Immunity: Allergy

Ann E Bancroft

Ferris State University

Abstract

The immune system is a highly complex arrangement of biochemical factors and cell mediated responses. In a certain genetically specific group, sensitivity to certain antigens creates a maladaptive immune response which causes individuals to respond via the IgE mediated pathway rather than the more adaptive IgG/IgM mediated pathway. In this paper, the pathophysiology, assessment, and pharmacological interventions involved in allergic responses will be discussed, including why certain individuals develop allergies.

Immunity: Allergy

Health in the human body relies in large part upon the immune system. When the immune system works in a homeopathic manner it identifies pathogens, prevents overgrowth of cells, and provides a multidimensional protection against non-self organisms and proteins that can cause harm to the human body. When an individual develops an allergic response to a substance the immune system responds differently than an individual without the allergic response. Common allergy triggers are pollen, bee stings, animal dander, medications, and foods such as nuts, milk, shellfish, and eggs (Simons, 2009). Recognition and management of allergic responses requires the health care practioners to be aware of the multiple factors that impact the process. In this paper, the pathophysiology, assessment, and pharmacological interventions involved in allergic responses will be discussed, including why certain individuals develop allergies.

# Pathophysiology

According to McCance and Huether (2014) an antigen is a protein that identifies something as self or non-self. Pathogens can be inhaled, ingested, absorbed through contact with skin or mucous membranes, or injected such as in the case of immunizations. In a normal immune response a pathogen enters the body lacking the identifying histocompatibility antigen (HLA) and therefore is identified by the body as foreign. Antigen presenting cells such as dendritic cells, macrophages, and B lymphocytes capture the pathogen, process it for presentation, and present the processed pathogen to T-helper cells. The T-helper cells immediately identify the pathogen and prepare the B and T cells to destroy this specific enemy. The B cells create antibodies that target and bind to the pathogen. The initial antibody created is IgM followed closely by IgG, both of which activate the complement cascade to destroy pathogens efficiently and interact with the inflammatory response to isolate, destroy, and clean up the pathogen and affected cells. The T cells differentiate after interaction with the T Helper cells, becoming T Killers or activating macrophages, T-regulatory cells, which mediate the extent of the immune response to prevent an over-reaction, and T-memory cells that remember the antigen, pass on this memory, and help create a more rapid, more thorough response when the same pathogen is encountered again (McCance and Huether, 2014).

In individuals with a predisposition to developing an allergic response, the antibody response that happens following a specific pathogen introduction does not follow the normal pathway; instead, IgE is the primary responder. IgE is a short lived antibody with a very profound interaction with mast cells (McCance and Huether, 2014). When in the presence of or bound to the antigen of the allergen, IgE reacts with the mast cells even if it is not currently bound to the antigen, which means it does not necessarily matter how much allergen has be contacted, but how much IgE has been released (McCance and Huether, 2014). The combination of IgE and mast cells causes the mast cells to degranulate. Mast cells are found in the loose connective tissues near blood vessels. They are found in high concentrations in areas likely to come into contact with environmental pathogens, including the skin, GI tract, and respiratory tract (McCance and Huether, 2014). Activation of the mast cells starts the inflammatory response by release of histamine which is a vasoactive protein that causes vasoconstriction of venules and vasodilatation of the larger vessels which floods the area involved with increased blood flow (McCance and Huether, 2014). At the same time, histamine causes increased vessel permeability which allows for easy and rapid dissemination of leukocytes to the affected area. Histamine also causes bronchial constriction through smooth muscle contraction. Mast cells also release a chemotactic factor that attracts leukocytes to the area, and in the case of anaphylactic shock, eosinophil chemotactic factor of anaphylaxis. Cytokines are released by mast cells leading to B cell proliferation, antibody production, and increased vascular permeability which leads to exudation (McCance and Huether, 2014). Chemotaxis calls neutrophils and eosinophils to the area leading to phagocytosis (Alves, 2013). Further exudation is led by leukotrienes and prostaglandin synthesis (Alves, 2013). Therefore, allergic reaction is overreaction of the immune system mediated by IgE antibodies instead of the normal response of IgG and IgM.

# Assessment

The hypersensitivity of an individual to an allergen causes either a localized inflammatory response or a systemic anaphylactic reaction (McCance and Huether, 2014). These responses can vary from rashes, localized swelling, sneezing, itchy watery eyes, nasal congestion, and difficulty breathing all the way to shock.

**Itching and Rashes**

Itching is caused by histamine binding with neural receptors in the affected areas, such as skin, eyes, or nasal passages (Buddenkotte & Steinhoff, 2010). Atopic dermatitis, which is the skin eruption manifestation of an allergic response, is often seen in asthma, allergic rhinitis, and IgE mediated food allergies as well as independent allergic responses (Wollenberg and Feichtner, 2013). Cytokine IL-31 produced by T cells induces pruritus after the inflammatory response has been initiated, causing skin eruptions or rashes.

**Respiratory**

Allergic rhinitis is characterized by nasal congestion and discharge, nasal or sinus itching, and sneezing and is generally experienced in either an early or late reaction (Min, 2010). The early reaction is identified by rapid onset of rhinorrhea and sneezing which disappears fairly quickly and is mediated by mast cell release of histamine, prostaglandins and leukotrienes acting within the nasal mucosa creating a release of clear fluid exudate (Min, 2010). The late reaction is identified by nasal congestion and resolves slowly. The late reaction is mediated by eosinophil chemotaxis which is initiated by the early reaction (Min, 2010). Many of the cells that are involved in allergic rhinitis such as macrophages and eosinophils cause cellular remodeling of the nasal airway, causing chronic congestion in individuals suffering from chronic allergic response (Min, 2010). Difficulty breathing is characterized by wheezing lung sounds, created by narrowed airways. Bronchoconstriction is caused by inflammatory processes including release of histamine and prostaglandins by mast cells which in turn cause smooth muscle constriction (Barnes, 2011). Chronic inflammatory response can lead to epithelial destruction and nerve exposure secondary to cytokines released by eosinophils (Min, 2010). This can lead to hypersensitivity to non-allergens and can cause the exposed nerves to release neuropeptides which in turn causes smooth muscle contraction in response to either allergen or non-allergen irritating inhalants (Min, 2010).

**Anaphylactic**

Anaphylactic reaction happens in individuals who have been previously exposed to the allergen, with or without a diagnosed allergic reaction, and involves a systemic severe reaction in which the individual experiences smooth muscle contraction in the airway causing airway constriction, vasodilation causing decreased blood pressure, increased mucous production which increases difficulty breathing, and pruritus (Vaca, 2013). The onset symptoms can occur immediately to an hour post exposure. The symptoms can degenerate into shock, cyanosis and hypoxia, and death if not treated promptly and effectively (Vaca, 2013).

**Testing**

Clinical testing for allergies include skin testing, in which allergens are introduced locally into the dermal layer and observed for localized reaction, radioallergosorbent test (RAST), and multiple allergen simultaneous test (MAST) (Min, 2010). Each testing method has its limitations, such as false negative or false positives in the skin testing, expense, use of radioactive isotopes, and inability to identify multiple IgE antibodies in the RAST, and low sensitivity in the MAST (min, 2010). The ability to definitively identify true allergic responses to specific allergens is still problematic. Asking an individual about previous allergy responses, possible exposure to allergens, assessing any rash or skin eruption, nasal occlusion or drainage, eyes for redness and tearing, sinus pressure or pain, and lung sounds for bronchial constriction may lead you to suspect an allergic response (Ball et al, 2015).

**Genetics**

Why do some people have allergic responses when many do not? The answer may lie within a study conducted in Finland that used 693 individuals who tested positive to sensitivity to timothy grass and 3726 control individuals who did not. Alves, Bruhn, Ramasamy, Wang, Holloway, Hartikainen, Jarvelin, Benson, Balding, and Coin (2013) conducted DNA analysis on these individuals, and through thorough testing determined genetic markers were present in a certain protein sequence within the genes that changed regulation of the complement cascade in individuals sensitized to a specific allergen. The researchers worked with and augmented the genome wide association study (GWAS) findings of genetic variations of allergic responses. They further broke the pathway down and determined that the CD4+ T cells gene expression is altered in those who were allergen sensitive. In all, the researchers discovered seven genes specifically associated with a positive response to pollen, confirmed two more already delineated by the GWAS, and implicated two of the genes in the interaction between T cells and the complement system.

**Pharmacology**

Due to the fact that allergies are largely IgE mediated, and IgE is a short lived antibody, allergic responses usually resolve independently once the allergen is removed. However, for those who experience chronic, unavoidable exposure to allergens or who experience acute moderate to severe reaction, pharmacological interventions are necessary. Pharmacological treatments of allergies lie within antihistamines and immunosuppressants.

**Antihistamines**

H1 antagonist antihistamines block the receptor sites for histamine, but do not prevent histamine release (Lehne, 2013). This works by preventing changes in the vascular network in the affected area and preventing the inflammatory response. H1 blockers also prevent mucous secretion in mucous membranes. Side effects include sedation, paradoxal excitation, dizziness, nausea, vomiting, diarrhea, constipation, drying of the mucous membranes, palpitations, and urinary hesitancy (Lehne, 2013). According to Min (2010) first generation antihistamines penetrate the blood-brain barrier and act upon the central nervous system, causing sedation and impaired motor skills, whereas second generation antihistamine have less affinity for crossing the barrier. Antihistamines need to be used with caution in individuals with high blood pressure, urinary retention issues, glaucoma, and/or mentation issues due to the anticholinergic effects of the drugs (Lehmann and Blaiss, 2006).

**Glucocorticoids**

Immunosuppressant glucocorticoids are used to reduce inflammatory response. They do this by interrupting the synthesis of prostaglandins, histamine, and leukotrienes (Lehne, 2013). Predictably, the use of glucocorticoids interferes with normal immune response, and can leave a patient vulnerable to infection. Other concerns are adrenal insufficiency, osteoporosis, unstable glucose metabolism, weakness, electrolyte imbalances, insomnia, anxiety, psychosis, and Cushing’s syndrome (Lehne, 2013). Of particular concern is use of glucocorticoids in individuals with glucose management issues, as glucocorticoids interfere with insulin sensitivity and decrease beta cell glucose management Dalmazi, Pagotta, Pasquali, and Vicennati, 2012). Long term use of glucocorticoids increases the possibility of adverse reaction.

**Anaphylaxis Treatment**

In the event of anaphylactic reaction, epinephrine is the drug of choice to thwart the inflammatory response of increased microvascular flow by causing immediate vasoconstriction systemically (Lehne, 2013). Supplemental oxygen is an appropriate method of supportive care (Vaca, 2013). Diphenhydramine is the antihistamine of choice in the anaphylactic reaction, and the addition of glucocorticoids will help manage the sequelae (Lehne, 2013).

**Immunotherapy**

Immunotherapy is the ideal intervention for the individual experiencing moderate to severe allergic response on a chronic level. Immunotherapy induces desensitization by reducing the IgE response and encouraging the less pathogenic IgG response by reducing antigen-specific T helper cells responsible for the stimulation of the IgE response, inducing T regulatory cells to limit the inflammatory response, and reducing inflammatory cell recruitment (Calderon et al, 2011). Immunotherapy is available in antigen specific injections and antigen specific oral therapies, although the oral therapies are slow to be introduced in the United States. The regimen is subcutaneous injections of specific antigen(s), titrated to a therapeutic dose known as a maintenance dose which is administered for three years or more (Min, 2010). There is a risk of anaphylactic reaction, which is greatly decreased in the oral therapies (Min, 2010).

**Conclusion**

The immune system is a highly complex arrangement of biochemical factors and cell mediated responses. In a certain genetically specific group, sensitivity to certain antigens creates a maladaptive immune response which causes individuals to respond via the IgE mediated pathway rather than the more adaptive IgG/IgM mediated pathway. Allergic responses vary in intensity and symptomology, including nasal congestion, itchy, watery eyes, rashes and itchy skin, difficulty breathing, and life threatening anaphylactic reaction. Pharmacological interventions include antihistamines, glucocorticoids, epinephrine, and immunological desensitization. Recognition and management of allergic responses requires the practioners to be aware of the multiple factors that impact the process.

References

Alves, A. C., Bruhn, S., Ramasamy, A., Wang, H., Holloway, J. W., Hartikainen, A. L., Jarvelin,

M. R., Benson, M., Balding, D. J., and Coin, L. J. M. (2013). Dysregulation of

complement and CD4+T cell activation pathways implicated in allergic response. *PLoS*

*ONE, 8*(10). 1-15. doi:.org/10.1371/journal.pone.0074821

Ball, J.W., Dains, J.E., Flynn, J.A., Solomon, B.S. & Stewart, R.W. (2015). Seidel’s guide to

physical examination (8th ed.)

Barnes, P. J. (2011). Pathophysiology of allergic inflammation. *Immunological Reviews.242*(1).

31-50. doi:10.111/j.1600-065X.2011.01020.x

Buddenkotte, J. & Steinhoff, M. ( 2010). pathophysiology and therapy in allergic and atopic

diseases. *European Journal of Allergy and Clinical Immunology. 65*(7). 805-821.

doi:10.111/j.1398-995.2010.01995.x

Calderon, M. A., Casale, T. B., Togias, A., Bousquet, J., Durham, S. R., & Demoly, P. (2011).

Allergen-specific immunotherapy for respiratory allergies: From meta-analysis to

registration and beyond. *Journal of Allergy and Clinical Immunology 127*(1). 30-38.

doi:10.1016/j.jaci.2010.08.024

Carpenter, C. J. (2010). A meta-analysis of the effectiveness of health belief model variables in

predicting behavior. *Health Communication*, *25*(8), 661-669.

doi:10.1080/10410236.2010.521906

Dalmazi, G. D., Pagotto, U., Pasquali, R., & Vicennati, V. (2012). Glucocorticois and type 2

diabetes: From physiology to pathology. *Journal of Nutrition and Metabolism.* vol. 2012,

Article ID 525093, 9 pages. doi:10.1155/2012/525093

Giddens, J.F. (2012). Concepts for nursing practice. St. Louis: Elsevier.

Lehne, R.A. (2013). Pharmacology for nursing care (8th ed.). St. Louis: Elsevier.

Lehmann, J. M. & Blaiss, M. S. (2006). Selecting the optimal oral antihistamine for patients with

allergic rhinitis. *Drugs. 66*(18). 2309-2319. Retrieved from <http://0->

ejournals.ebsco.com.libcat.ferris.edu/Direct.asp?AccessToken=954Q9IX8X5PDDXR59I

DRQRXQPI1M8MIJQI&Show=Object&msid=603996343

McCance, K.L., & Huether, S.E. (2014). Pathopshysiology (7th ed.). St. Louis: Elsevier

Min, Y. (2010). The pathophysiology, diagnosis, and treatment of allergic rhinitis. *Allergy,*

*Asthma & Immunology Research. 2*(2). doi:.org/10.4168/aair.2010.2.2.65

Simons, F. E. R. (2009). Anaphylaxis. *Journal of Allergy and Clinical* *Immunuology. 125*(2).

S161-S181. doi:10.1016/j.jaci.2009.12.981

Vaca, V. M. Jr. (2013) Anaphylaxis. *Nursing 2013. 43*(11).

doi:10.1097/01.NURSE.0000435204.03647.3f

Wollenberg, A. & Feichtner, K. (2013) Atopic dermatitis and skin allergies- update and

outlook. *European Journal of Allergy and Clinical Immunology. 68*(12). 1509-1519.

doi:10.111/all.12324