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: medicinal products obtained from human and animal blood, blood plasma (except whole blood). History of development (timeline) and use. Classification by origin (human albumin preparations; human immunoglobulin preparations; blood coagulation factor preparations containing one of the blood coagulation factors or their combination) with examples.

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 various groups of immunobiological agents, study:
• history of development,
• classification,
• 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: УК-1.1.3, УК-1.2.1, УК-1.2.2, УК-1.2.3., УК-1.3.1, УК-1.3.2., УК-6.1.1., УК-6.2.1, УК-6.2.2, УК-6.3.1, УК-6.3.2, УК-6.3.3, УК-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 (IMP) are medicinal products intended to form active or passive immunity, or to diagnose the presence of immunity (vaccines, toxoids, toxins, serums, immunoglobulins and allergens). Immunobiological medicinal products: medicinal products obtained from blood, blood plasma of humans and animals (except whole blood). History of development (timeline) and use. Classification by origin (human albumin preparations; human immunoglobulin preparations; blood coagulation factor preparations containing one of the blood coagulation factors or their combination) with examples.

Analysis of theoretical material according to the classification of immunobiological agents.

History of development (timeline) and application.

There is probably no other biological process that has been studied as long and intensively as the biochemistry of blood coagulation. The earliest stage is the research of Hippocrates and Aristotle (459-377) on stopping bleeding and the description of the fibers in the blood that are necessary for coagulation. It was only in 1731 that Petit outlined a scientific approach to the physiology of hemostasis, concluding that bleeding stops when a blood clot forms, part of which sticks to the inner surface of the vessel. The invention of the microscope played a huge role in the development of blood diagnostics. The Dutch scientist Antonio van Leeuwenhoek, who lived in the 17th century, is known not only as the creator of microscopes, but also as the discoverer of the simplest organisms. Thus, Leeuwenhoek discovered ciliates, erythrocytes, described bacteria, yeast, lens fibers, epidermal scales of the skin, the structure of muscle fibers and the eyes of insects. The ability to examine the tissues and fluids of the human body, and primarily blood, allowed the development of such a science as hematology. This is a branch of laboratory science that studies the properties of blood and its changes in a particular disease.

Wars, which by the 20th century were becoming increasingly bloody, played an important role in the development of hematology, one of the branches of laboratory diagnostics. For example, hematology began to develop rapidly during the First World War. Blood transfusions were necessary

for the wounded with large blood losses, and they began to be used quite actively then. When transfusing, the compatibility of the blood of the donor and recipient is important. In 1901, the Viennese scientist Karl Landsteiner discovered three blood groups in humans (for which he was awarded the Nobel Prize in 1930). A year later, the fourth group was identified. A few years later, blood transfusions became a mass procedure. At the beginning of the 20th century, they began to study group affiliation, the Rh factor, blood compatibility and learned how to correctly select blood for transfusion.

Biological products derived from human and animal blood are used to treat infectious diseases, toxin damage, various forms of hemophilia, immunological and metabolic disorders, congenital or acquired hypoproteinemia, and to compensate for blood loss. Unfortunately, until the late 1980s, their clinical use resulted in numerous transmissions of viral infections and severe non-infectious complications. Manufacturers lacked the knowledge to scientifically assess the possible relationship between the quality, efficacy, and safety of blood products and the processes used. Currently, the safety and quality of such products has improved, but the scale of their production and the range of products have increased, and the production itself has become internationalized, which suggests significantly greater consequences from an accidental error than it was 30 years ago.

Classification by origin (human albumin preparations; human immunoglobulin preparations; blood coagulation factor preparations containing one of the blood coagulation factors or a combination of them) with examples.

Medicines obtained from blood, blood plasma of humans and animals (except whole blood).

Human albumin (Human serum albumin)

A product obtained by fractionating blood, plasma, placenta, and serum from healthy donors. Maintains colloid-osmotic (oncotic) blood pressure, increases BCC, and increases blood pressure. Promotes the penetration of tissue fluid into the bloodstream. Is a source of protein.

Indications. Contraindications. Side effects.

Human coagulation factor IX (Human coagulation factor IX)

A hemostatic agent used in hemophilia B. During the blood clotting process, coagulation factor IX is activated by factor XIa. The active form of coagulation factor IX, factor IXa, in combination with coagulation factor VIII activates factor X, which in turn promotes the conversion of prothrombin to thrombin and the formation of a fibrin clot.

Indications. Contraindications. Side effects.

Human blood coagulation factor VII (Human blood coagulation factor VII)

Vitamin K-dependent factor of normal human plasma, a component of the extrinsic pathway of the blood coagulation system. It is a zymogen of serine protease factor VIIa, which initiates the extrinsic pathway of the blood coagulation system. Administration of human coagulation factor VII concentrate increases the concentration of factor VII in plasma and provides temporary correction of the coagulation system defect in patients with coagulation factor VII deficiency.

Indications. Contraindications. Side effects.

Human coagulation factor VIII (Human coagulation factor VIII)

A hemostatic agent used in hemophilia A. Promotes the conversion of prothrombin to thrombin and the formation of a fibrin clot.

Indications. Contraindications. Side effects.

Human plasma for fractionation

Human plasma for fractionation is used as a substance for the production of human blood products.

Indications. Contraindications. Side effects.

Human immunoglobulin normal

Human Ig, replenishing the deficiency of antibodies, reduces the risk of developing infections in patients with primary and secondary immunodeficiency.

Modern immunoglobulin preparations are divided into three groups:

I. Standard preparations - contain mainly IgG (normal human immunoglobulin for intravenous administration).

II. Standard specific (hyperimmune) preparations - contain mainly IgG, but have a higher content of antiviral antibodies.

III. Enriched IVIG preparations - contain antibodies
of classes IgG, IgM, IgA against pathogenic viruses and bacteria.

Indications. Contraindications. Side effects.

Von Willebrand factor (human von Willebrand factor)

The introduction of von Willebrand factor allows to correct hemostatic deviations in patients with a deficiency of this factor (von Willebrand disease) at two levels:

Von Willebrand factor restores platelet adhesion to the vascular subendothelium at the site of injury (it can bind to the subendothelium and to the platelet membrane), providing primary hemostasis, which is manifested in a decrease in bleeding time. This effect appears immediately and largely depends on the level of multimerization of the active substance.

Von Willebrand factor promotes delayed correction of concomitant deficiency of factor VIII (produced by the patient's body), stabilizes the content of this factor, preventing its rapid degradation.

Von Willebrand factor replacement therapy normalizes the blood coagulation factor VIII after the first injection. This effect is long-term and persists during subsequent injections of Wilfactin alone.

Preparation of factors (VIII and von Willebrand) of blood coagulation)

A hemostatic agent used in hemophilia A. Promotes the conversion of prothrombin to thrombin and the formation of a fibrin clot.

Indications. Contraindications. Side effects.

Medicines obtained from the blood and blood plasma of animals (except whole blood).

Classified by origin of the drug:

1. Drugs obtained from pig blood plasma.

- Protein-peptide complex from pig blood leukocytes is an immunomodulator, a natural complex of natural antimicrobial peptides and cytokines - universal stimulants of the immune system with the activity of a factor that inhibits the migration of macrophages, interleukin 1 (IL-1), IL-6, tumor necrosis factor (TNF), transforming growth factor secreted by leukocytes of the peripheral blood of a pig.

It has antiviral, antimicrobial and antifungal effects. The drug stimulates the functional activity of phagocytic cells (monocytes and neutrophils): activates phagocytosis, cytokine production (IL-1, TNF), induces antitumor cytotoxicity of macrophages, regulates cell migration to the site of inflammation, increases the activity of natural killers. The drug has antioxidant activity, reduces the development of inflammatory reactions, stimulates regeneration and epithelialization of wound defects. Contraindications. Side effects.

2. Preparations obtained from the blood plasma of calves, bulls and other types of cattle.

- *Deproteinized hemoderivative of calf blood (Actovegin)*

An antihypoxant with three types of effects: metabolic, neuroprotective and microcirculatory. Increases oxygen absorption and utilization; inositol phospho-oligosaccharides included in the drug have a positive effect on glucose transport and utilization, which improves cellular energy metabolism and reduces lactate formation under ischemic conditions. As part of complex therapy: cognitive impairment, including post-stroke cognitive impairment and dementia; peripheral circulatory disorders and their consequences; diabetic polyneuropathy.

Contraindications. Side effects.

- *Deproteinized dialysate from the blood of healthy dairy calves (Solcoseryl)*

Solcoseryl is a deproteinized hemodialysate containing a wide range of low-molecular components of cellular mass and blood serum of dairy calves with a molecular weight of 5000 D (glycoproteins, nucleosides and nucleotides, oligopeptides, amino acids). Solcoseryl has been found to have the following properties: improves oxygen and glucose transport to cells under hypoxic conditions; increases the synthesis of intracellular ATP and promotes an increase in the share of aerobic glycolysis and oxidative phosphorylation; activates reparative and regenerative processes in tissues; stimulates fibroblast proliferation and vascular collagen synthesis. Indications. Contraindications. Side effects. -NovoSeven RT analogue of Eptacog alpha (activated) Hemostatic agent containing trace amounts of bovine IgG protein and other bovine proteins. Recombinant blood coagulation factor VIIa. In therapeutic doses, it binds to a large amount of tissue factor, forming a complex that enhances the initial activation of factor X. In the presence of calcium ions and anionic phospholipids, it is capable of activating factor X on the surface of activated platelets, acting "bypassing" the coagulation cascade system. It acts only at the site of damage and does not cause systemic activation of the coagulation process. Indications. Contraindications. Side effects.

3. Preparations from animals of different species.

- Heterologous immunoglobulins Thymoglobulin (rabbit immunoglobulin); Antilympholin (goat or rabbit immunoglobulin); Atgam (horse immunoglobulin); ATG-Fresenius (rabbit immunoglobulin). Heterologous serums and immunoglobulins are medicinal products containing purified immunoglobulins and/or their fragments obtained from serum or plasma of animals of various species immunized with the corresponding antigens.

Preparations of heterologous immunoglobulins and serums are used in the complex therapy of a number of infectious diseases, as well as for emergency prevention. Indications. Contraindications. Side effects.

- «Hematogen».

Hematogen is a food supplement based on black albumin, a protein obtained by processing defibrinated dry animal blood. Indications. Contraindications. Side effects.

- *Fibrin films*

Fibrin from stabilized human and animal (pig, horse) blood is used to produce fibrin film. It is used as a plastic material for ulcers, poorly healing wounds and burns. Indications. Contraindications. Side effects.

Analyze 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

Приложение 1

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 // ЭБС

"Консультант студента" : [сайт]. - URL : https://www.studentlibrary.ru/book/ISBN9785970447048.html

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 B, D и C : 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. - M. : 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)