

## MEDICAL SCIENCES

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### ALLERGIC DISEASES IN CHILDREN FROM MOTHERS WITH AN ALLERGIC HISTORY AND ASPECTS FORMATION OF FOOD INTEGRABILITY

*The article includes data from a literature analysis on aspects of allergopathology in children, which are important for physicians, especially pediatricians, and the study of this problem remains an open question.*

**Key words:** *young age, distribution, aspects, growth, diseases.*

Allergic diseases are currently characterized by steady growth, so the problem of diagnosis and treatment remains the focus of attention of many researchers and doctors. The particular relevance of this issue for pediatricians is also due to the fact that more than half of all new cases of allergic diseases have their first manifestations from an early age.

As noted by the authors of the literature, the concept of "tolerance" to dietary proteins can be considered in two aspects: Formation of tolerance of dietary proteins during the formation of the immunological phenomenon of "oral tolerance", when the immune system is utero and then learns not to respond to a born baby active on a wide range of proteins that enter enterally.

This process begins in utero, continues actively in the first months of life and in early childhood. The possibility of influencing the mechanisms of formation of such a "primary" tolerance is the basis of modern approaches to the prevention of PA; In children who are allergic to food proteins, tolerance to these proteins can form over time. For different proteins, the frequency of formation of such a "secondary" tolerance is different - it is highest among proteins of cow's milk and chicken eggs. The formation of tolerance is much less common with allergies to peanuts, fish, and other allergens. The formation of food tolerance primarily depends on a genetic predisposition to the development of allergic diseases.

An analysis of the literature showed that the duration of breastfeeding and, in the absence of breast milk, the choice of a mixture, the timing of the introduction of complementary foods, the choice of products for administration, the state of the gastrointestinal tract and the composition of the intestinal microflora, the state of innate and humoral immunity, are of great importance. Of course, children from the risk group for the formation of allergic diseases (the presence of allergic diseases in parents or siblings) are more likely to develop them. So, in the case of an allergic disease in one of the parents, the risk of developing an allergic disease exceeds the population by 30-40%, and if there is an allergy in both parents, by 50-80%. According to some

reports, due to the presence of 25 burdened heredities for allergic diseases, up to 30% of newborns have a high risk of their development.

The authors noted the fact that during pregnancy, in the ratio of T helper cells (Th1 / Th2) in the mother, regardless of the presence or absence of an allergic disease, Th2 dominates. This physiological mechanism reduces the risk of T-associated placental rejection. The immune system preserves the dominant Th2 type and supports the production of immunoglobulin (Ig) E in the baby during the prenatal period, and after birth, under the influence of certain factors, the Th2 type of the immune response switches to the Th1 type of the immune response. Under the influence of genetic and external factors in some children, the balance between Th1 / Th2 is disturbed, which can lead to a significant imbalance in the immune response and an increase in IgE production in the first year of a child's life.

According to most researchers, the early intake of a foreign antigen and the state of its own intestinal microbiota affect the Th1 / Th2 balance through special mechanisms of innate and acquired immunity. At the same time, there is convincing evidence that strict elimination of allergens can inadvertently contribute to an increased risk of developing allergic diseases, including due to the lack of the possibility of tolerance to these allergens. This is true for both food and inhalant allergens. Due to the lack of convincing data in favor of the effectiveness of strict elimination measures during pregnancy, the previous recommendations were postponed until six months of age and strict elimination measures for allergenic products during pregnancy were rejected. It is also not recommended to avoid probable inhalation allergens during pregnancy and during the neonatal period.

Further analysis of literature showed that experimental animal studies support the hypothesis of tolerogenic properties of breast milk. This is mediated through tolerogenic cytokines, such as transforming growth factor (TGF), which contribute to the regulation of the ratio of T cell populations in the intestines of the newborn. Allergy to cow's milk proteins rarely devel-

ops in exclusively breast-fed infants. As well as a prospective study of children from birth fed a standard formula based on cow's milk during the first days of life, showed an association with an increased risk of developing allergies to cow's milk proteins, especially in children with a hereditary predisposition to allergies. Introduction to the feeding of children in maternity hospitals with standard mixtures based on cow's milk increases the risk of allergies compared with children receiving breast milk or mixtures based on hydrolyzed proteins. However, only breastfeeding also does not exclude the risk of a possible allergy to cow's milk proteins. Based on this, many experts strongly recommend maintaining breastfeeding for as long as possible, but if a mixture is needed, it is better to use a standard milk mixture for children with a genetic predisposition to allergies. In a large, multicenter, randomized trial conducted by von Berg A. et al. 2252 newborns at risk who received a mixture based on moderately hydrolyzed whey protein or a mixture based on highly hydrolyzed whey protein and highly hydrolyzed casein were included. Newborns who were breastfed were excluded from the analysis (N = 945). According to the results of the study, it turned out that there was a significant decrease in the frequency of formation of the syndrome of atopic 27 dermatitis / eczema at 1, 3, 6 and 10 years in children who received hydrolyzed mixtures. Immunological mechanisms of oral tolerance Currently, dendritic cells (DC) currently play a key role in the formation of either an allergic reaction to food allergens or oral tolerance.

There are several subclasses of DC with regulatory functions that are present in the intestine and therefore are potentially important for the formation of oral tolerance. Conventional myeloid DCs and plasmacytoid DCs of Peyer's patches have unique regulatory functions and can contribute to the formation of oral tolerance. DCs have the ability to suppress the immune response, most likely by inducing the differentiation of naive T cells into regulatory T cells (Treg). CD103 + DC, located mainly in the own plate of the mucous membrane, capture the antigen and migrate to the mesenteric lymph nodes, where they initiate the formation of regulatory T cells. It has been shown that the capture of antigens in M cells of Peyer's patches is also involved in the induction of oral tolerance, although it seems that mesenteric lymph nodes are the main recognition zone of T cells. In general, when the components of the accepted "harmless" food are captured by DC of the intestinal mucosa, regulatory T cells are formed that support the induction of oral tolerance. These cells surround natural or induced CD 4 + CD25 + Foxp3 +, TGF- $\beta$ -producing Th3 and IL-10-producing Treg1 cells. In experimental studies in mice, it was shown that CD103 + DCs cause differentiation of Foxp3 + - regulatory T cells due to mechanisms involving TGF- $\beta$  and retinoic acid (PK), which comes from food. Oral tolerance caused by a partial hydrolyzed mixture based on serum proteins of cow's milk leads to the induction of regulatory 28 Treg or Th1, a decrease in the relative number of Th2 in mesenteric lymph nodes.

Treg and T-effectors accumulate in their own plate of the mucous membrane, where they can participate in

an effective immune response directed against specific antigens. In experimental studies, tolerance caused by a partial hydrolyzed mixture based on serum proteins of cow's milk was associated with an increase in the percentage of Foxp3 + Treg and CD103 + DC in mesenteric lymph nodes. Previous studies have shown that infant formula with the addition of indigestible oligosaccharides containing neutral short galactooligosaccharides and long-chain fructooligosaccharides in a 9: 1 ratio cause functional suppression involving regulatory Treg. Mixtures containing neutral short galactooligosaccharides and long-chain fructooligosaccharides in combination with 9: 1: 1 pectic acid oligosaccharides support the development of a population of tolerogenic DC and regulatory T cells. Epithelial mediators, such as PK and TGF- $\beta$ , can indirectly contribute to this effect, since they induce CD103 + DC. In the case of allergic sensitization, the plasmacytes produce specific IgE, which rush to the mast cell membrane, followed by their degranulation upon repeated contact with the allergen. The timing of the formation of tolerance in children allergic to BMD (Protein of cow's milk). The timing of the formation of tolerance in these patients with PA and, accordingly, the timing of elimination measures for allergies to BMD are individual. The frequency of formation of milk protein tolerance in children who were allergic to BMD in the first year of life with non-IgE-mediated form of allergy to BMD can reach 100% by 5 years, while with an IgE-mediated form these figures are significantly lower.

So, according to Saarinen KM. with co-authors, 29 with IgE-mediated allergy, tolerance to BMD develops in 74% of children by 5 years old and in 85% by 8-9 years of age. According to Elizur A. et al, this occurs in 41% of children by 2 years of age and in 57% of children by 4 years of age. The least optimistic prognosis of the formation of tolerance to BMD in the IgE-mediated form, gives J.M. Skripak, who co-authored the largest number of clinical observations (807 patients), was 19% at 4 years old, 64% at 12 years old and 79% at 16 years of age. This means that every fifth child with an IgE-mediated allergy to BMD, which started at an early age, does not tolerate milk even at the age of 16. Factors affecting the timing of the formation of tolerance to BMD and the duration of the elimination diet Normally, priming by lymphocytes of BMD begins prenatally. Subsequently, a pronounced immune response to BCM and other dietary proteins is noted in the first months of life. An increase in the level of IgG, including the IgG1 subclass, is a physiological reaction to the introduction of a foreign protein. The level of specific IgG antibodies rises within a few weeks after the introduction of infant formula into the diet and reaches a peak after 3-4 months. Small amounts of specific IgE are also part of the physiological response to foreign cow's milk proteins. However, significant production of specific IgE for BMP in combination with clinical manifestations is a diagnostic criterion for the IgE-mediated form of PA for milk proteins, and is also a predictor of its persistence. Moreover, a periodic examination with an assessment of the level of specific IgE allows predicting the development of tolerance.

Thus, based on the literature data, we can say about the appropriateness of further study of this problem in pediatrics.

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### ЖЕЛЧЕГОННЫЕ СВОЙСТВА КОМПЛЕКСНОГО ВВЕДЕНИЯ ФЕРАЗОНА С ЛИПОВИТОЛОМ, КАРВИОЛОМ И ЛИМОНЕОЛОМ НА ЗДОРОВЫХ КРЫСАХ И МОРСКИХ СВИНКАХ

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### CHOLERIC PROPERTIES OF COMPLEX ADMINISTRATION OF PHERASON WITH LIPOVITOL, CARVIOL AND LIMONEOL ON HEALTHY RATS AND GUINEA PIGS

#### Резюме

Данная статья посвящена желчегонным свойствам комплексного введения Феразона+липовитола, Феразона +лимонеола, Феразона+карвиола в дозах 0,5 -0,02 г/кг на здоровых белых крысах и морских свинках. Экспериментальными исследованиями установлено, что испытуемые средства в указанных дозах оказывают заметный желчегонный эффект как на белых крысах, так и на морских свинках. Наряду с