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The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED 1812 • ISSN 0028-4793 • WWW.NEJM.ORG

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SOCIETY Volume 346(17), 25 April 2002, pp 1320-1322

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[Table of Contents](#) | [Browse TOC](#)

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Links

[Complete Reference](#)
[Catalogo Biblioteca ISS](#)

Outline

- [REFERENCES](#)

Graphics

- [Figure 1](#)

Recent History

[GO](#)

[Previous Page](#)

The Nuts and Bolts of Peanut Allergy

[Editorial]

Long, Aidan.

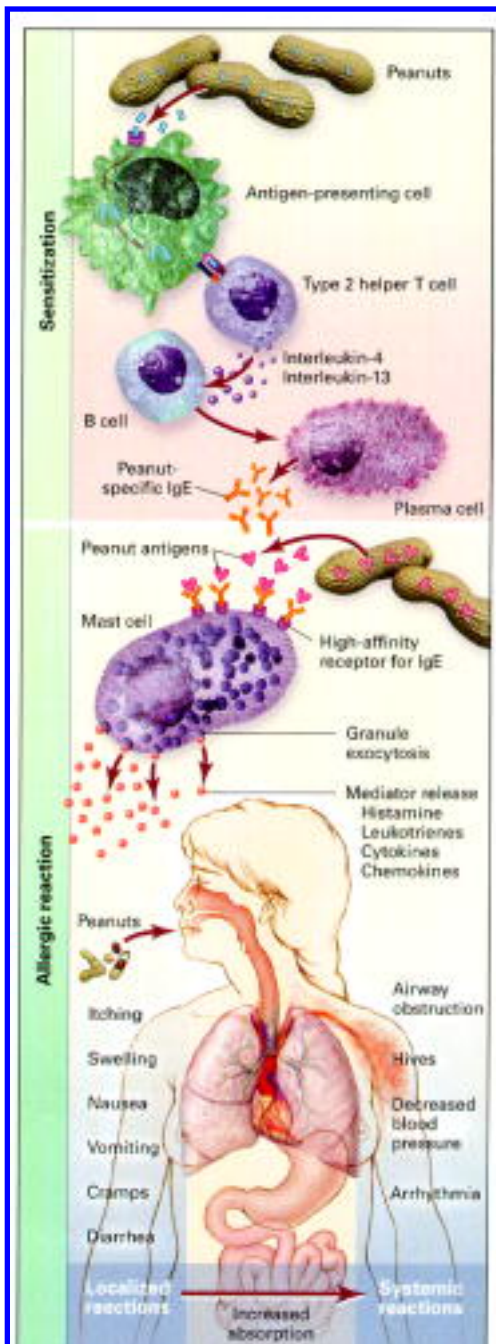
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In this issue of the Journal, Sampson [\[1\]](#) reviews the clinical features of allergy to peanuts. The question is why, in a small but apparently increasing percentage of the

population, does the ingestion of a seemingly innocuous and healthful food result in an allergic reaction?

The clinical manifestations of an allergic reaction to foods are the end result of an orchestrated series of events involving the immune system that have their origins in a prior exposure to the offending allergen ([Figure 1](#)). During the initial exposure, which may occur in utero, during breast-feeding, or in early childhood, antibodies of the IgE isotype, which are highly specific for epitopes on the surface of the food allergen (usually proteins or glycoproteins), are elaborated. The propensity to produce IgE antibodies against commonplace substances is the hallmark of the allergic diathesis. The factors underlying this propensity remain incompletely understood but appear to include exposure to allergens as well as a genetic predisposition. Exposure through mucosal surfaces, such as those of nasal passages and the respiratory and gastrointestinal tracts, seems to increase the risk of sensitization, whereas parenteral exposure, such as through subcutaneously administered immunotherapy, seems to increase the likelihood of tolerance. The threshold for sensitization most likely differs among patients. Multiple genes probably underlie atopy. Much recent attention has been focused on regions of chromosome 5q, which contains a tightly linked cluster of genes encoding interleukin-3, 4, 5, 9, 12, and 13 and granulocyte-macrophage colony-stimulating factor, and chromosome 11q, which encodes part of the high-affinity receptor for IgE (Fc(epsilon)RI). [\[2,3\]](#)

Figure 1. The Mechanism of Sensitization and Allergic Reaction.



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IgE antibodies differ from IgM, IgG, and IgA antibodies in that, to a large extent, they become cell-bound rather than circulate in the bloodstream or percolate through other body fluids. IgE binds to cells that express Fc(epsilon)RI (a receptor for its distinctive (epsilon) chain), notably mast cells and basophils and, possibly, eosinophils. Each Fc (epsilon)RI contains an (alpha) chain, a (beta) chain, and two (gamma) chains, which protrude into the cytoplasmic compartment of the cell. The Fc portion of the IgE antibody molecule (specifically the C(epsilon)3 domain) binds the (alpha) chain of the

Fc(epsilon)RI, leaving the antigen-binding region of the antibody molecule free to bind allergen.

Subsequent exposure to the allergen - for example, through the ingestion of peanuts - results in highly specific binding between epitopes on the surface of the allergenic protein or glycoprotein and the antigen-binding regions of the cell-bound IgE. Cross-linking cell-bound IgE antibodies by multivalent allergen in this manner initiates a sequence of intracellular events that culminates in the discharge from mast cells and basophils of chemical mediators that are responsible for the clinical characteristics of allergic reactions. The pathways involved in signal transduction and mast-cell activation include several critical steps, beginning with the aggregation of the (alpha) chains of Fc(epsilon)RI and followed by phosphorylation of the (beta) and (gamma) chains, activation of phospholipase C and other linked pathways, the generation of second messengers, and transcriptional gene activation. [4] These biochemical reactions result in exocytosis of intracellular granules, leading to the release of preformed chemical mediators, the synthesis of lipid-derived mediators (prostaglandins and leukotrienes), and the generation of inflammatory cytokines.

Within minutes after allergen binding, mast cells and basophils release histamine and serine proteases from their granules into the extracellular fluid. These mediators are responsible for the acute symptoms of allergic reactions. The newly synthesized lipid mediators, cytokines, and chemokines are released hours later and cause late-phase allergic reactions and the inflammatory-cell infiltrate at the site of allergen exposure that occurs in chronic allergic diseases, and they may also be responsible for biphasic reactions.

Acute symptoms predominate in allergic reactions to food, and as pointed out by

Sampson, they can be life-threatening or even fatal in rare instances. The rapid onset and severity of these symptoms result in part from the relatively extensive exposure to the allergen that ingestion affords and, more important, the rapid access of the ingested allergen to the systemic circulation, which leads to the activation of sensitized mast cells in the lungs, skin, and other tissues and organs. Exposure to food allergens through the digestive tract not only causes localized activation of mast cells and local symptoms (abdominal pain, vomiting, cramping, and diarrhea) but also increases intestinal permeability, permitting the passage of large molecules, such as intact allergenic proteins or glycoproteins, into the systemic circulation. [\[5\]](#)

The specific molecules in peanuts that contain the allergenic epitopes have been identified. The two dominant ones - Ara h 1 and Ara h 2 - are seed-storage glycoproteins that have a molecular mass of 65 kD and 17.5 kD, respectively. [\[6\]](#)

Several of the common characteristics of food allergens have been identified, such as being present in high concentrations (as is true of storage proteins in peanuts) and being relatively resistant to digestion and heat, but such features are also common in nonallergenic components of foods. Indeed, as described by Sampson, exposure of the main peanut allergen to high heat during roasting may actually increase the allergenicity of the protein.

Clinical food allergy is increasingly being recognized thanks in part to the exemplary work of Sampson and his colleagues. However, the fundamental questions of why food allergy develops in one person and not another and why only some foods are frequently implicated in this process remain to be answered.

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REFERENCES

1. Sampson HA. Peanut allergy. N Engl J Med 2002;346:1294-9. [\[Context Link\]](#)
2. Borish L. Genetics of allergy and asthma. Ann Allergy Asthma Immunol 1999;82:413-24. **Catalogo Biblioteca ISS Bibliographic Links** [\[Context Link\]](#)
3. Cookson W. The alliance of genes and environment in asthma and allergy. Nature 1999;402: Suppl:B5-B11. **Catalogo Biblioteca ISS Bibliographic Links** [\[Context Link\]](#)
4. Kinet JP. The high-affinity IgE receptor (Fc epsilon RI): from physiology to pathology. Annu Rev Immunol 1999;17:931-72. **Catalogo Biblioteca ISS Bibliographic Links** [\[Context Link\]](#)
5. Sanderson IR, Walker WA. Uptake and transport of macromolecules by the intestine: possible role in clinical disorders (an update). Gastroenterology 1993;104:622-39. **Catalogo Biblioteca ISS Bibliographic Links** [\[Context Link\]](#)
6. Breiteneder H, Scheiner O. Molecular and biochemical classification of plant-derived food allergens. J Allergy Clin Immunol 2000;106:27-36. **Catalogo Biblioteca ISS Bibliographic Links** [\[Context Link\]](#)

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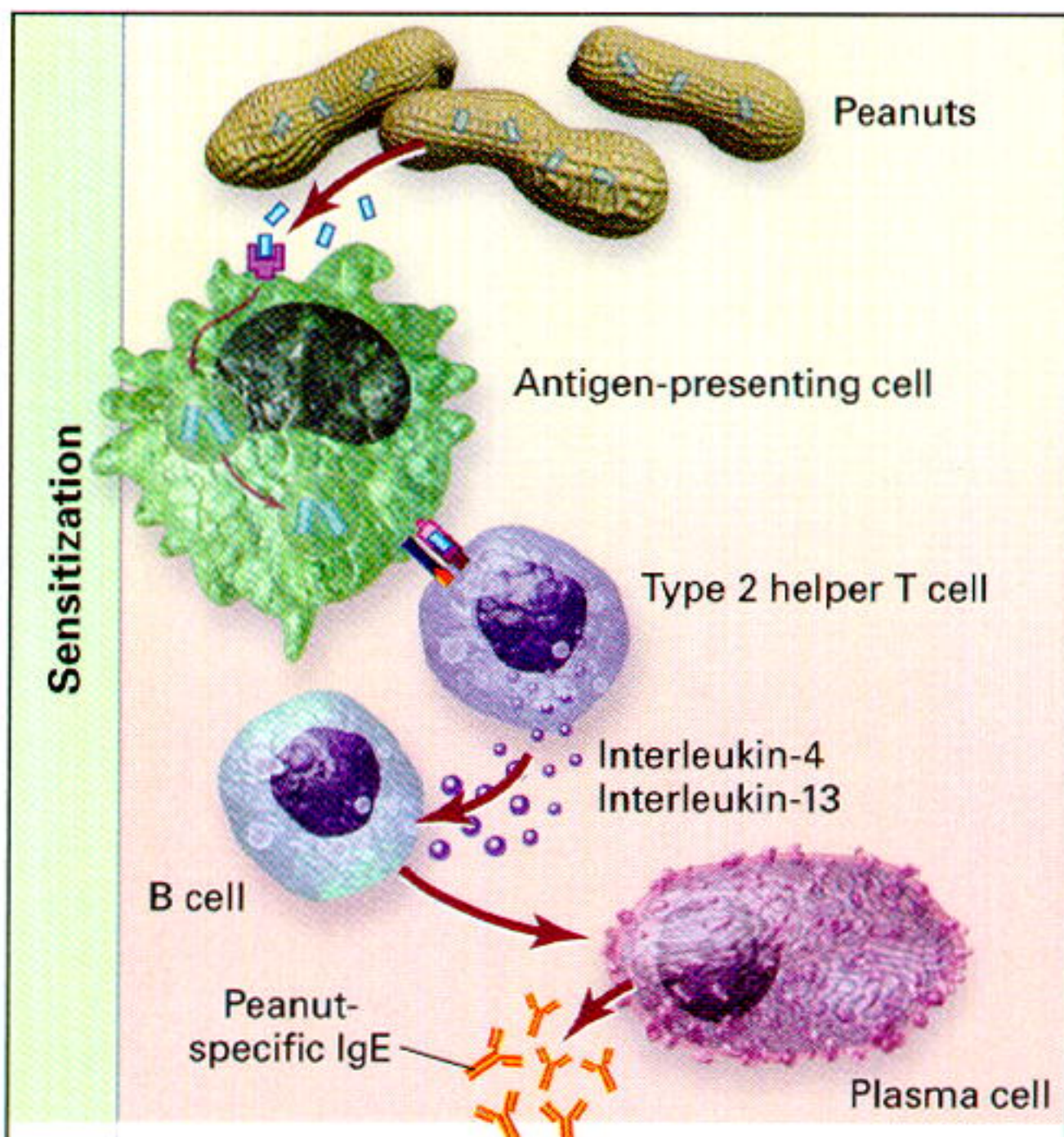
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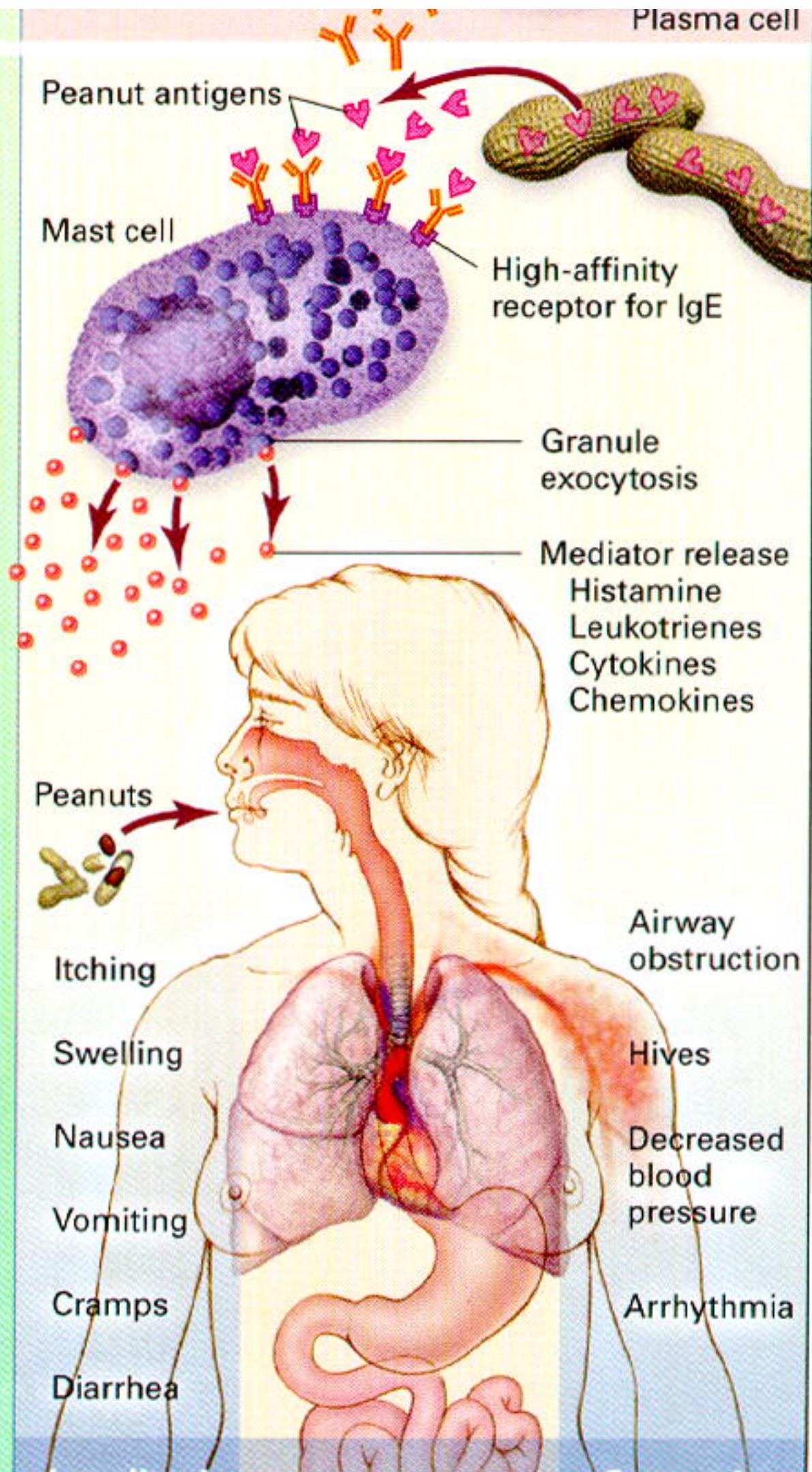
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Figure 1



Allergic reaction



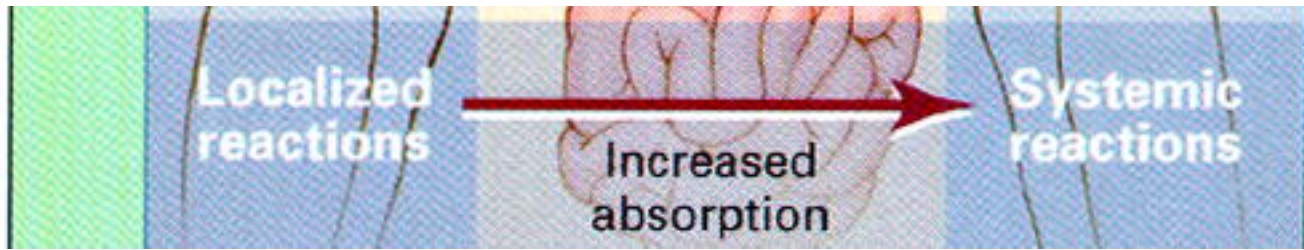


Figure 1. The Mechanism of Sensitization and Allergic Reaction.

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