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# INVESTIGATION OF ALLERGIC REACTIONS IN HELMINTHIASIS

**Abstract**

Identification and characterization of allergens associated with helminth infestations is important. These allergens belong to common allergens and have different biological functions. The activity of some allergens associated with helminth infestations has been studied and it has been determined that during helminth infestations, various substances are produced in the host's body, and some of them stimulate the synthesis of specific IgE, and a few of them cause allergic reactions.

The activity of allergens associated with helminth infestations (the ability to induce IgE-mediated inflammation) has been studied clinically and experimentally. In several epidemiological studies, it has been established that IgE response to helminths is a risk factor for asthma and atopy (i.e. susceptibility to allergies). Revision of existing diagnostic methods and standards of allergic processes in helminthiasis, and research on molecular mechanisms of metabolism of allergens related to helminth infestations should be continued.

***Keywords****: Helminthiasis, immune system, antigens, allergy, IgE*

## Introduction

Helminth allergens are common allergens and have different biological functions. The role of helminth allergens in allergic reactions and symptoms in helminths has not yet been fully investigated.

During helminth invasions, various substances form in the host body, and some of them stimulate the synthesis of specific IgE, while a small percentage cause allergic reactions. At the same time, the frequency and intensity of allergic reactions are formed depending on the state of the immune system.

Considering the importance of the identification and characterization of allergens associated with helminth invasions, their allergen activity (ability to induce IgE-mediated inflammation) has been clinically and experimentally investigated (Caraballo, 2018: 99–102). It has been found in some epidemiological studies that the IgE response to helminth is a risk factor for asthma and atopic allergy (i.e. predisposition to allergies).

The official WHO website provides information on the specific antigen (known as Asc s 1 or ABA-1) and two cross-reacting allergens (Asc l 3 and Asc l 13). The role of 3 helminth allergens (ASC 15, ASC 13 (tropomatosis), and ASC 113 (glycation transferase)) in diagnosing allergies in helminth invasions is of particular importance.

During helminth invasions, the body responds to different allergens with different symptoms (Webb, Nampijja, Kaweesa, Kizindo, 2016, 1156-1169; Nkurüngi, Kabagenyi, Nampijja, 2018: 40). Studies among children in Venezuela have seen an increase in asthma and other respiratory diseases. The purpose of these studies was to investigate the possible relationship between the development of bronchial hyperactivity in children and the immune response to **Ascarislumbricoides.** The study was conducted and evaluated on 470 schoolchildren living in the village. Functional tests of the lungs in children found that 20% of them had bronchial hyperactivity. The prevalence of ascariasis and the intensity of invasiveness were determined by examination of feces.

IgE triggers have been set using the modified ELISA method. The results found that IgE against invasion of *Ascaris* lumbricoides caused bronchial hyperactivity among rural children from endemic areas.

During the migration phase of the larvae of*Ascaris*lumbricoides, asthmatic symptoms are common, sometimes involving Löffler syndrome. These changes are also noted at the cellular and molecular level (Caraballo, Acevedo, Zakzuk, 2019: 41; 6). In addition, polyclonal non-stimulation of B cells is observed during ascaridosis (Lee, Xie, 1995: 1246–1254).

*Examination* of A.lumbricoides excretor using immunoblotting and spectrometry suggests that the allergen *is specific to A.* lumbricoides species (Ahumada, Zakzuk, Coronado, Aglaz, Araujo, Briza, et al. 2020: 13; 8).

Cough is also noted as one of the allergy symptoms during the course of ascaridosis. The larvae that pass into the owner's gastrointestinal system gradually develop and pass through the blood vessel system and lungs into the respiratory tract. The presence of larvae in the uterus causes increased sputum exposure, coughing (Ahmad, Arifin, Nolan, Lok, Anuar, Noordin, 2021: 11; 6). Other helminths have also been studied in this aspect.

**Strongiloidosis.** Strongyloidosis is often asymptomatic, but in some cases causes allergic diseases of the respiratory system or allergic dermatitis. In laboratory conditions, experiments on mice infected with strongiloid have shown that this helminth is known to cause eosinophilic inflammation, thickening of the bronchus walls, and asthma symptoms (Araujo, de Jesus Pereira, de Moura Pereira, Moreira, de Rezende, Rodrigues, et al. 2016: 3107–3117).

*S.stercoralis--antigens* are recognized by IgE, IgE-dependent histamine exposure increases, and a positive skin reaction is noted at this time. Another helminth secretory that helps strongiloidosis larvae penetrate the skin is metalloprotease. 100 %of patients with S.stercoralis IgE-induced recombinant protein rA133 are recognized by IgE but are not recognized by those infected with other parasites.

The rate of immunosuppression during helminths depends on the type of helminth and the intensity of the invasion and the genetic characteristics of the host organism. Studies on animal models have found that specific IgE antibodies, along with eosinophils, can destroy helminth larvae. Other types of immune mechanisms have been found in these studies using different helmets (Vacca, Le Gros, 2022: 1212-23; Caraballo, Coronado, 2018: 113-119), but their clinical significance should be further investigated.

All these molecules are allergens and they induce IgE, some of which have been investigated for allergen activity (the ability to cause allergic inflammation), which is important in determining their

clinical significance (Caraballo, Valenta, Puerta, Pomes, Zakzuk, Fernandez-Caldas, et al. 2020: 13; 5). This consideration applies to common allergens but is especially important for helminths (Caraballo, Zakzuk Acevedo, 2021: 1–13).

Invasions in humans can manifest themselves with chronic cough and aggravation of asthma (de las Marinas, Martorell, Felix, 2012: 286-7; Hazan, Orscheln, Kertz, 2022: 2562-4; Salam, Sharaan, Jackson, 2020).

Strongyloidiasis antigens cause IgE-dependent histamine secretion and positive skin reactions in basophiles (Neva, Gam, Maxwell, 2001: 567–572).

Several antigens associated with IgE of Strongilodosis have been investigated. For example, NIE is a larva component recognized by the human IgE. Strongilodose is another secretory metalloprotease with IgE reactivity that helps larvae penetrate the skin (Varatharajalu, Parandaman, Ndao, 2011: 115–122). *S.stercoralis* IgE-induced recombinant rA133 is identified in 100% of infected patients.

There is experimental and epidemiological evidence of asthma in toxocariasis (Mendonca, Veiga, Dattoli, Figueiredo, Fiaccone, Santos, 2012). Meta-analysis examinations show that children infected with toxocaria are more likely to have asthma than those who are uninfected. Identification of components related to IgE has not been fully carried out in these parasites, although several components of human-specific antitopes have been identified.

**Ankylostomidoses.** Most studies about these nematodes have noted that it has an immunosuppressive effect on the human body. Ankylostomies are shown to cause an allergic reaction in the human body during life cycle. Migration of parasitic larvae from the lungs causes Löffler syndrome.

Ankylostoma secretes the IgE-binding molecule Na-ASP-2, which is structurally similar to SmVALs (Kelleher, Darwiche, Rezende, Farias, Leite, Schneiter, 2014: 2186–2196). Na-ASP-2 can cause positive skin reactions. Both calreticulin and Na-ASP-2 have been investigated as vaccines against ankylostoma helminths (Bethony, Loukas, Smout, 2005: 1743-1745; Winter, Davies, Brown, Stolnik, Pritchard, 2005: 139–146).

High titre of IgE is already detected in children infected with helminth in endemic zones at age 3 (Zakzuk, Acevedo, Cifuentes, Bornacelly, Sanchez, Ahumada, 2013: 788–797). Thus, the detection of specific IgE is more important for determining atopy in areas endemic to the helm. Eosinophilia is observed in both asthmatic patients (Price, Rigazio, Campbell, Bleecker, Corrigan, Thomas, 2015: 849-858) and those infected with helminthosis.

In tropical climatic endemic areas, the rise of eosinophils is more dependent on ascaridosis. Therefore, studies of helminth invasion by examination of feces can help determine the cause of eosinophilia in the blood in asthmatic patients living in endemic zones with tropical climates.

The similarity of inflammatory mechanisms in allergies and parasitoses necessitates a revision of existing diagnostic methods and standards. At the onset of the disease, a specific absence of clinical signs and overlapping symptoms can lead to a misdiagnosis. For this reason, comparative analysis of similar and different symptoms of these diseases and metabolic pathways of molecular mechanisms of allergy should be studied. Research methods for differential diagnostics have been presented in this direction.

Scientific background work in allergy and parasitology indicates that it is advisable to perform a parallel allergy and parasitological examination in patients with non-specific symptoms. This approach helps to diagnose accurately and early and perform effective therapy.

Immune processes and reactions that occur during helminth invasions and allergic diseases may be similar (Cooper, Figueiredo, Rodriguez, 2023: e12232).

An infected organism is usually more likely to react to this invasion if the invasion occurs accidentally in an area that is not endemic to it. At this time, hyperallergic reactions such as Löffler syndrome or eosinophilic pneumonia may occur, which require treatment with corticosteroids (Araujo, de Jesus Pereira, de Moura Pereira, Moreira, de Rezende, Rodrigues, 2016: 3107–3117).

Occasionally, infection with parasites causes a similar severe allergic response to food allergens in the body.

Intestinal nematodes cause symptoms of impaired gastrointestinal functions, such as general weakness of the body, diarrhea, and abdominal pain (Ravi, Ramachandran, Thompson, 2002: 73–81).

After infection with helminths, the immune system is activated. This process includes T and B lymphocytes, regulatory T cells, eosinophils, neutrophils, basophils, etc. (Dunne, Webster, Smith, 1997: 79–89). T cells are important in regulating the immune response. T-cell cells (Th) stimulate humoral and cellular activity, depending on the activation of a given subpopulation. Th1 is involved in the induction of a cell-type immune reaction, while Th2 mediates a humoral immune reaction. At this time, the blood is characterized by increased amounts of IL-4, IL-5, and IL-13, as well as high titration of eosinophilia and IgE (van den Biggelaar, van Ree, Rodrigues, 2000: 1723-1727). It persists through the action of IL-4, which is described as a key cytokine in the pathogenesis of allergic diseases. Parasites are the most powerful inductors of the Th2-type immune response (Santiago, Hafalla, Kurtis, Aligui, Wiest, Olveda, 1998: 94-104), but are involved in this process in adult dendric cells. Stimulation of Th2 cells leads to secretion of IgE and IgG antitopes by plasma cells and causes eosinophilia (Fitzsimmons, Stewart, Hoffmann, 2004: 371–6).

Both acute and delayed allergic reactions can occur without Ig involvement and with involvement (Schramm, Hamilton, Balog, Wuhrer, Gronow, Beckmann, 2009: 4–14). Proteins with cytotoxic properties include protein (MBP accounts for more than 50% of them), eosinophilic peroxidase (EPX), eosinophilic cationic protein (ECP), and eosinophilic derivative, neuro-toxin (EDN). These proteins play an important role in eliminating helminths. Laboratory tests indicate significant eosinophilia in both allergic diseases and helminth invasions (IL-1β, IL-2, IL-12, and tumor necrosis factor-alpha (TNF-α)). Cytokines that develop inflammation are involved in the regulation of inflammation (Medeiros, Figueiredo, Almeida, Matos, Araujo, Cruz, 2003: 947–951).

Natural regulatory mechanisms that protect the host organism from inflammatory or autoimmune reactions during parasitic diseases, such as T cells (Trig), play a role in tolerance to autoantigens and reducing reactions to alien particles (Wordemann, Diaz, Heredia, Collado Madurga, Ruiz Espinosa, Prado, 2008: 180-186). Parasites secrete a number of specific metabolites that directly affect the host organism. They affect T cells and can alter the function of proliferation or apoptosis (Sangsupawanich, Mahakittikun, Chongsuvivatwong, Mo-suwan, Choprapawon, 2010: 29-34), which affects the balance of their Th1/Th2/Treg response. In addition, some helminths induce apoptosis of different immune cell populations (i.e. programmed death) (Falcone, Telford, Hooi, 2009: 1343–50).

Some helminths affect antithelial levels by converting IgG4, an expression of genes that encode IgE antitheses. Unlike IgG4 IgE, they are not involved in the elimination of parasites, the presence of which indicates the development of allergen tolerance (Phillips, Coward, Pritchard, Hewitt, 2003: 165-171). The parasite disrupts the homeostasis of the infected human body. However, studies have shown that the antagonism between the parasite and the possessor does not always harm the possessor organism. In addition to the pathological effects of invasion due to the evolutionary long-term link between the parasite and the host organism, helminths affecting the maintenance of immune homeostasis may be observed (Medeiros, Figueiredo, Almeida, Matos, Araujo, Cruz, 2003: 947-951).

**Conclusion.** In recent years, studies on the inhibition of an inflammatory reaction by some intestinal nematodes have been able to prove that some types of parasitic invasion are alternatives to the treatment of autoimmune diseases and allergies (Balfour, Zalka, Lazova, 2002: 368-370). Research into the molecular mechanisms of metabolism of allergens associated with helminth invasions should be continued.

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