

VOLGOGRAD STATE MEDICAL UNIVERSITY

DEPARTMENT OF PHARMACOLOGY AND BIOINFORMATICS

Methodological recommendations for students for practical classes
«Immunobiological and gene therapy drugs»

Thematic block: **Immunobiological drugs**

Class topic:

Immunobiological medicinal products - blood products. Classification by action: drugs of complex action (plasma products and albumin solutions), immunologically active and hemostatic (cryoprecipitate, prothrombin complex, fibrinogen and individual coagulation factors of the B02BD subgroup).

Pharmaceutical faculty

1. Class aims

- learn to analyze and classify the action of immunobiological agents based on the totality of their pharmacological properties, mechanisms and localization of action;
- learn to evaluate the possibilities of using immunobiological agents for adequate pharmacotherapy.

2. TASKS:

1. For immunobiological agents of complex action, study:
 - classification of drugs (plasma preparations and albumin solutions), immunologically active and hemostatic (cryoprecipitate, prothrombin complex, fibrinogen and individual coagulation factors of the B02BD subgroup),
 - their use in medical practice.
2. For individual immunobiological groups and drugs, study:
 - pharmacodynamics of substances (effects, localization of action)
 - pharmacokinetics of substances (absorption, distribution, chemical transformations in the body, elimination routes),
 - main side effects and toxicity,
 - main indications and contraindications for use,
 - routes of administration.

3. THE FOLLOWING PRACTICAL SKILLS ARE PRACTISED DURING THE LESSON:

- ability to evaluate the possibilities of using various immunobiological agents based on ideas about their properties;
- ability to analyze the action of human albumin preparations; human immunoglobulin preparations; blood clotting factor preparations containing one of the blood clotting factors or a combination of them, based on the totality of their pharmacological properties, mechanism and localization of action.

4. ORDER OF CONDUCTING CLASSES:

Venue: classroom of the Department of Pharmacology and Bioinformatics.

Time: 2 AH

Competencies to be developed: YK-1.1.3, YK-1.2.1, YK-1.2.2, YK-1.2.3., YK-1.3.1, YK-1.3.2., YK-6.1.1., YK-6.2.1, YK-6.2.2, YK-6.3.1, YK-6.3.2, YK-6.3.3, YK-6.3.4, ОПК-1.1.1., ОПК-

1.2.1, ОПК-1.2.2., ОПК-1.3.1, ОПК-6.1.1, ОПК-6.2.1, ОПК-6.3.1, ПК-7.1.1, ПК-7.2.1, ПК-7.3.1.

4.1 Technological map of the lesson

Part	№	Class stage	Time
1	1	Checking the students present at the lesson, lesson mode, lesson topic.	5 min
	2	Checking the initial level of students' knowledge (written survey).	10 min
	3	Survey on the topic of the lesson.	45 min
	4	Independent work of students (on prescriptions with analysis of the most complex prescriptions (if any in the topic), analysis of errors in medical prescriptions written by students; work with synonyms).	15 min
	5	Checking independent work	5 min
	6	Summing up the lesson. Assignment for the next lesson.	5 min
	7	Cleaning of workplaces.	5 min

4.2 Demonstrations

1. Demonstration of advertising brochures on this topic during a survey on the topic of the lesson.

4.3 Lesson plan

4.3.1 Introductory remarks by the teacher.

4.3.2 Analysis of theoretical material.

4.3.3 Conducting the test

Plan for analyzing theoretical material.

Immunobiological medicinal products - blood products.

Blood products are medicinal products obtained from donor blood. There are complex action products, immunologically active (immunoglobulins) and hemostatic products.

Classification by action: complex action products (plasma products and albumin solutions), immunologically active and hemostatic (cryoprecipitate, prothrombin complex, fibrinogen and individual coagulation factors of the B02BD subgroup).

Analysis of theoretical material according to the classification of immunobiological blood products.

Complex action drugs include plasma and albumin solutions; they simultaneously have a hemodynamic and anti-shock effect. Fresh frozen plasma has the greatest effect due to the almost complete preservation of its functions. Other types of plasma - native (liquid), lyophilized (dry) - significantly lose their therapeutic properties during the manufacturing process, and their clinical use is less effective. Fresh frozen plasma is obtained by plasmapheresis or centrifugation of whole blood with rapid subsequent freezing (in the first 1-2 hours after blood is taken from the donor). It can be stored for up to 1 year at 1°-25° and below. During this time, it retains all blood coagulation factors, anticoagulants, and components of the fibrinolysis system. Immediately before transfusion, fresh frozen plasma is thawed in water at a temperature of 35-37° (to speed up the thawing of the plasma, the plastic bag in which it is frozen can be kneaded in warm water with your hands). Plasma should be transfused immediately after warming within the first hour in accordance with the attached instructions for use. Flakes of fibrin may appear in thawed plasma, which does not prevent it from being transfused through standard plastic systems with filters. Significant turbidity and the presence of massive clots indicate poor quality of the plasma: in this case, it cannot be transfused. Repeated freezing and thawing of plasma is not allowed.

Fresh frozen plasma transfused to a patient must be of the same blood group as the patient's blood according to the AB0 system. In emergency cases, in the absence of single-group plasma,

transfusion of group A(II) plasma is permitted to patients with blood group 0(I), group B(III) plasma to patients with blood group 0(I), and group AB(IV) plasma to patients with any blood group; a group compatibility test is not performed. Transfusions of fresh frozen plasma are indicated for thrombohemorrhagic syndrome, burn disease, purulent-septic processes, prolonged compression syndrome, as well as hemorrhagic diathesis caused by a deficiency of plasma coagulation factors, including hemophilia A and B, massive blood loss (with blood loss of more than 25% of the volume, transfusion of fresh frozen plasma is combined with transfusion of red blood cells, preferably washed red blood cells), etc. Fresh frozen plasma is also used in patients with recurrent thrombosis of blood vessels, especially caused by a deficiency of natural anticoagulants (antithrombin III, proteins C and S, etc.), against the background of heparin therapy and the use of fibrinolytic drugs (for example, streptokinase). It is transfused with rheologically active drugs (for example, rheopolyglucin) in case of lymphatic circulation disorders. In hemophilia, transfusions of fresh frozen plasma are performed in the absence of concentrate of blood coagulation factor VIII (cryoprecipitate) at 300-500 ml 3-4 times a day. In thrombohemorrhagic syndrome, the daily dose of fresh frozen plasma is 1-2 liters or more, heparin is also administered drip in small doses (up to 20,000 U per day) and contrical in large quantities (up to 60,000 U per day).

Transfusion of fresh frozen plasma to several patients from one plastic bag or bottle is prohibited; it also cannot be left for subsequent transfusions after the plastic bag or bottle has been depressurized. Transfusion of fresh frozen plasma is contraindicated in patients sensitized to parenteral administration of protein. To prevent pathological reactions, a biological test is performed, as with whole blood transfusion. Albumin is produced in the form of 5, 10 and 20% solutions. Along with purified albumin, the drug "protein" is widely used, containing admixtures of a- and b-globulins. Due to the introduction of stabilizers, albumin solutions can withstand pasteurization, inactivating hepatitis and HIV viruses. Albumin is indicated for various types of shock - traumatic, surgical, burn, as well as for edema caused by disorders of the protein composition of the blood, with disorders of albumin synthesis in the liver and its large loss (for example, with cirrhosis of the liver, ascites, burns). Concentrated albumin solutions are used in cases where it is necessary to limit the volume of fluid introduced into the body, for example, with traumatic brain injury accompanied by cerebral edema, heart failure. Albumin (5% solution) is advisable to use in case of blood loss, when it is necessary to normalize blood pressure. In case of massive bleeding, the administration of albumin should be combined with transfusions of red blood cells. Albumin in the form of a 10% solution is usually used in pediatric practice. Plasma immunoglobulins isolated during blood fractionation constitute a group of immunological preparations with specific activity against infectious diseases. Normal human immunoglobulin (gamma globulin) is most widely used in clinical practice. Specific immune preparations with targeted action against influenza, tick-borne encephalitis, tetanus, etc. have a high therapeutic effect. Highly sensitive immunoglobulin is used in the treatment of idiopathic thrombocytopenic purpura. Immunoglobulin preparations are administered intramuscularly. Purified immunoglobulins suitable for intravenous use are much more effective due to the fact that when they enter the bloodstream directly, the protein is not subject to breakdown by tissue proteases.

Hemostatic preparations include cryoprecipitate, prothrombin complex, fibrinogen.

Cryoprecipitate contains large amounts of antihemophilic globulin (coagulation factor VIII) and von Willebrand factor, as well as fibrinogen, fibrin-stabilizing factor XIII, and other protein impurities. The preparations are produced in plastic bags or vials in frozen or dried form. They are used for hemophilia A, von Willebrand disease, and some other types of bleeding.

In hemophilia B, hemorrhagic disease of the newborn and overdose of indirect anticoagulants (pelentan, phenylin), prothrombin complex (PPSB, or CSF) is used - a complex of II, VII, IX and X blood coagulation factors; if it is absent, fresh frozen plasma is administered intravenously.

Fibrinogen has limited use: it is indicated for bleeding caused by fibrinogen deficiency. In hypofibrinogenemia caused by thrombohemorrhagic syndrome, its replacement, like other blood coagulation factors, should be carried out with fresh frozen plasma, since purified fibrinogen is not balanced with natural anticoagulants and can undergo coagulation in the patient's bloodstream, which increases pulmonary and renal failure. Fresh frozen plasma contains enough fibrinogen to replenish its deficiency in the body.

In addition to intravenous drugs, there is a group of hemostatic agents used locally to stop external bleeding that occurs during surgical interventions. These include thrombin, fibrin film, hemostatic sponge, biological antiseptic tampon, etc. The main active ingredient of these agents is thrombin, which causes the formation of a clot as a result of the conversion of fibrinogen K into fibrin, which thromboses the lumen of blood vessels at the site of bleeding. The use of hemostatic drugs on the damaged surface of parenchymatous organs is especially effective.

Fibrin films and sponges, due to their mechanical properties, are used not only to stop bleeding, but also as a plastic material, for example, in the treatment of burn disease, trophic ulcers. In neurosurgical practice, fibrin films are successfully used to compensate for the deficiency of the dura mater. Isogenic films can be left in the patient's body during surgery, which is impossible when using a heterogeneous drug due to the risk of sensitization of the body with a foreign protein.

According to the Anatomical Therapeutic Chemical (ATC) classification system (ATC), blood coagulation factor preparations belong to the B02BD group, which is subdivided into:

- B02BD01 Coagulation Factors IX, II, VII and X in comb
- B02BD02 - Coagulation Factor VIII
- B02BD03 - Coagulation Factor VIII inhibitors
- B02BD04 - Coagulation Factor IX
- B02BD05 - Coagulation Factor VII
- B02BD06 - Von Willebrand Factor and Coagulation Factor VIII in Combination
- B02BD07 Coagulation Factor XIII
- B02BD08 - Eptacog alpha activated (coagulation factor VIIa)
- B02BD09 Nonacog alpha
- B02BD10 - Von Willebrand Factor
- B02BD11 Catridecacog
- B02BD13 Coagulation Factor X
- B02BD14 Susoctocog alfa • B02BD15 Valoctocogen roxaparvovec • B02BD16 Ethranacogen desaparvovec • B02BD30 – Thrombin

Understand the mechanism of action of each group of drugs. Pharmacological effects. Features of use in medical practice. Pay attention to side effects.

4.3.5. Independent work of students:

1. Work with the reference book "Synonyms of medicines", conduct a search and write out in the workbook synonyms of medicines on this topic.

4.3.6 Checking the students' independent work.

4.3.7 Summing up the lesson. Answering students' questions.

4.3.8 Concluding remarks by the teacher.

Составитель
доцент, к.м.н.

К.А. Гайдукова

Перечень рекомендуемой литературы, включая электронные учебные издания:

1. Харкевич Д. А. Фармакология : учебник / Харкевич Д. А. - 11-е изд., испр. и доп. - М. : ГЭОТАР-Медиа, 2015. - 755, [5] с. : ил. - Текст : непосредственный.
2. Харкевич, Д. А. Фармакология : учебник / Д. А. Харкевич. - 13-е изд., перераб. - Москва : ГЭОТАР-Медиа, 2022. - 752 с. : ил. - ISBN 978-5-9704-6820-3. - Текст : электронный // ЭБС "Консультант студента" : [сайт]. - URL : <https://www.studentlibrary.ru/book/ISBN9785970468203.html>
3. Фармакология : учебник / под ред. Р. Н. Аляутдина. - 6-е изд., перераб. и доп. - Москва : ГЭОТАР-Медиа, 2022. - 1104 с. - ISBN 978-5-9704-6819-7. - Текст : электронный // ЭБС "Консультант студента" : [сайт]. - URL : <https://www.studentlibrary.ru/book/ISBN9785970468197.html>
4. Майский, В. В. Фармакология с общей рецептурой : учебное пособие / В. В. Майский, Р. Н. Аляутдин. - 3-е изд., доп. и перераб. - Москва : ГЭОТАР-Медиа, 2017. - 240 с. - ISBN 978-5-9704-4132-9. - Текст : электронный // ЭБС "Консультант студента" : [сайт]. - URL : <https://www.studentlibrary.ru/book/ISBN9785970441329.html>
5. Аляутдин, Р. Н. Фармакология. Ultra light : учеб. пособие / Р. Н. Аляутдин. - Москва : ГЭОТАР-Медиа, 2012. - 584 с. - ISBN 978-5-9704-1985-4. - Текст : электронный // ЭБС "Консультант студента" : [сайт]. - URL : <https://www.studentlibrary.ru/book/ISBN9785970419854.html>
6. Онкология : учебник / М. И. Давыдов, Ш. Х. Ганцев [и др.]. - Москва : ГЭОТАР Медиа, 2020. - 920 с. : ил. - ISBN 978-5-9704-5616-3. - Текст : электронный // ЭБС "Консультант студента" : [сайт]. - URL : <https://www.studentlibrary.ru/book/ISBN9785970456163.html>
7. Онкология : учебник / под ред. С. Б. Петерсона. - 2-е изд., перераб. и доп. - Москва : ГЭОТАРМедиа, 2018. - 288 с. : ил. - ISBN 978-5-9704-4704-8. - Текст : электронный

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8. Онкология / под ред. Чиссова В. И., Давыдова М. И. - Москва : ГЭОТАР-Медиа, 2014. - 1072 с. - ISBN 978-5-9704-3284-6. - Текст : электронный // ЭБС "Консультант студента" : [сайт]. - URL : <https://www.studentlibrary.ru/book/ISBN9785970432846.html>

9. Медицинская микробиология, вирусология и иммунология : Т. 1 : учебник / под ред. Зверева В. В., Бойченко М. Н. - Москва : ГЭОТАР-Медиа, 2020. - 448 с. - ISBN 978-5-9704-5835-8. - Текст : электронный // ЭБС "Консультант студента" : [сайт]. - URL : <https://www.studentlibrary.ru/book/ISBN9785970458358.html>

10. Медицинская микробиология, вирусология и иммунология : Т. 2 : учебник / под ред. Зверева В. В., Бойченко М. Н. - Москва : ГЭОТАР-Медиа, 2021. - 472 с. - ISBN 978-5-9704-5836-5. - Текст : электронный // ЭБС "Консультант студента" : [сайт]. - URL : <https://www.studentlibrary.ru/book/ISBN9785970458365.html>

11. Этиотропная терапия острых вирусных инфекций у детей : учеб. пособие для спец. 06010365 "Педиатрия" / Крамарь Л. В., Арова А. А., Желудков Ю. А. и др. - Волгоград : Изд-во ВолгГМУ, 2012. - 156 с. - Текст : непосредственный.

12. Иоанниди Е. А. Хронические вирусные гепатиты В, D и С : этиопатогенез, эпидемиология, клиника, лечение и профилактика : учеб. пособие / Иоанниди Е. А., Божко В. Г., Беликова Е. А., Александров О. В. ; ВолгГМУ Минздрава РФ. - Волгоград : Изд-во ВолгГМУ, 2016. - 71, [1] с. : табл. - Текст : электронный // ЭБС ВолгГМУ : электронно-библиотечная система. - URL: http://library.volgmed.ru/Marc/MObjectDown.asp?MacroName=%D5%F0%EE%ED%E8%F7%E2%E8%F0%F3%F1_%E3%E5%EF%E0%F2%E8%F2%FB_2016&MacroAcc=A&DbVal=47

13. Kharkevitch D.A., Pharmacology / Kharkevitch D.A. - М. : ГЭОТАР-Медиа, 2008. - 672 с. - ISBN 5-9704-0264-8 - Текст : электронный // ЭБС "Консультант студента" : [сайт]. - URL : <http://www.studentlibrary.ru/book/ISBN5970402648.html> (дата обращения: 28.02.2020). - Режим доступа : по подписке.

Перечень профессиональных баз данных, информационных справочных систем, электронных образовательных ресурсов, рекомендуемых для подготовки:

1. <http://vrachirf.ru/> - Информационный портал Врачи России
2. <https://pharmarf.ru> – информационный портал Фарма России
3. <https://www.rlsnet.ru/> - РЛС (регистр лекарственных средств России) (информационная справочная система)
4. <http://www.drugs.com> - Информационная база о лекарственных препаратах (информационная справочная система)
5. <https://grls.pharm-portal.ru/> - государственный реестр лекарственных средств.
6. <http://elibrary.ru> – Электронная база, электронных версий периодических изданий на платформе Elibrary.ru (профессиональная база данных)
7. <http://www.consultant.ru/> – Справочно-правовая система «Консультант-Плюс» (профессиональная база данных)