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ALLERGY AS A FORM OF PATHOLOGICAL RESPONSE: A COMPREHENSIVE REVIEW

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Allergies represent a maladaptive form of pathological reactivity in which the immune system responds inappropriately to typically harmless environmental antigens. This inappropriate response can lead to tissue damage and clinical disease.

The classical Gell and Coombs classification framework serves as a foundational model, delineating four types of hypersensitivity: Type I, which involves IgE-mediated immediate hypersensitivity; Type II, characterized by cytotoxic reactions mediated by IgG or IgM; Type III, which is immune complex-mediated; and Type IV, associated with delayed T-cell-mediated responses.

Furthermore, contemporary nomenclature has expanded to incorporate additional categories, such as tissue-driven and direct chemical responses, reflecting significant advances in immunology and precision medicine.

Mechanistically, Type I hypersensitivity reactions occur when allergens cross-link immunoglobulin E (IgE) on mast cells and basophils, which triggers the rapid release of histamine, leukotrienes, and prostaglandins. This initial response is followed by a late-phase reaction driven by T-helper 2 (Th2) cytokines, including interleukin-4 (IL-4), interleukin-5 (IL-5), and interleukin-13 (IL-13) (Nakamura, 2021).

In contrast, Type II hypersensitivity reactions involve antibody-dependent cellular cytotoxicity and complement activation targeting cell surface antigens. Type III hypersensitivity reactions arise from the deposition of antigen-antibody complexes within tissues, which activates the complement system and recruits neutrophils.

Type IV hypersensitivity reactions are mediated by memory T lymphocytes and macrophages, manifesting hours to days following exposure.

Genetic and environmental factors play a crucial role in the development of allergies. Recent research has identified epigenetic modifications, particularly DNA methylation of allergy-related genes, in children diagnosed with eczema, rhinitis, and asthma. This observation suggests a shared pathway that influences phenotypic expression.

Furthermore, environmental exposures, including allergen concentrations influenced by climatic conditions, as well as allergen characteristics such as hydrophilicity and airborne persistence, significantly contribute to the risk of developing these diseases.

The concept of altered reactivity is fundamental to the understanding of allergies, particularly illustrated by drug hypersensitivity reactions (DHRs). These reactions represent Type B adverse events that are characterized by their dose-independent nature, unpredictability, and immunological mediation.

Recent theoretical frameworks, such as the Protein-Homeostasis-System (PHS) hypothesis, suggest that allergic diseases originate from immune responses targeting small etiological substances. In this context, mast cells and eosinophils serve as critical regulators of these immune processes.

Overall, allergy exemplifies a model of pathological reactivity that integrates molecular immunology with clinical medicine, thereby carrying significant implications for diagnosis, therapy, and prevention.