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# Complement cascade and humoral-IgE skin cream

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## Abstract

During acute infection, antibodies establish the strength or weakness of the immune response. The body's immunoglobulin signature may affect the complement cascade (innate immunity) and pro-inflammatory response. The review discusses immunoglobulin E (IgE) and its effect on the complement cascade. Specifically, the expression of IgE may affect complement cascade immunopathology. More specifically, IgE expression may inhibit the degranulation of mast cells and basophils by anaphylatoxins. Research explores if humoral-IgE skin cream therapy can reduce morbidity and mortality during acute infection.

**Keywords:** Complement; Cytokine; IgE; Infection; Mast Cells; Skin Cream

## 1. Introduction

The complement cascade is part of innate immunity and a crucial defense mechanism against invading pathogens. The complement cascade affects opsonization, lysis, and inflammation and bridges the innate and adaptive immune system [1]. In addition, it enhances (i.e., complements) the ability of phagocytic cells and antibodies to remove pathogens from the body [2].

Inflammation increases when pathogen-bound IgG, IgM, and IgA antibodies activate the complement cascade to release glycoproteins called anaphylatoxins. Anaphylatoxins C3a and C5a bind to receptors on mast cells and basophil cells (i.e., C3aR and C5aR), triggering non-IgE-mediated degranulation [3, 4]. Degranulation is a rapid and excessive release of signaling molecules into the bloodstream leading to cytokine storms, endothelial lesions, thromboses, respiratory distress syndrome, and death [5, 6, 7]. IgE antibodies cannot activate complement through the classical pathway [8].

Allergies can engender a healthy immune response to harmful viruses [9, 10]. Researchers have concluded that the allergic phenotype has likely saved the lives of many more mammals than have ever died from allergy, justifying the positive role of IgE in our evolution [11].

Humoral-IgE skin cream therapy supports a healthy immune response to acute infection by balancing Th1 and Th2 responses. Th1 and Th2 cells play a vital role in immunity. Th1 and Th2 responses are required at different time points to eradicate an infectious agent. Th1 cells stimulate the cellular immune response, participate in the inhibition of macrophage activation and stimulate B cells to produce IgM and IgG1. Th2 stimulates the humoral-IgE immune response, promotes B cell proliferation, and induces antibody production through IL-4 expression [12].

Mast cells and basophil cells are potent effector cells of the innate immune system and play a critical role in immune regulation and host defense against infection [13]. Humoral-IgE skin cream therapy may inhibit effector cell

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degranulation during acute infection. Specifically, steric factors may hinder degranulation by anaphylatoxin when cytokinergic IgE binds to high-affinity receptors (FcεRI) on mast cells and basophil cells.

## 2. Mast Cells

Cytokinergic IgE, in the absence of antigen, induces cytokine secretion by mast cells. In addition, cytokinergic IgE generates a positive feedback loop for mast cell activation; the release of anti-inflammatory cytokines IL-4 and IL-13 stimulates mast cell survival and class switching to IgE in B cells [14].

Forced allergen-specific IgE production may dampen the complement cascade; IgE bound to mast cells increase steric hindrance and shielding of complement receptors on the mast cells, inhibiting anaphylatoxin-induced degranulation. Humoral-IgE skin creams preferably induce the production of cytokinergic IgE to allergens that are not prevalent in the host's natural environment. Hyper-IgE may have a long-term effect on the complement cascade, increasing the incidence and prevalence of recurrent infections. Job Syndrome (IgE > 1000 IU/mL) [15] is a rare, primarily immunodeficiency caused by a genetic mutation [16]. Hyper-IgE causes recurrent infections [17].

## 3. Basophil Cells

Research shows that basophil cells are reduced in severe COVID-19 [18]. Interleukin-4 (IL-4) is an anti-inflammatory, pleiotropic cytokine produced in response to receptor activation by basophil cells. In addition, IL-4 is essential for B cell secretion of IgE and augments the production of IgG1 in vivo, class switching of IgG1 to IgE High-affinity IgE [19, 20, 21].

Forced allergen-specific IgE development may dampen the complement cascade; IgE bound to basophil cells increases steric hindrance and shielding of complement receptors on the basophil cells, inhibiting anaphylatoxin-induced degranulation. Humoral-Ige skin creams preferably induce the production of cytokinergic IgE to antigens that are not prevalent in the host's natural environment.

## 4. Humoral- IgE Skin Cream

Viruses are constantly evolving; the innate and adaptive immune systems work together to fight off infection [22]. A low serum IgE profile can produce a harmful immune response to viral infection. The usually accepted upper limit of serum IgE is between 150 and 300 UI/ml [23]. In moderate and severe COVID-19 patients, almost no positive IgE was detected [24].

Humoral-IgE skin creams are taught in the United States patent application number 20210015912 A1 (2019) titled, "Topical hyper-allergenic composition and method of treating using the same" [25].

## 5. Conclusion

As viruses evolve, measures to support a robust and healthy immune response continue. Allergies may mediate the complement cascade to reduce inflammation during acute infection. Research explores if humoral-IgE skin cream therapy can effectively dampen the complement cascade to decrease morbidity and mortality during acute infection.

## Compliance with ethical standards

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*Disclosure of conflict of interest*

Michael John Dochniak is the co-founder of Alleam-it Corporation, Minnesota, USA.

## References

[1] Dunkelberger, J., Song, WC. Complement and its role in innate and adaptive immune responses. Cell Res 20, 34–50 (2010).

[2] Janeway CA Jr, Travers P, Walport M, et al. Immunobiology: The Immune System in Health and Disease. 5th edition. New York: Garland Science; 2001. The complement cascade and innate immunity.

[3] Merle NS, Church SE, Fremeaux-Bacchi V, Roumenina LT. Complement System Part I - Molecular Mechanisms of Activation and Regulation. Front Immunol. 2015 Jun 2; 6:262.

[4] Ng N, Powell CA. Targeting the Complement Cascade in the Pathophysiology of COVID-19 Disease. J Clin Med. 2021 May 19;10(10):2188.

[5] Schroeder HW Jr, Cavacini L. Structure and function of immunoglobulins. J Allergy Clin Immunol. 2010 Feb;125(2 Suppl 2): S41-52.

[6] Chouaki Benmansour, N., Carvelli, J., & Vivier, E. (2021). Complement cascade in severe forms of COVID-19: Recent advances in therapy. European journal of immunology, 51(7), 1652–1659.

[7] DE Yang. Handbook of biologically active peptides. Kastin A, editor. Academic press; 2013 Jan 26, Pages 625-630.

[8] Encyclopedia of Respiratory Medicine (Second Edition) 2006, Pages 409-415.

[9] Dochniak MJ. Cytokine Storm Interference. International Journal of Science and Research Archive, 2021, 04(01), 185–187.

[10] Dochniak MJ. Allergies, acute infections, and humoral skin creams. International Journal of Biology and Pharmacy Research Updates, 2022, 02(01), 014–016.

[11] Pritchard DI, Falcone FH, Mitchell PD. The evolution of IgE-mediated type I hypersensitivity and its immunological value. Allergy. 2021 Apr;76(4):1024-1040.

[12] Infante-Duarte C, Kamradt T. Th1/Th2 balance in infection. Springer Semin Immunopathol. 1999;21(3):317-38.

[13] Huang H, Li Y. Mechanisms controlling mast cell and basophil lineage decisions. Curr Allergy Asthma Rep. 2014 Sep;14(9):457.

[14] Bax HJ, Keeble AH, Gould HJ. Cytokinergic IgE Action in Mast Cell Activation. Front Immunol. 2012 Aug 6; 3:229.

[15] Ponsford MJ, Klocperk A, Pulvirenti F, Dalm VASH, Milota T, Cinetto F, Chovancova Z, Rial MJ, Sediva A, Litzman J, Agostini C, van Hagen M, Quinti I, Jolles S. Hyper-IgE in the allergy clinic--when is it primary immunodeficiency? Allergy. 2018 Nov;73(11):2122-2136.

[16] Freeman AF, Holland SM. The hyper-IgE syndromes. Immunol Allergy Clin North Am. 2008 May;28(2):277-91, viii.

[17] Hafsi W, Yarrarapu SNS. Job Syndrome. [Updated 2022 Aug 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK525947/

[18] Murdaca G, Di Gioacchino M, Greco M, Borro M, Paladin F, Petrarca C, Gangemi S. Basophils and Mast Cells in COVID-19 Pathogenesis. Cells. 2021 Oct 14;10(10):2754.

[19] Luzina IG, Keegan AD, Heller NM, Rook GA, Shea-Donohue T, Atamas SP. Regulation of inflammation by interleukin-4: a review of "alternatives". J Leukoc Biol. 2012 Oct;92(4):753-64.

[20] Smiley, S. T., Kaplan, M. H., and Grusby, M. J. (1997). Immunoglobulin E Production in the Absence of Interleukin-4-Secreting CD1-dependent Cells. Science 275, 977–979.

[21] He JS, Subramaniam S, Narang V, Srinivasan K, Saunders SP, Carbajo D, Wen-Shan T, Hidayah Hamadee N, Lum J, Lee A, Chen J, Poidinger M, Zolezzi F, Lafaille JJ, Curotto de Lafaille MA. IgG1 memory B cells keep the memory of IgE responses. Nat Commun. 2017 Sep 21;8(1):641.

[22] InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. The innate and adaptive immune systems. [Updated 2020 Jul 30]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279396/

[23] Laurent J, Noirot C, Ansquer JC, Laurent G, Kestenbaum S, Lagrue G. Comment définir le taux normal des IgE sériques chez l'adulte? (How to define the normal level of serum IgE in adults?). Ann Med Interne (Paris). 1985;136(5):419-22.

[24] Guo Y, Li T, Xia X, Su B, Li H, Feng Y, Han J, Wang X, Jia L, Bao Z, Li J, Liu Y, Li L. Different Profiles of Antibodies and Cytokines Were Found Between Severe and Moderate COVID-19 Patients. Front Immunol. 2021 Aug 19; 12:723585.

[25] Dochniak MJ, inventor; Alleam-it Corporation, assignee. Topical hyper-allergenic composition and method of treating using the same. United States Patent application number 20210015912 A1. 16 July 2019