoietin drugs: pharmacodynamics properties, indications, side effects.
23. Classification of drugs influencing on leucopoiesis. Leucopoiesis drugs stimulants: pharmacodynamics properties, indications, side effects.
24. Classification of angioprotectors. Mechanism of action, effects, indications, of vegetal, animal, and synthetic origin drugs

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

1.) Brief characteristics of compulsory drugs:

Down: Drug nomenclature: 1. Heparin. 2. Nandroparin. 3. Enoxaparin. 4. Protamine sulfate 5. Ethylbiscoumacetate. 6. Warfarin 7. Alteplase. 8. Streptokinase. 9. Ticlopidine. 10. Fibrinogen. 11. Menadione. 12. Aminocaproic acid. 13. Carbasocrome.. 14. Ferrous sulphate. 15. Fercoven. 16. Cyanocobolamin (B_{12}). 17. Folic acid. 18. Sodium nucleinate.

Across:1. Dosage forms. 2. Way of administration. 3. Dosages (the upper limit for a single administration and along the course of 24 hours, as well as the maximum therapeutic dose). 4. Mechanism of action. 5. Indications and contraindications. 6. Side effects.

2.) Questions on medical prescriptions

To prescribe following drugs in all possible medicinal forms:1. Heparin. 2. Nandroparin. 3. Enoxaparin. 4. Protamine sulfate 5. Ethylbiscoumacetate. 6. Warfarin 7. Alteplase. 8. Streptokinase. 9. Ticlopidine. 10. Fibrinogen. 11. Menadione. 12. Aminocaproic acid. 13. Carbasocrome.. 14. Ferrous sulphate. 15. Fercoven. 16. Cyanocobolamin (B_{12}). 17. Folic acid. 18. Sodium nucleinate.

Drugs used in (for): treatment and prevention of deep vein thrombosis, treatment and prevention of pulmonary arteri thromboembolia, diseminated intravascular coagulopathy, overdosage with indirect anticoagulants, overdosage with direct anticoagulants, prevention of postoperative thrombembolia, prophylaxis of peripheral arteri thrombosis, thrombosis prophylaxis in myocardial infarction,

thrombembolia prophylaxis in atrial fibrilation, prophylaxis of cerebrovascular thrombosis, stopping parenchimatous and capillary bleeding, haemophilia, gastrointestinal and lungs bleeding, hemorrhages caused by hyperfibrinolysis,
iron deficiency anemia, B_{12} deficiency anemia, folic acid deficiency anemia, aplastic anemia, hemolytic anemia, leucopenia.

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 1

Comparative characteristics of direct and indirect anticoagulants

Parameter		Direct anticoagulants	Indirect anticoagulants
Mechanism of action	inactivating clotting factors		
	coagulation factors synthesis distiurbance		
Activity	"in vivo"		
	"in vitro"		
Onset of action			
Cumulative properties			
Duration of action			
Antagonists			

Note. Indicate the effect by the "+" sign.

Table 2

Comparative characteristics of standard heparin and low molecular weight heparin

Parameters	Standard Heparin	Low molecular weight Heparin
Molecular weight kDA		
Inactivation of factor IIa (thrombin) (- / +)		

Inactivation of factor Xa (prothrombin III) (- / +)		
Anticoagulant effect		
Duration of action (hours)		
Maximal effect		
Treatment monitoring		
Bioavailability after s/c administration		
Half life		
Bleeding risk		
Property to cause thrombocitopenia		

Table 3

The comparative characteristic of fibrinolytic drugs

Parameters		Streptokinase	Streptodecase	Urokinase	Alteplase
Activation of transformation of profibrinolysin into fibrinolysin	in thrombus				
	in plasma				
Duration of action (hours)					
The risk of bleeding (often / rarely)					
The presence of pyrogenic and allergic reactions					

Table 4

Indications of hemostatic drugs

Indications	Thrombin	Fibrinogen	Menadion	Aminocaproic acid	Protamine sulfate
Bleeding from small vessels					
Bleeding due to hyperfibrinolysis					
Bleeding due to hypofibrinogenemia					
Overdosage of direct anticoagulants					
Overdosage of indirect anticoagulants					
Treatment of varicose veins dilation of lower extremity					

Table 5

Comparative characteristisc of antianemic drugs

Parameters	Iron drugs	B-12 drugs	Folic acid preparation
Drugs			
Pharmacokinetic properties			
Pharmacodynamic properties			
Indications			
Side effects			

Table 6

The comparative characteristic of drugs regulating erythro- and leukopoiesis

Growth factors	Drugs	Way of administration	Indication	Side efect
Erythropoietin				

The colony-stimulating macrophage granulocyte factor				
The colonially stimulating granulocytic factor				

8.) Solve the case:

Two patients with thrombosis were hospitalized. Patient A - with deep vein thrombosis, patient B - with inferior extremities arteri thrombosis.

Which drugs will you prescribe for patients treatment?

Explain the choosing drugs according to their mechanism of action.