MODERN MEDICINE AND PRACTICE
https://inovatus.es/index.php/ejmmp
EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE
Vol. 4 No. 2 (Feb - 2024) EJMMP ISSN: 2795-921X

GENERAL PATHOGENESIS OF ALLERGIC REACTIONS

Karabayev Aminjon Gadayevich
Head of Department of Physiology Department of the Samarkand State Medical University

Varsha Gopakumar Nair, Chetan Ram, Sarkisova Victoria
Lecturer of Physiology Department of the Samarkand State Medical University

Abstract: Allergy (allergia from allos - other, ergon - action) is a different action compared to immune reactions. Allergy is a state of increased and qualitatively perverted reaction to substances with antigenic properties and even without them. Allergies differ from immunity in that the allergen itself does not cause damage.

Key words: acid phosphatase, ribonuclease, cathepsins, collagenase, elastase.

Classification of allergens: exoallergens and endoallergens.

Exoallergens:

1) infectious:

a) bacterial, b) viruses, c) fungi,

2) pollen of flowering plants, poplar fluff, dandelion, ragweed, cotton,

3) superficial (or epiallergens),

4) household - house and library dust, as a product of the life activity of house mites, are specific to a particular apartment,

5) food products - especially for children - cow's milk, chicken eggs, chocolate, citrus fruits, strawberries, fish, crabs, lobsters, cereals,

6) medications - especially medicinal serums.

7) products of chemical synthesis.

Endoallergens:

a) natural (primary): lens and retina, tissues of the nervous system, thyroid gland, male gonads,

b) secondary (acquired), induced from one’s own tissues under the influence of external influences: infectious:

- intermediate tissue damaged under the influence of a microbe;
- complex microbe+tissue, virus+tissue; non-infectious:
- cold, burn, irradiation;

General pathogenesis of allergic reactions (3 stages):

1. Immunological (AT formation),

2. Pathochemical (isolation of BAS substrates) and

3. Pathophysiological (clinical manifestations).

Immunological stage - upon exposure to an allergen, allergic antibodies are produced and accumulated within 2-3 weeks - active sensitization. And it can be passive (when administering ready-made antibodies with serum, it takes at least two hours to fix the antibody to the tissue), and lasts for 2-4 weeks. Allergies are strictly specific. All ATs appear non-simultaneously - first IgE - "reagins" - the main allergic ATs. IgE has a high affinity for skin and tissues. Blocking antibodies - IgG - appear during the recovery period, easily combine with antigen in the blood and block its contact with reagins - perform a protective role. The titer of reagins is judged by the titer of IgG hemagglutinins, because there is a certain dependence [1].

Reagin type of tissue damage (type I):

immunological stage: Reagins with their Fc (constant fragment) end are fixed on the corresponding receptors of mast cells and basophils;

nerve receptors of blood vessels, smooth muscles of the intestinal bronchi and blood cells. T

he other end of the antigen-binging fragment of the variable part performs an antibody function by binding to antigen, and 1 IgE molecule can bind 2 antigen molecules. Because IgE is synthesized in the lymphatic tissue of the mucous membranes and lymph nodes (Peyer's patches, mesenteric and bronchial), therefore, with the reagin type of damage, the shock organs are the respiratory organs, intestines, conjunctiva = an atypical form of bronchial asthma, hay fever, urticaria, food and drug allergies, helminthiases. If the same antigen enters the body, or it is present after the initial entry, then it binds to IgE-ATs, both circulating and fixed on mast cells and basophils [3].

The cell is activated and the process transitions to the pathochemical stage. Activation of mast and basophil cells (degranulation) leads to the release of various mediators. Immediate type allergy mediators:

1. Histamine.

2. Serotonin.

3. Slowly reacting substance (slowly acting substance - MAD).

4. Heparin.

5. Platelet-activating factors.

6. Anaphylotoxin.

7. Prostaglandins.

8. Eosinophilic chemotactic factor of anaphylaxis and high molecular weight neutrophil chemotactic factor.

9. Bradykinin.

Pathophysiological stage. It has been established that the basis of the action of mediators is an adaptive, protective value. Under the influence of mediators, the diameter and permeability of small vessels increases, the chemotaxis of neutrophils and eosinophils increases, which leads to the development of various inflammatory reactions. An increase in vascular permeability promotes the release of immunoglobulins and complement into the tissue, ensuring inactivation and elimination of the allergen. The resulting mediators stimulate the release of enzymes, superoxide radical, MDV, etc., which plays an important role in anthelmintic protection. But the mediators also have a damaging effect: an increase in the

permeability of the microvasculature leads to the release of fluid from the vessels with the development of edema and serous inflammation with an increase in the content of eosinophils, a drop in blood pressure and an increase in blood clotting. Bronchospasm and spasm of intestinal smooth muscles develop, and increased secretion of the glands. All these effects are clinically manifested in the form of an attack of bronchial asthma, rhinitis, conjunctivitis, urticaria, edema, itching, and diarrhea. Thus, from the moment of connection of AG with AT, the 1st stage ends. Cell damage and release of mediators is the 2nd stage, and the effects of the mediators are the 3rd stage. Clinical features depend on the predominant involvement of the target organ (shock organ), which is determined by the predominant development of smooth muscles and fixation of AT on the tissue [2].

Anaphylactic shock generally proceeds in a standard way: a short erectile stage, after a few seconds - a torpid stage.

- in a guinea pig - predominantly bronchospasm (asthmatic type of shock),
- in dogs - spasm of the sphincters of the hepatic veins, stagnation of blood in the liver and intestines - collapse,
- in a rabbit - predominantly spasm of the pulmonary arteries and stagnation of blood in the right half of the heart,
- in humans - all components: a drop in blood pressure due to blood redistribution and impaired venous return, an attack of suffocation, involuntary urination and defecation, skin manifestations: urticaria (urticaria), swelling (oedema), itching (pruritus).

Atopy is the absence of a point of contact, occurs naturally only in humans and has a pronounced hereditary predisposition. There is no need for prior contact with the allergen; readiness for allergies has already been formed: bronchial asthma, hay fever, urticaria (to citrus fruits), Quincke's edema, migraine. The pathogenesis of these diseases is similar. Clinical features depend on the predominant involvement of the target organ (shock organ), which is determined by the predominant development of smooth muscles and fixation of AT on the tissue.

Bronchial asthma (asthma bronchiale) - an attack of suffocation with difficulty in exhaling - bronchospasm, swelling of the mucous membrane, copious mucus secretion and blockage of the bronchi. Hay fever (pollinosis from pollen pollen): allergic rhinitis and conjunctivitis, swelling of the mucous membrane, lacrimation, often itching due to pollen.

Skin manifestations: Quincke's edema due to cosmetics and food allergens (deep layers of facial skin are affected) and urticaria (if superficial layers of skin are affected - to creams, ointments, powders).

Migraine (hemicrania): periodic severe headache on one side - allergic swelling of one half of the brain to food, less often to drugs [4]. Type II damage - cytotoxic: Abs formed on the Ag cells of the cells attach to the cells and cause their damage or even lysis, since the cells of the body acquire autoallergenic properties under the influence of various reasons, for example, chemicals, often drugs due to:

1) conformational changes in the Ag cell,

2) membrane damage and the appearance of new Ags,

3) the formation of complex allergens with a membrane, in which the chemical plays the role of a hapten.

Lysosomal enzymes of phagocytic cells, bacterial enzymes and viruses act similarly on the cell. The resulting antibodies belong to the IgG or IgM classes. They connect with their Fab end to the corresponding cell Ags. Damage can be caused in 3 ways:

1) due to activation of complement - complement-mediated cytotoxicity, in which active fragments are formed that damage the cell membrane,

2) due to the activation of phagocytosis of cells coated with G4 opsonin antibodies,

3) through activation of antibody-dependent cytotoxicity.

After connection with the cell, conformational changes occur in the F region at the end of the antibody, to which K cells (killer T lymphocytes and null cells) attach. During the pathochemical stage, the complement system (serum protein system) is activated. Lysis of target cells develops with the combined action of components from C5b to C9. The process involves the superoxide anion radical and lysosomal enzymes of neutrophils.

Pathophysiological stage. In the clinic, the cytotoxic type of reaction can be one of the manifestations of drug allergies in the form of leukocytopenia, thrombocytopenia, hemolytic anemia, with allergic blood transfusion reactions, with hemolytic disease of newborns due to the formation of Rh-positive IgG to fetal erythrocytes in the Rh-negative mother. However, the effect of cytotoxic antibodies does not always end with cell damage - with a small amount of antibodies, the phenomenon of stimulation can be obtained (antireticular cytotoxic serum by A.A. Bogomolets for stimulating immune mechanisms, pancreatotoxic serum by G.P. Sakharov for the treatment of diabetes mellitus). Some forms of thyrotoxicosis are associated with the long-term stimulating effect of naturally formed autoantibodies to the thyroid gland [5]. Damage by immune complexes (AG + AT) – type III - (synonyms - immunocomplex, Arthus type). On AG, which has a soluble form, the body forms AT of G and M classes (precipitating) capable of forming a precipitate in vitro when combined with AG. Immune reactions constantly occur in the body with the formation of the Ag+AT complex, because Some antigens constantly enter the body from the outside or are formed endogenously, but these reactions are an expression of the protective or homeostatic function of the immune system and are not accompanied by damage. However, under certain conditions, the AG + AT complex can cause damage and the development of disease through complement activation, release of lysosomal enzymes, generation of superoxide radical and activation of the kallikrein-kinin system. Many exo- and endogenous antigens and allergens are involved in the formation of immune complexes: antibiotics, sulfonamides, antitoxic serums, homologous gamma globulins, food products, inhalation allergens, bacteria and viruses. The formation of the immune complex depends on the site of entry or formation of Ag. The damaging effect is usually caused by complexes formed in a small excess of antigen with a molecular weight of 900,000 - 1 million daltons.

Pathochemical stage.

Under the influence of the complex and in the process of its removal, a number of mediators are formed for phagocytosis and digestion of the complex: these are complement, lysosomal enzymes (acid phosphatase, ribonuclease, cathepsins, collagenase, elastase); kinins, causing spasm of bronchial smooth muscles, vasodilation, chemotaxis of leukocytes, pain effect, increased permeability of the microcirculatory bed. Activation of Hageman factor (XII) and (or) the plasmin system and the release of histamine, serotonin, platelet-activating factor, which causes platelet aggregation on the endothelium and the release of histamine and serotonin from platelets, can also occur. Pathophysiological stage: circulating immune complexes are deposited in the vessels of the glomeruli of the kidneys and cause various types of glomerulonephritis, in the lungs - alveolitis, in the skin - dermatitis. In severe cases, inflammation can take on an alterative character with tissue necrosis, partial or complete thrombosis, and hemorrhage. Initially, neutrophils predominate in the lesion, actively phagocytizing immune complexes, releasing lysosomal enzymes and factors that increase permeability and chemotaxis for macrophages. Macrophages accumulate in the site of inflammation and phagocytose destroyed cells, cleaning the affected area. Inflammation ends with the proliferation of cellular elements. The third type of immune damage is leading in the development

of serum sickness, exogenous allergic alveolitis, some cases of drug and food allergies, and a number of autoimmune diseases (lupus erythematosus, rheumatoid arthritis). With significant complement activation, systemic anaphylaxis can develop in the form of anaphylactic shock [4]. Serum sickness is an immediate allergic disease caused by the administration of heterologous or homologous serums or serum preparations and is characterized by predominant inflammatory damage to blood vessels and connective tissue, which develops 7-12 days after the administration of foreign serum. In response to the introduction of antigens, various classes of antigens are formed in the body, mainly precipitating ones. Immune complexes are formed and undergo phagocytosis, as in a normal immune reaction. But due to certain conditions (a certain amount of the allergen/AT complex, a small excess of allergen, and other factors), this complex is deposited in the vascular wall, its permeability increases, complement is activated, and mediators are released. Symptoms of serum sickness develop after 6-8-12 days: body temperature begins to rise, papulovesicular rashes appear on the skin (urticaria) up to hemorrhagic ones, most often at the site of injection of AG. The rash is accompanied by severe itching and hemodynamic disorder. Immune complexes are more often deposited in the glomeruli of the kidneys (glomerulonephritis) with swelling and proliferation of endothelial cells and mesangiocytes and narrowing or obliteration of the lumen of the glomerular capillaries. Often enlarged spleen, damage to the heart (from angina attacks to MI), lungs (emphysema, acute edema). In the blood - leukopenia with relative lymphocytosis, sometimes thrombocytopenia, glypoglycemia. Treatment depends on the form of the disease: in severe cases in the form of anaphylactic shock, emergency care is required, steroid hormones, antihistamines are prescribed, in case of edema - diuretics, etc. Characteristics of HRT - T-type of allergic response (autoimmune diseases, tuberculin-type reactions and contact dermatitis). The stages are the same. In the immunological stage, within 10-12 days, a clone of sensitized T-lymphocytes accumulates, into the cell membrane of which structures are built that act as ATs, capable of combining with the corresponding allergen.

Lymphocytes do not need to be fixed; they are the repository of allergy mediators. Upon repeated application of the allergen, T-lymphocytes diffuse from the bloodstream to the site of application and combine with the allergen. Under the influence of the immuno-allergo-receptor + allergen complex, lymphocytes are irritated (pathochemical stage) and release HRT mediators:

1) skin reactivity factor,

2) lymphocyte blast transformation factor,

3) transfer factor,

4) chemotaxis factor,

5) macrophage migration inhibitory factor (MIF),

6) lymphotoxin,

7) interferon,

8) a factor that stimulates the formation of endogenous pyrogens by macrophages,

9) mitogenic factors.

Clinically, stage 3 is a focus of allergic exudative inflammation of dense consistency. The leading place among HRT is autoimmune diseases.

Pathogenesis of autoimmune diseases due to endoallergens: There are three possible options:

1) the formation of autoATs to primary allergens that enter the blood when the corresponding organ is damaged (since in utero during the formation of the immune system they did not come into contact with lymphocytes, were isolated by histo-hematological barriers or developed after birth),

2) production of sensitized lymphocytes against foreign flora that have common specific antigen determinants with human tissues (group A streptococcus and heart and kidney tissue, E. coli and colon tissue, timothy grass glycoproteins and UDP glycoproteins),

3) removal of the inhibitory effect of T-suppressors, disinhibition of suppressed clones against their own tissues, components of the cell nucleus, causes generalized inflammation of the connective tissue - collagenosis [3].

Diagnosis of allergic diseases - the search for a specific allergen, is based on serological and cellular reactions based on the antibodies or lymphocytes present in the allergic person. To identify the reagin type of sensitization:

1) radioallergosorbent test (RAST),

2) radioimmunosorbent test (RIST),

3) direct skin test,

4) Praustnitz-Kustner reaction,

5) Shelley test.

To identify the cytotoxic type:

a) various variants of the immunofluorescence method,

b) Coombs test,

c) Steffen reaction,

d) radioimmunological method.

To identify the immune complex type:

a) various methods for determining circulating immune complexes,

b) determination of the rheumatoid complex,

c) various methods for determining precipitating antibodies. Diagnosis of HRT - identification of mediator effects:

1) direct skin test,

2) blast transformation reaction,

3) reaction of inhibition of macrophage migration,

4) lymphotactic effect.

Allergy treatment - specific:

1. Etiotropic - prevention, cessation and elimination of the allergen: with medications, food, hay fever, household allergens. Specific to HNT is hyposensitization (fractional, continuous long-term administration of the allergen to the patient in increasing doses). Pathogenetic therapy - to identify the leading type of allergic reaction and have a blocking effect on the development of each stage. In the immunological stage, levamisole and thymus hormones are used, which regulate the immune response. In the pathochemical stage: with the reagin type of blockade, the release of mediators from mast cells: intal, ketotifen, antihistamines, histaglobulin (histaminopexy), antiserotonin drugs. For cytotoxic and immunocomplex types, antienzyme drugs inhibit the activity of proteolytic enzymes and thereby block the complement systems and kallikrein, etc. At the pathophysiological stage, treatment depends on the type of allergy.

2. Desensitization - urgent removal of sensitization in order to prevent anaphylactic shock. Three types:

1) natural - after suffering anaphylactic shock (for 2 weeks),

2) nonspecific - introduction of the allergen under the protection of anesthesia and antihistamines,

3) specific according to Bezredko A.M. (repeated fractional doses every 30 minutes 2-3 times).

The first small doses bind the bulk of the AT, losing the minimal reaction, and then the main dose of the drug.

3. Nonspecific - symptomatic: bronchodilators, antihistamines, anti-inflammatory hormones, anticoagulants for type 3 immune damage.

Literature:

1. Kurbonova G. A., Lapasova Z. K. CURRENT VIEWS ON IRON DEFICIENCY ANAEMIA IN PATIENTS WITH CARDIOVASCULAR DISEASE //The American Journal of Medical Sciences and Pharmaceutical Research. – 2022. – Т. 4. – №. 03. – С. 59-64.
2. Khidirovna L. Z. et al. Significance of Syndrome Teetering in Development of Residual Pain Syndrome in Patients Operated for Lumbar Osteochondrosis //Texas Journal of Multidisciplinary Studies. – 2022. – Т. 6. – С. 59-63.
3. Sherali K., Zebiniso L., Gulbahor K. Features Of Anthropometric Indicators Of Children Of The First Year Of Life Born Of Mothers In The State Of Hypothyrozis //The American Journal of Medical Sciences and Pharmaceutical Research. – 2020. – Т. 2. – №. 09. – С. 64-68.
4. Хакимова Л., Лапасова М., Лапасова З. The use of innovative learning methods in high educational establishments as a stage of implementation of improving the quality of the educational process //Общество и инновации. – 2022. – Т. 3. – №. 1/S. – С. 121-125.
5. Khidirovna L. Z. Primary and Secondary Hyperalgesia //Scholastic: Journal of Natural and Medical Education. – 2023. – Т. 2. – №. 5. – С. 99-104.
6. Vladimirovna S. V. et al. Analysis of Women's Reproductive and Somatic Health, Hospitalized for Endometrial Hyperplasia and Uterine Bleeding //Eurasian Medical Research Periodical. – 2023. – Т. 17. – С. 91-96.
7. Лапасов С. Х. и др. Инновационные подходы в диагностике язвенной болезни у взрослых в первичном звене здравоохранения: обзор литературы //Здоровье, демография, экология финно-угорских народов. – 2018. – №. 4. – С. 68-72.
8. Khidirovna L. Z. et al. Significance of Syndrome Teetering in Development of Residual Pain Syndrome in Patients Operated for Lumbar Osteochondrosis //Texas Journal of Multidisciplinary Studies. – 2022. – Т. 6. – С. 59-63.
9. Sarkisova V., Xegay R., Numonova A. ENDOCRINE CONTROL OF THE DIGESTION PROCESS. GASTROINTESTINAL ENDOCRINE CELLS //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 582-586.
10. Sarkisova V. ASPECTS OF THE STATE OF THE AUTONOMIC NERVOUS SYSTEM IN HYPOXIA //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 977-982.
11. Vladimirovna S. V. Epidemiology, Theories Of The Development, Conservative And Operative Treatment Of The Endometriosis //The Peerian Journal. – 2023. – Т. 15. – С. 84-93.

12. Vladimirovna S. V. About the Causes of Endometrial Hyperplasia and Forms of Endometrial Hyperplasia //Global Scientific Review. – 2023. – Т. 12. – С. 25-32.
13. Sarkisova V., Xegay R. Causes, Diagnosis, Conservative And Operative Treatment Of Uterine Myoma //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 198-203.
14. Саркисова В. В. Патогенетические отношения артериальной гипертензии и сопротивления инсулина //IQRO. – 2023. – Т. 2. – №. 1. – С. 727-731.
15. Vladimirovna S. V. PATHOGENETIC RELATIONSHIPS OF ARTERIAL HYPERTENSION AND INSULIN RESISTANCE //IQRO. – 2023. – Т. 2. – №. 1. – С. 685-691.
16. Sarkisova V., Regina X. РОЛЬ БРАДИКИНИНА В ПРОТЕКАНИИ ОСНОВНЫХ ЖИЗНЕННЫХ ПРОЦЕССОВ //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 587-593.
17. Sarkisova V., Numonova A., Xegay R. Аспекты Состояния Вегетативной Нервной Системы При Гипоксии //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 228-231.
18. Sarkisova V., Alvi I. THE PROBLEM OF COMORBIDITY OF AFFECTIVE DISORDERS AND PERSONALITY DISORDERS //Science and innovation. – 2023. – Т. 2. – №. D5. – С. 170-177.
19. Sarkisova V. et al. BIPOLAR AFFECTIVE DISORDER (BAR) //Science and innovation. – 2023. – Т. 2. – №. D5. – С. 165-169.
20. Sarkisova V. et al. CYTOKINE PROFILE IN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS (WEGENER'S) //Science and innovation. – 2023. – Т. 2. – №. D11. – С. 336-343.
21. V. Sarkisova, Z. Lapasova, F. Shernazarov, O. Rakhmanov INFLAMMATORY DISEASES OF THE PELVIC WOMEN ORGANS // SAI. 2023. №D11. URL: https://cyberleninka.ru/article/n/inflammatory-diseases-of-the-pelvic-women-organs (дата обращения: 31.01.2024).
22. Шерназаров Фаррух,Шерназаров Самандар,Курбаниязова В.Е.,Виктория Саркисова Владимировна. (2023). Клиническое значение микробиоты кишечника у новорожденных с геморрагической болезнью. IQRO , 2(2), 867–877. Retrieved from http://wordlyknowledge.uz/index.php/iqro/article/view/893
23. V. Sarkisova, I. Alvi THE PROBLEM OF COMORBIDITY OF AFFECTIVE DISORDERS AND PERSONALITY DISORDERS // SAI. 2023. №D5. URL: https://cyberleninka.ru/article/n/the-problem-of-comorbidity-of-affective-disorders-and-personality-disorders (дата обращения: 31.01.2024).
24. Саркисова В., Абдурахманова К. Роль гормональных препаратов в терапии гиперпластических процессов эндометрия и в частности при миоме матки //Журнал вестник врача. – 2014. – Т. 1. – №. 1. – С. 167-168.
25. Джуманов Б. и др. Применение инструментальных методов исследование в диагностике острого аппендицита у беременных //Журнал проблемы биологии и медицины. – 2014. – №. 1 (77). – С. 9-12.
26. Sarkisova V., Xegay R. Causes, Diagnosis, Conservative And Operative Treatment Of Uterine Myoma //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 198-203.
27. Sarkisova V., Numonova A., Xegay R. АНТИБИОТИКОРЕЗИСТЕНТНОСТЬ ИЛИ БОРЬБА С ГЛОБАЛЬНОЙ УГРОЗОЙ XXI ВЕКА //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 232-241.

28. Sarkisova V. et al. CYTOKINE PROFILE IN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS (WEGENER'S) //Science and innovation. – 2023. – T. 2. – №. D11. – C. 336-343.
29. Vladimirovna S. V. et al. TORCH-Complex //Scholastic: Journal of Natural and Medical Education. – 2023. – T. 2. – №. 6. – C. 183-187.