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Effect of Bisphenol A on Formation and Process of Allergic Reaction - Review

Denis Bažány*, Hana Greifová, Nikola Štefunková, Tomáš Jambor, Katarína Tokárová, Norbert Lukáč

Institute of Applied Biology, Faculty of Biotechnology and Food Sciences, Slovak University of Agriculture in Nitra, Tr. A. Hlinku 2, 949 76 Nitra, Slovak Republic

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Abstract

One of the possible immunomodulatory effects of BPA is the alteration the allergy process and asthma. The growth in the prevalence of asthma around the world roughly corresponds with the rise in the widespread usage of certain chemicals. Despite the fact that asthma is a complicated and varied condition brought on by exposure to a variety of environmental factors and genetic predispositions, many classes of chemicals that are frequently present in the surrounding environment and are linked to endocrine disruption have recently been linked to the disease's pathogenesis. BPA is endocrine disrupting chemical compound made up of two phenol rings joined by a methyl bridge and two methyl functional groups adhered to the bridge. BPA is ingested by humans, inhaled via home dust, and exposed through the skin. An allergy is an aberrant immunological reaction to an antigen, such as a protein or allergen. An ingested or breathed allergen encounters the epithelium as its initial barrier. The inflammatory condition and increased permeability of the epithelial barrier are associated with allergic inflammatory disorders, and this suggests that the epithelium barrier is more sensitive to allergen sensitization. The existing literature and scientific publications do not adequately address the direct influence of bisphenols on the development and influence of the allergic process. Multiple authors discuss how bisphenol affects specific allergic response components. We may conclude that exposure to bisphenol A alters the allergic response based on the findings of the studies and the analysis of the literature.

1. Introduction

The consequences of ambient chemical exposure on the immune system, particularly the emergence of allergies, have attracted a lot of attention in recent years. Epidemiologic research suggests that there is widespread exposure to endocrine disrupting substances that are generated in large quantities, such as phthalates and bisphenol A (BPA) **(Robinson a Miller 2015)**. For almost 50 years, BPA has been a commonly used synthetic chemical in the production of polycarbonate plastics, epoxy resin, and other polymers. BPA is also present in non-food items such toys, thermal paper, and medical devices **(Mourot-Bousquenaud et al. no date)**. Concerns over the possible impact of environmental contaminants have been raised as a result of the relatively short timeframe in which the frequency of asthma and allergy illnesses has increased **(Bousquet et al. 2011)**. Certain pollutants, such as those frequently used in the production of plastic, have been linked to an increased risk of infection as well as the onset of allergies and asthma in the early years of life **(Winans et al. 2011)**. Increased permeability and an inflammatory condition of epithelial barriers, which are believed to be sensitive to allergen sensitization, are associated with allergic airway disorders **(Loffredo et al. 2020)**. The question of whether Bisphenol A can interact with components of the immune system to have negative health effects is still of attention **(Kimber et al. 2022)**. The European Food Safety Authority (EFSA) has conducted a comprehensive analysis of the potential of adverse effects of BPA exposure on humans, leading to a reduction of the recommended tolerated daily intake level from 50 µg/kg body weight per day to 5 µg/kg body weight per day **(EFSA. 2015)**. Because of its widespread use over time, bisphenol A is still present in large quantities in the human environment, even with the restrictions. From the perspective that these chemicals are imposed upon us early in childhood, a precise knowledge of these compounds' immunomodulatory effects is essential. One of the possible immunomodulatory effects of BPA is the alteration the allergy process and asthma. The growth in the prevalence of asthma around the world roughly corresponds with the rise in the widespread usage of certain chemicals. Despite the fact that asthma is a complicated and varied condition brought on by exposure to a variety of environmental factors and genetic predispositions, many classes of chemicals that are frequently present in the surrounding environment and are linked to endocrine disruption have recently been linked to the disease's pathogenesis **(Kwak et al. 2009)**.

2. Bisphenol A

BPA is endocrine disrupting chemical compound made up of two phenol rings joined by a methyl bridge and two methyl functional groups adhered to the bridge **(Kang et al. 2006)**. It is

*Corresponding author: xbazany@uniag.sk
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a white, crystalline substance with a melting point of 156 °C and a molecular weight of 228.29 g/mol **(Legeay a Faure 2017)**. In the 1930s, it was discovered that the monomer bisphenol A (BPA) could stimulate the female reproductive system in rats just like estrone. BPA was initially created as a synthetic estrogen in the 1890s **(Rochester 2013)**. Consequently, BPA has found its way into a wide range of consumer goods, such as PVC, food packaging, dental sealants, thermal receipts, plastics (in the form of a polymer, such as polycarbonate [#7] plastic), and plastics. Because polycarbonate plastics have high impact strength, hardness, toughness, transparency, resistance to temperatures between approximately -40 °C and 145 °C, and resistance to many acids and oils, they are used in the production of compact disks, automotive lenses, household appliances, food packaging, and plastic bottles **(Staples et al. 1998)**. BPA is ingested by humans, inhaled via home dust, and exposed through the skin **(Vandenberg et al. 2012)**. According to the research, oral intake is the most common way that BPA is exposed to people, especially when food is contaminated by hazardous containers. For instance, following the pasteurization process, food may contain BPA released from aluminum cans. Furthermore, it has been shown that using plastic baby bottles for longer periods of time and at higher temperatures can accelerate polycarbonate hydrolysis and cause BPA to leak out of the bottle **(Nam et al. 2010)**. Recent research has linked high BPA levels to reduced sperm count, diabetes, obesity, cardiovascular illness, and polycystic ovarian disease **(Fenichel et al. 2013)**. Following absorption, BPA undergoes glucuronidation in the liver, where it is primarily eliminated through bile but is also eliminated through urine. This chemical molecule is found in blood in a nonconjugated state, which suggests internal exposure. If it is detected in the urine, it means that the chemical was exposed internally, that the first passage's conjugation was unsuccessful, or that the compound was not removed or deconjugated properly. It can accumulate in adipose tissue since it is lipophilic. Aside from age and gender, other factors influencing BPA metabolism include physiological state and liver function **(Almeida et al. 2018)**. Furthermore, by competing with endogenous E2, BPA can function as an antiestrogen and prevent the estrogenic response **(Richter et al. 2007)**. BPA may also be antiandrogenic, inhibiting the effects of natural androgens, and it can bind to androgen receptors directly **(Sohoni a Sumpter 1998)**. It has been demonstrated that BPA binds to thyroid receptors and influences thyroid function in both agonistic and antagonistic ways **(Moriyama et al. 2002)**. Additionally, BPA interacts with various organs and physiological systems, such as the immunological system, the developing central nervous system, and the endocrine pancreas. The scientific community, government agencies, and the general public have shown a continuing interest in evaluating the possible health hazards linked to BPA exposure as a result of recent findings about the environmental spread of BPA and its prevalence in humans and wildlife **(Wetherill et al. 2007)**.

3. Allergy in general

An allergy is an aberrant immunological reaction to an antigen, such as a protein or allergen. Allergies to certain substances are more likely to cause allergies to other substances, and while many allergies have a genetic basis, their prevalence seems to be rising. Frequently encountered allergens include pollen, dust mites, mold, pet dander, nuts, shellfish, proteins from milk and eggs, and latex; however, in numerous instances, the allergen identity is uncertain **(Scully 2013)**. The prevalence of allergic diseases, such as rhinitis, asthma, and food allergies, is rising, especially among industrialized countries **(Bieren a Harris 2016)**. The process of allergy formation involves two steps. Sensitization is the initial phase. When a foreign protein enters the body, the immune system detects it as an antigen, such as one found in food. It produces an immunological response that includes T cells that have been sensitized to a particular antigen or specific antibodies. Because the antibodies or lymphocytes carry the information required to recognize the relevant antigen, they are referred to as "specific." If the antibody is an IgE antibody, it will react to the allergen by causing an allergic reaction, which is an inflammatory response. Therefore, allergy is more than just the presence of antibodies; it also refers to disease **(Terr 2001)**. It can be challenging to consider mast cells and immunoglobulin E (IgE) antibodies in other contexts due to their strong and convincing associations with the pathophysiology of anaphylaxis and other acute allergic reactions **(Galli a Tsai 2012)**. It is widely accepted that the development of the acute symptoms of various allergic conditions can be significantly influenced by antigen specific IgE antibodies as well as the mast cells, one of the main effector cells of allergy. The primary mechanism in acute allergy reactions is the antigen-dependent activation of tissue mast cells with specific IgE attached to their surface **(Galli a Tsai 2012)**. The immunoglobulin isotype that has the lowest concentration in the bloodstream, IgE, cannot fix complement and has a poor placental transit rate. Some people with allergic illnesses or parasite infections may have noticeably higher plasma concentrations of it **(Gould a Sutton 2008)**. The prevalence of food and allergy-related conditions ranges from 5–10% and 5–25%, respectively, and over the past century, allergies have become more prevalent globally. Increased exposure to endocrine disruptors (ED) and alterations in the environment, including different food components and indoor and outdoor air quality, have been associated with a rise in the incidence of allergy diseases **(Sicherer a Sampson 2014)**. The most important factor in the formation of an allergy is the exposure to substances that can induce or alter it during prenatal development. As adjuvants, compounds that cause irritation, inflammation, change microflora, alter how allergens are processed and presented, or directly affect immune cell function or differentiation may cause tolerance to break down. This can lead to the development of allergic reactions to specific proteins. Since the immune system is still developing in the early stages of life, exposure to substances that impact it while a woman is pregnant or during the early stages of life might have long-lasting negative effects **(Dietert a Zelikoff 2008)**.

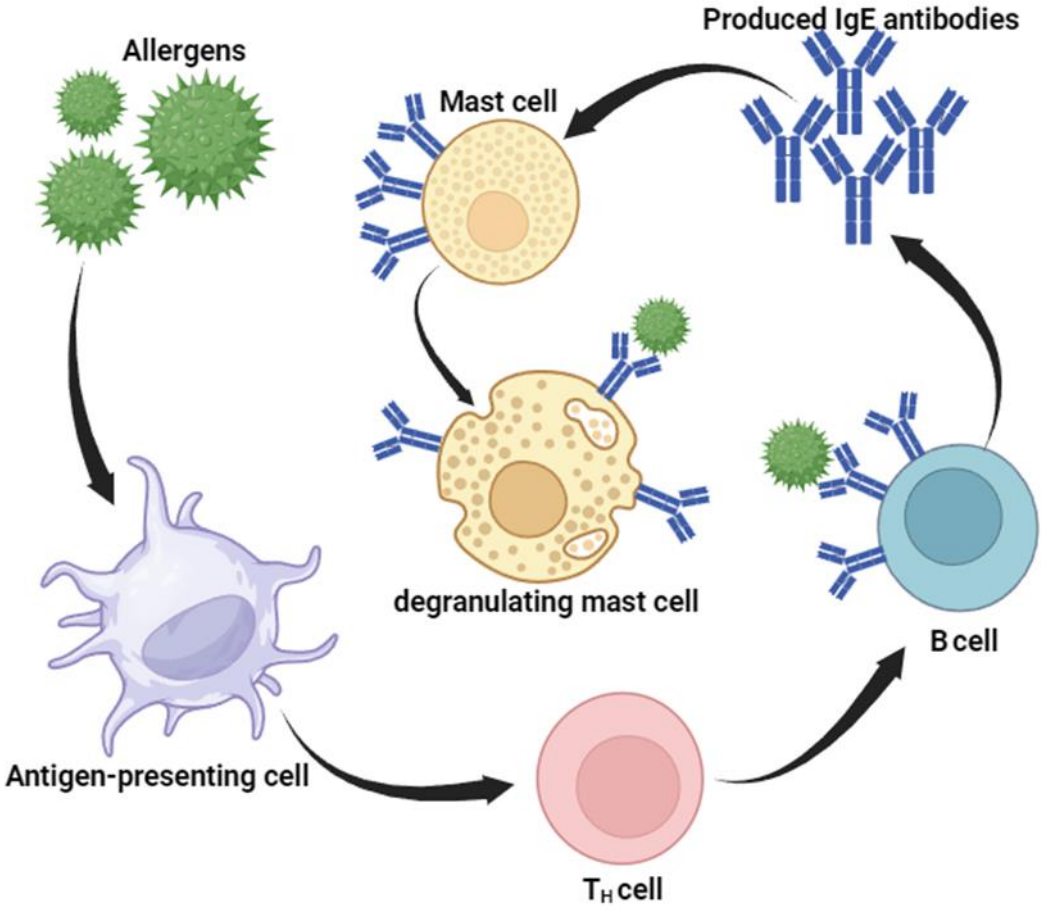

Figure 1 (González de Olano a Alvarez-Twose 2018) The mechanism of type I hypersensitivity reactions in allergic inflammation. Following the first exposure, an allergen is delivered to TH cells by antigen-presenting cells; this aids in the control of cellular immunity and promotes B cells to produce particular IgE antibodies and switch isotypes. When antigens are exposed again, they cross-link FcεRI and antigen-IgE complexes on the mast cells´ surface, activating and degranulating the mast cells.

4. Links between bisphenols and allergy

An ingested or breathed allergen encounters the epithelium as its initial barrier. The inflammatory condition and increased permeability of the epithelial barrier are associated with allergic inflammatory disorders, and this suggests that the epithelium barrier is more sensitive to allergen sensitization **(Loffredo et al. 2020)**. This initial barrier can be triggered by various endocrine disrupting chemicals. Synthetic or naturally occurring chemical substances known as "xenoestrogens" can imitate the properties of estrogen and have an estrogenic impact on organisms, interfering with the endocrine system's production of estrogen **(Donohue et al. 2013)**. Because of this, they are sometimes referred to as "environmental hormones" at times. Recent research has demonstrated that low-level, continuous, non-toxic exposure to bisphenols poses a major environmental risk associated with a wide range of human ailments, including allergy illnesses **(Houston a Ghosh 2020)**. Additionally, many studies have indicated that BPA may make allergy conditions more severe, including rhinitis, allergic asthma, and allergic dermatitis. Studies where mice were used as laboratory models have shown increased lung inflammation and airway lymphocytic responses after bisphenol exposition **(Bauer et al. 2012)**. According to research conducted on humans, scientists found a correlation between rising maternal urine BPA concentrations and a higher risk of respiratory tract infections and asthma symptoms in offspring. Additionally, concentrating on human data, it was discovered that mothers of infants suffering from allergy diseases had considerably higher urinary BPA levels than those of newborns not suffering from allergic diseases. Prenatal exposure to toxic pollutants may have detrimental effects on the developing immune and respiratory systems, damage the ability to fight infections for a long time, and raise the likelihood of allergic reactions in later life **(Donohue et al. 2013)**. According to research on animals and *in vitro*, BPA may play a part in the etiology of most allergic diseases. Urinary BPA is strongly linked to allergic asthma because it may function as a TH2 or allergy sensitizer and trigger particular IgE responses **(Kim et al. 2017)**. Increased BPA exposure has been linked in several studies to the onset of atopy or wheezing. Additionally, they indicate that the clinical phenotype is altered by the timing and length of BPA exposure. Epidemiological research has not conclusively demonstrated that BPA raises the incidence of allergy and asthma; nonetheless, by modifying immune cell activity and cytokine release, it may raise the likelihood of a Th2 response **(Robinson a Miller 2015)**. T helper cell type 2 mechanisms can also be directly altered by the presence of endocrine-disrupting chemicals. The synthesis of interleukin-4 (IL-4), IL-5, and IL-13 is a hallmark of the T helper type 2 (Th2) immune response, which is an essential defense against helminths that invade cutaneous or mucosal areas. Furthermore, it is essential to the pathophysiology of allergic disorders such allergic diarrhea and asthma **(Koyasu a Moro 2011)**. Numerous research has also been conducted about the impact of bisphenol A on allergic reactions. Some of them are summarized in Table 1.

Table 1 Studied impact of bisphenol A on allergic and/or immune reactions.

Authors	Chemical compound used	Laboratory model	Method of application	Results
(Nygaard et al. 2015)	Bisphenol A	Mice	Intragastric gavage	BPA (100 μg/ml) led to elevated eosinophil counts in bronchoalveolar lavage fluid (BALF) and a rise of IgE levels in the airway allergy model. BPA altered splenocyte cytokines and decreased mouse mast cell protease (MMCP)-1 blood levels but did not affect clinical anaphylaxis or antibody responses in the food allergy and tolerance studies. Finally, BPA exposure throughout the early stages of life via drinking water only slightly increased allergic reactions in a mouse model of airway allergy at high doses.
(Wang et al. 2020)	Bisphenol A	Allergy rhinitis mice	Subcutaneous injection	Both the amount of Th2 cells and the mRNA expression of the Th2- and GATA-3-related cytokines, IL-4 and IL-13, were increased by BPA. BPA inhibited Foxp3, Helios, and Treg cells, as well as the Treg-related cytokine IL-10 at the mRNA levels. Therefore, IgE-mediated inflammation of the nasal mucosa is responsible for AR symptoms. Authors discovered that exposure to BPA greatly raised OVA-specific serum IgE levels and allergy symptoms; hence, BPA had an immediate impact on experimental AR. Authors assessed BPA's direct impact on inflammation caused by allergies.
(Yanagisawa et al. 2022)	Bisphenol S	Mice	Oral administration	Moderate-dose BPS (BPS-M) combined with OVA significantly increased OVA-specific IgE and IgG1, pulmonary inflammation, and airway hyperresponsiveness in comparison to OVA alone. Moreover, the lungs' levels of the proteins CCL11/Eotaxin, IL-13, IL-33, and interleukin (IL)-5 rose. Conversely, these allergic reactions were diminished in the high-dose BPS+OVA group. BPS-M with OVA stimulated antigen-presenting cells, including the typical dendritic cell subset (cDC2), and increased the total number of cells in mesenteric lymph nodes cells (MLN). Following OVA restimulation, the culture supernatant exhibited an increase in both cell proliferation and Th2 cytokine production (IL-4, IL-5, and IL-13). Therefore, by boosting Th2-polarized responses and activating the MLN cells, oral exposure to low-dose BPS can exacerbate allergic asthmatic reactions.
(Misme-Aucouturier et al. 2022)	Bisphenol A	BALB/cJRj mice	Oral administration	Authors assessed the impact of direct oral exposure to BPA at 4 μg/kg bw/d, which corresponds to a tolerated daily intake (TDI), in a mouse model of allergy. They looked at the humoral and cellular immune responses, intestinal physiology, and symptoms associated with food allergies and investigated the connection between alterations in the gut microbiota and oral BPA exposure. After being exposed to BPA, markers of intestinal permeability and food allergies rose. The inflammation associated with food allergies was also found to be aggravated by a modulated humoral and T-cell response. Furthermore, food allergies-induced microbial diversity was reduced and gut dysbiosis was brought on by BPA exposure.
(Tajiki-Nishino et al. 2018)	Bisphenol A	BALB/c mice, human epidermal keratinocytes (HEKs) and bronchial epithelial (BEAS-2B) cells	Oral administration	High dosages of BPA significantly downregulated the ear-swelling response in the allergic dermatitis model. The allergic airway inflammation model showed the opposite response to BPA administration, with notable increases in local cytokine levels, total IgE levels in serum, and red coloration in the lung. Human epidermal keratinocytes (HEKs) and bronchial epithelial (BEAS-2B) cells were used in in *vitro* tests to validate the *in vivo* findings. The *in vivo* findings were corroborated by a notable increase in cytokine release from BEAS-2B cells in the BPA-treated group, but not from HEKs. Findings suggest that allergic airway inflammation is directly

				aggravated by BPA exposure, whereas allergic dermatitis is not affected.
(Loffredo et al. 2020)	Bisphenol A	Mice	Oral administration	The skin, gut, and airways expressed more innate inflammatory mediators when exposed to BPA through the water supply or inhalation, which created a systemic para-inflammatory response. Chronic systemic exposure to BPA was found to be sufficient in a murine tolerogenic antigen challenge model to cause airway sensitization to harmless chicken egg ovalbumin, even in the absence of any adjuvants. The impact of oral BPA exposure on allergic reactions in adult and juvenile mice has been examined by the authors; BPA was only found to be an aggravating or exacerbating factor in the development of allergic airway inflammation.
(Alizadeh et al. 2006)	Bisphenol A	Mice	Oral administration	Treatment with BPA led to decreased titers of total IgE ($P<0.01$) and greater levels of IgG2a ($P<0.05$) in the water-fed groups. This was followed by higher levels of IFN-γ ($P<0.05$) and IL-12 ($P<0.05$) with intact IL-4. Examined in OVA-fed groups, the chemical produced less IFN-γ ($P<0.05$) but no change in overall or OVA-specific IgE or -IgG2a production. Additionally, BPA decreased lymphocyte proliferation to Con A in groups fed water ($P<0.05$), but not in animals that were tolerated. The data show that BPA increases Th1 immune responses but has no discernible impact on developed OVA tolerance.
(Koike et al. 2018)	Bisphenol A	C3H/HeJJcl mice	Intratracheal administration	Exposure to OVA + BPA increased the number of total cells and activated antigen-presenting cells (MHC class II+ CD86+, CD11c+), as well as the production of Th2 cytokines (i.e. IL-4 and IL-5). It also increased the infiltration of inflammatory cells and the protein expression of Th2 cytokines/chemokines (e.g., interleukin (IL)-13 and IL-33) in the lungs. Additionally, anti-inflammatory corticosterone serum levels, spleen function, and estrogen receptor 2 messenger RNA (mRNA) expression in the lungs were all affected by exposure to OVA + BPA. These results imply that BPA exposure at low doses may exacerbate allergic airway inflammation by stimulating Th2 responses through immune system disturbance.

5. Conclusion

The existing literature and scientific publications do not adequately address the direct influence of bisphenols on the development and influence of the allergic process. Multiple authors discuss how bisphenol affects specific allergic response components. The primary focus is on modulating T-lymphocyte and mast cell activity. The majority of the cellular response that contributes to the development of an allergic reaction is represented by these cells. The vast majority of authors examine allergic reactions using mice as their laboratory model, since they are the most suitable animal. Human studies have shown that the content of bisphenol A in the mother's urine during pregnancy plays a crucial role in the fetus's exposure to the chemical. It is also crucial to possess knowledge that suggests modifying the synthesis of IgE, the primary antibody responsible for an allergic reaction. We may conclude that exposure to bisphenol A alters the allergic response based on the findings of the studies and the analysis of the literature. We believe it is crucial to add to the understanding of the immunomodulatory effects of common endocrine disruptors like bisphenol A in the human environment.

Declaration of interest

The authors declare no conflicts of interest.

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References

1. Alizadeh, M., Ota, F., Hosoi, K., Kato, M., Sakai, T., & Satter, M. A. (2006). Altered allergic cytokine and antibody response in mice treated with Bisphenol A. *The Journal of Medical Investigation*, 53(1,2), 70–80. https://doi.org/10.2152/jmi.53.70
2. Almeida, S., Raposo, A., Almeida-González, M., & Carrascosa, C. (2018). Bisphenol A: Food Exposure and Impact on Human Health. *Comprehensive Reviews in Food Science and Food Safety*, 17(6), 1503–1517. https://doi.org/10.1111/1541-4337.12388
3. Bauer, S. M., Roy, A., Emo, J., Chapman, T. J., Georas, S. N., & Lawrence, B. P. (2012). The Effects of Maternal Exposure to Bisphenol A on Allergic Lung Inflammation into Adulthood. *Toxicological Sciences*, 130(1), 82–93. https://doi.org/10.1093/toxsci/kfs227
4. Bieren, J. E., & Harris, N. L. (2016). Microbiome and Allergy. In M. J. H. Ratcliffe (Ed.), Encyclopedia of Immunobiology (pp. 336–345). Academic Press. https://doi.org/10.1016/B978-0-12-374279-7.16005-9
5. Bousquet, J., Anto, J., Auffray, C., Akdis, M., Cambon-Thomsen, A., Keil, T., Haahtela, T., Lambrecht, B. N., Postma, D. S., Sunyer, J., Valenta, R., Akdis, C. A., Annesi-Maesano, I., Arno, A., Bachert, C., Ballester, F., Basagana, X., Baumgartner, U., Bindslev-Jensen, C., …

Zuberbier, T. (2011). MeDALL (Mechanisms of the Development of ALLergy): An integrated approach from phenotypes to systems medicine. *Allergy*, 66(5), 596–604. https://doi.org/10.1111/j.1398-9995.2010.02534.x
6. Dietert, R. R., & Zelikoff, J. T. (2008). Early-life environment, developmental immunotoxicology, and the risk of pediatric allergic disease including asthma. *Birth Defects Research Part B: Developmental and Reproductive Toxicology*, 83(6), 547–560. https://doi.org/10.1002/bdrb.20170
7. Donohue, K. M., Miller, R. L., Perzanowski, M. S., Just, A. C., Hoepner, L. A., Arunajadai, S., Canfield, S., Resnick, D., Calafat, A. M., Perera, F. P., & Whyatt, R. M. (2013). Prenatal and postnatal bisphenol A exposure and asthma development among inner-city children. *Journal of Allergy and Clinical Immunology*, 131(3), 736-742.e6. https://doi.org/10.1016/j.jaci.2012.12.1573
8. Fenichel, P., Chevalier, N., & Brucker-Davis, F. (2013). Bisphenol A: An endocrine and metabolic disruptor. *Annales d'Endocrinologie*, 74(3), 211–220. https://doi.org/10.1016/j.ando.2013.04.002
9. Galli, S. J., & Tsai, M. (2012). IgE and mast cells in allergic disease. *Nature Medicine*, 18(5), 693–704. https://doi.org/10.1038/nm.2755
10. González de Olano, D., & Alvarez-Twose, I. (2018). Mast Cells as Key Players in Allergy and Inflammation. *Journal of Investigational Allergology and Clinical Immunology*, 28, 365–378. https://doi.org/10.18176/jiaci.0327
11. Gould, H. J., & Sutton, B. J. (2008). IgE in allergy and asthma today. *Nature Reviews Immunology*, 8(3), Article 3. https://doi.org/10.1038/nri2273
12. Houston, T. J., & Ghosh, R. (2020). Untangling the association between environmental endocrine disruptive chemicals and the etiology of male genitourinary cancers. *Biochemical Pharmacology*, 172, 113743. https://doi.org/10.1016/j.bcp.2019.113743
13. Kang, J.-H., Kondo, F., & Katayama, Y. (2006). Human exposure to bisphenol A. *Toxicology*, 226(2), 79–89. https://doi.org/10.1016/j.tox.2006.06.009
14. Kim, E.-H., Jeon, B.-H., Kim, J., Kim, Y.-M., Han, Y., Ahn, K., & Cheong, H.-K. (2017). Exposure to phthalates and bisphenol A are associated with atopic dermatitis symptoms in children: A time-series analysis. *Environmental Health*, 16(1), 24. https://doi.org/10.1186/s12940-017-0225-5
15. Kimber, I., Woeffen, N., & Sondenheimer, K. (2022). Bisphenol A, TH17 cells, and allergy: A commentary. *Journal of Immunotoxicology*, 19(1), 93–99. https://doi.org/10.1080/1547691X.2022.2113842
16. Koike, E., Yanagisawa, R., Win-Shwe, T.-T., & Takano, H. (2018). Exposure to low-dose bisphenol A during the juvenile period of development disrupts the immune system and aggravates allergic airway inflammation in mice. *International Journal of Immunopathology and Pharmacology*, 32, 2058738418774897. https://doi.org/10.1177/2058738418774897
17. Koyasu, S., & Moro, K. (2011). Type 2 innate immune responses and the natural helper cell. *Immunology*, 132(4), 475–481. https://doi.org/10.1111/j.1365-2567.2011.03413.x
18. Kwak, E. S., Just, A., Whyatt, R., & Miller, R. L. (2009). Phthalates, Pesticides, and Bisphenol-A Exposure and the Development of Nonoccupational Asthma and Allergies: How Valid Are the Links? *The Open Allergy Journal*, 2, 45–50. https://doi.org/10.2174/1874838400902010045
19. Legeay, S., & Faure, S. (2017). Is bisphenol A an environmental obesogen? Fundamental & Clinical Pharmacology, 31(6), 594–609. https://doi.org/10.1111/fcp.12300
20. Loffredo, L. F., Coden, M. E., & Berdnikovs, S. (2020). Endocrine Disruptor Bisphenol A (BPA) Triggers Systemic Para-Inflammation and is Sufficient to Induce Airway Allergic Sensitization in Mice. *Nutrients*, 12(2), Article 2. https://doi.org/10.3390/nu12020343
21. Misme-Aucouturier, B., De Carvalho, M., Delage, E., Dijoux, E., Klein, M., Brosseau, C., Bodinier, M., Guzylack-Piriou, L., & Bouchaud, G. (2022). Oral exposure to bisphenol A exacerbates allergic inflammation in a mouse model of food allergy. *Toxicology*, 472, 153188. https://doi.org/10.1016/j.tox.2022.153188
22. Moriyama, K., Tagami, T., Akamizu, T., Usui, T., Saijo, M., Kanamoto, N., Hataya, Y., Shimatsu, A., Kuzuya, H., & Nakao, K. (2002). Thyroid Hormone Action Is Disrupted by Bisphenol A as an Antagonist. The *Journal of Clinical Endocrinology & Metabolism*, 87(11), 5185–5190. https://doi.org/10.1210/jc.2002-020209
23. Mourot-Bousquenaud, M., Langonné, I., Buchheit, M., Muller, S., Coiscaud, A., Mathiot, J., Jacquenet, S., & Battais, F. (2023). Identification of the allergenic sensitizing potential of bisphenol A substitutes used in the industry. *Contact Dermatitis*, 1-13. https://doi.org/10.1111/cod.14452
24. Nam, S.-H., Seo, Y.-M., & Kim, M.-G. (2010). Bisphenol A migration from polycarbonate baby bottle with repeated use. *Chemosphere*, 79(9), 949–952. https://doi.org/10.1016/j.chemosphere.2010.02.049
25. Nygaard, U. C., Vinje, N. E., Samuelsen, M., Andreassen, M., Groeng, E.-C., Bølling, A. K., Becher, R., Lovik, M., & Bodin, J. (2015). Early life exposure to bisphenol A investigated in mouse models of airway allergy, food allergy and oral tolerance. *Food and Chemical Toxicology*, 83, 17–25. https://doi.org/10.1016/j.fct.2015.05.009
26. Richter, C. A., Birnbaum, L. S., Farabollini, F., Newbold, R. R., Rubin, B. S., Talsness, C. E., Vandenbergh, J. G., Walser-Kuntz, D. R., & vom Saal, F. S. (2007). In vivo effects of bisphenol A in laboratory rodent studies. *Reproductive Toxicology*, 24(2), 199–224. https://doi.org/10.1016/j.reprotox.2007.06.004
27. Robinson, L., & Miller, R. (2015). The Impact of Bisphenol A and Phthalates on Allergy, Asthma, and Immune Function: A Review of Latest Findings. *Current Environmental Health Reports*, 2(4), 379–387. https://doi.org/10.1007/s40572-015-0066-8
28. Rochester, J. R. (2013). Bisphenol A and human health: A review of the literature. *Reproductive Toxicology*, 42, 132–155. https://doi.org/10.1016/j.reprotox.2013.08.008
29. Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs | EFSA. (2015, January 21). https://www.efsa.europa.eu/en/efsajournal/pub/3978
30. Scully, C. (2013). 3 - Diagnosis: Investigations. In C. Scully (Ed.), Oral and Maxillofacial Medicine (Third Edition) (pp. 21–37). Churchill Livingstone. https://doi.org/10.1016/B978-0-7020-4948-4.00003-9
31. Sicherer, S. H., & Sampson, H. A. (2014). Food allergy: Epidemiology, pathogenesis, diagnosis, and treatment. Journal of Allergy and Clinical *Immunology*, 133(2), 291-307.e5. https://doi.org/10.1016/j.jaci.2013.11.020
32. Sohoni, P., & Sumpter, J. (1998). Several environmental oestrogens are also anti-androgens. *Journal of Endocrinology*, 158(3), 327–339. https://doi.org/10.1677/joe.0.1580327
33. Staples, C. A., Dome, P. B., Klecka, G. M., Oblock, S. T., & Harris, L. R. (1998). A review of the environmental fate, effects, and exposures of bisphenol A. *Chemosphere*, 36(10), 2149–2173. https://doi.org/10.1016/S0045-6535(97)10133-3
34. Tajiki-Nishino, R., Makino, E., Watanabe, Y., Tajima, H., Ishimota, M., & Fukuyama, T. (2018). Oral Administration of Bisphenol A Directly Exacerbates Allergic Airway Inflammation but Not Allergic Skin Inflammation in Mice. *Toxicological Sciences*, 165(2), 314–321. https://doi.org/10.1093/toxsci/kfy132
35. Terr, A. I. (2001). CHAPTER 44—Nutrition and Food Allergy. In A. M. Coulston, C. L. Rock, & E. R. Monsen (Eds.), Nutrition in the Prevention and Treatment of Disease (pp. 701–714). Academic Press. https://doi.org/10.1016/B978-012193155-1/50046-5
36. Vandenberg, L. N., Colborn, T., Hayes, T. B., Heindel, J. J., Jacobs, D. R., Jr., Lee, D.-H., Shioda, T., Soto, A. M., vom Saal, F. S., Welshons, W. V., Zoeller, R. T., & Myers, J. P. (2012). Hormones and Endocrine-Disrupting Chemicals: Low-Dose Effects and Nonmonotonic Dose Responses. *Endocrine Reviews*, 33(3), 378–455. https://doi.org/10.1210/er.2011-1050
37. Wang, Y., Cao, Z., Zhao, H., Ren, Y., Hao, L., & Gu, Z. (2020). Bisphenol A Exacerbates Allergic Inflammation in an Ovalbumin-Induced Mouse Model of Allergic Rhinitis. *Journal of Immunology Research*, 2020, e7573103. https://doi.org/10.1155/2020/7573103
38. Wetherill, Y. B., Akingbemi, B. T., Kanno, J., McLachlan, J. A., Nadal, A., Sonnenschein, C., Watson, C. S., Zoeller, R. T., & Belcher, S. M. (2007). In vitro molecular mechanisms of bisphenol A action. Reproductive *Toxicology*, 24(2), 178–198. https://doi.org/10.1016/j.reprotox.2007.05.010
39. Winans, B., Humble, M. C., & Lawrence, B. P. (2011). Environmental toxicants and the developing immune system: A missing link in the global battle against infectious disease? *Reproductive Toxicology*, 31(3), 327–336. https://doi.org/10.1016/j.reprotox.2010.09.004
40. Yanagisawa, R., Koike, E., Win-Shwe, T.-T., & Takano, H. (2022). Effects of Oral Exposure to Low-Dose Bisphenol S on Allergic Asthma in Mice. *International Journal of Molecular Sciences*, 23(18), Article 18. https://doi.org/10.3390/ijms231810790