Johns Hopkins Engineering

Immunoengineering

Allergy and Autoimmunity

Allergies

JOHNS HOPKINS
WHITING SCHOOL
of ENGINEERING

Allergies

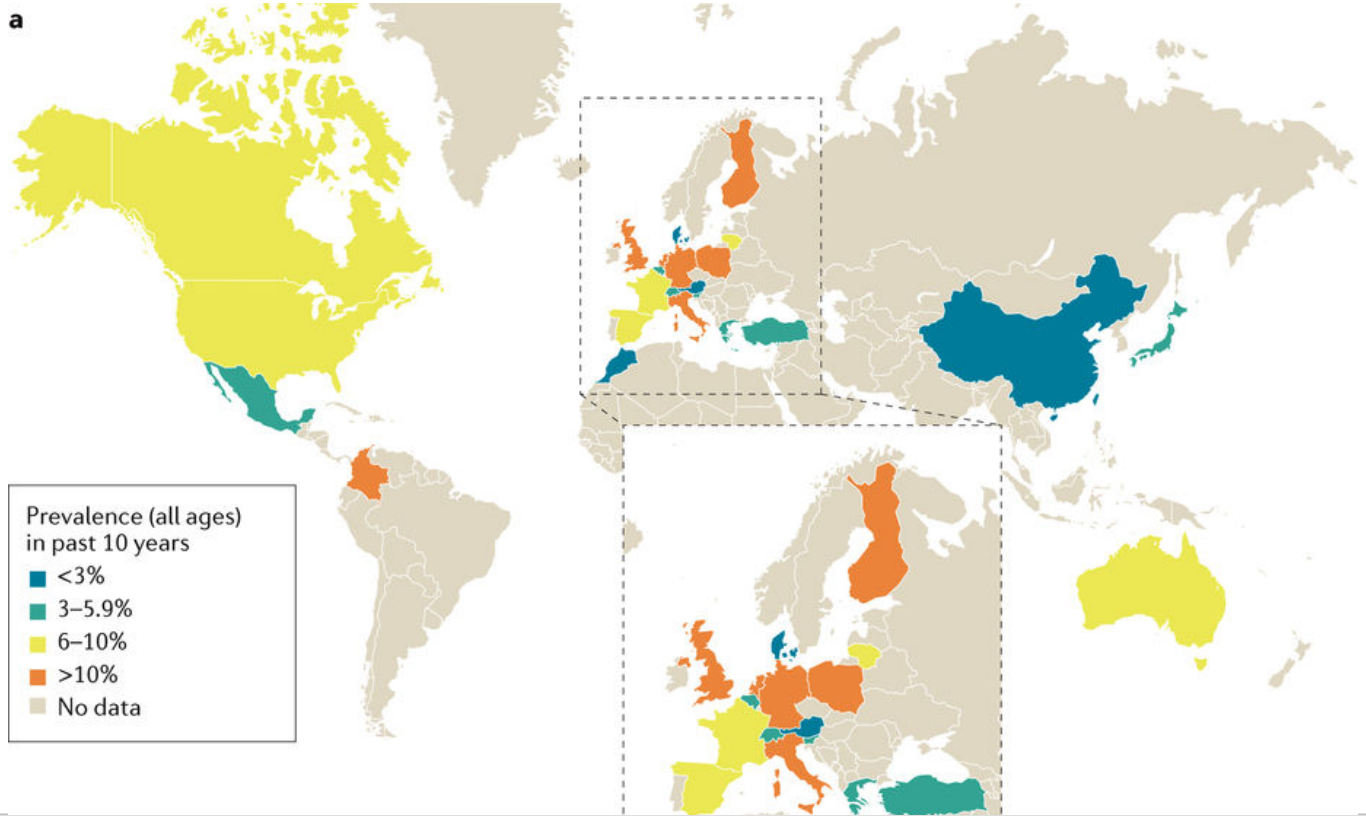
http://allergena.blogspot.com/2015/01/what-is-difference-between-anaphylaxis.html

Will Smith in *Hitch*

- Hyperactivity to environmental antigen that majority of population is tolerized to
- Why?

http://allergena.blogspot.com/2015/01/what-is-difference-between-anaphylaxis.html

Food Allergy Prevalence



Renz, H. *et al*. Food allergy. *Nat. Rev. Dis. Primers* **4**, 17098 (2018).

Clinical Effects of Allergic Reaction

Table 1 | **Food hypersensitivity (allergic) disorders by predominant organ affected**

Target organ	IgE-mediated disorders	Predominantly non-IgE-mediated disorders*	Non-IgE-mediated (cellular) disorders
Skin	• Generalized urticaria • Acute contact urticaria • Angio-oedema • Erythematous morbilliform rash • Flushing	Atopic dermatitis	• Contact dermatitis • Dermatitis herpetiformis
Lungs	• Allergic rhinoconjunctivitis • Acute bronchospasm	Asthma	Food-induced pulmonary haemosiderosis (Heiner syndrome)
Gastrointestinal tract	• Oral allergy syndrome • Acute gastrointestinal spasm	• Eosinophilic oesophagitis • Eosinophilic gastritis • Eosinophilic gastroenteritis	• Food protein-induced enterocolitis syndrome • Food protein-induced proctocolitis syndrome • Food protein-induced enteropathy syndrome • Coeliac disease
Cardiovascular system	• Hypotension • Dizziness and/or fainting	NA	NA
Generalized reaction‡	• Anaphylaxis • Food-associated exercise-induced anaphylaxis • NSAID-associated, aspirin-associated or alcohol-associated food-induced anaphylaxis	NA	NA
Other	• Uterine cramping and contractions • Feeling of 'pending doom'	NA	NA

IgE, immunoglobulin E; NA, not applicable. *Disorders associated with IgE hypersensitivity. ‡Involving two or more organ systems.

Renz, H. *et al*. Food allergy. *Nat. Rev. Dis. Primers* **4**, 17098 (2018).

Types of Reactions

IgE-mediated allergic reactions			
Reaction or disease	**Common allergens**	**Route of entry**	**Response**
Systemic anaphylaxis	Drugs Venoms Food, e.g. peanuts Serum	Intravenous (either directly or following oral absorption into the blood after oral intake)	Edema Increased vascular permeability Laryngeal edema Circulatory collapse Death
Acute urticaria (wheal-and-flare)	Animal hair Insect bites Allergy testing	Through skin Systemic	Local increase in blood flow and vascular permeability Edema
Seasonal rhinoconjunctivitis (hay fever)	Pollens (ragweed, trees, grasses) Dust-mite feces	Contact with conjunctiva of eye and nasal mucosa	Edema of conjunctiva and nasal mucosa Sneezing
Asthma	Danders (cat) Pollens Dust-mite feces	Inhalation leading to contact with mucosal lining of lower airways	Bronchial constriction Increased mucus production Airway inflammation
Food allergy	Peanuts Tree nuts Shellfish Fish Milk Eggs Soy Wheat	Oral	Vomiting Diarrhea Pruritis (itching) Urticaria (hives) Anaphylaxis (rarely)

Figure 14.2 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

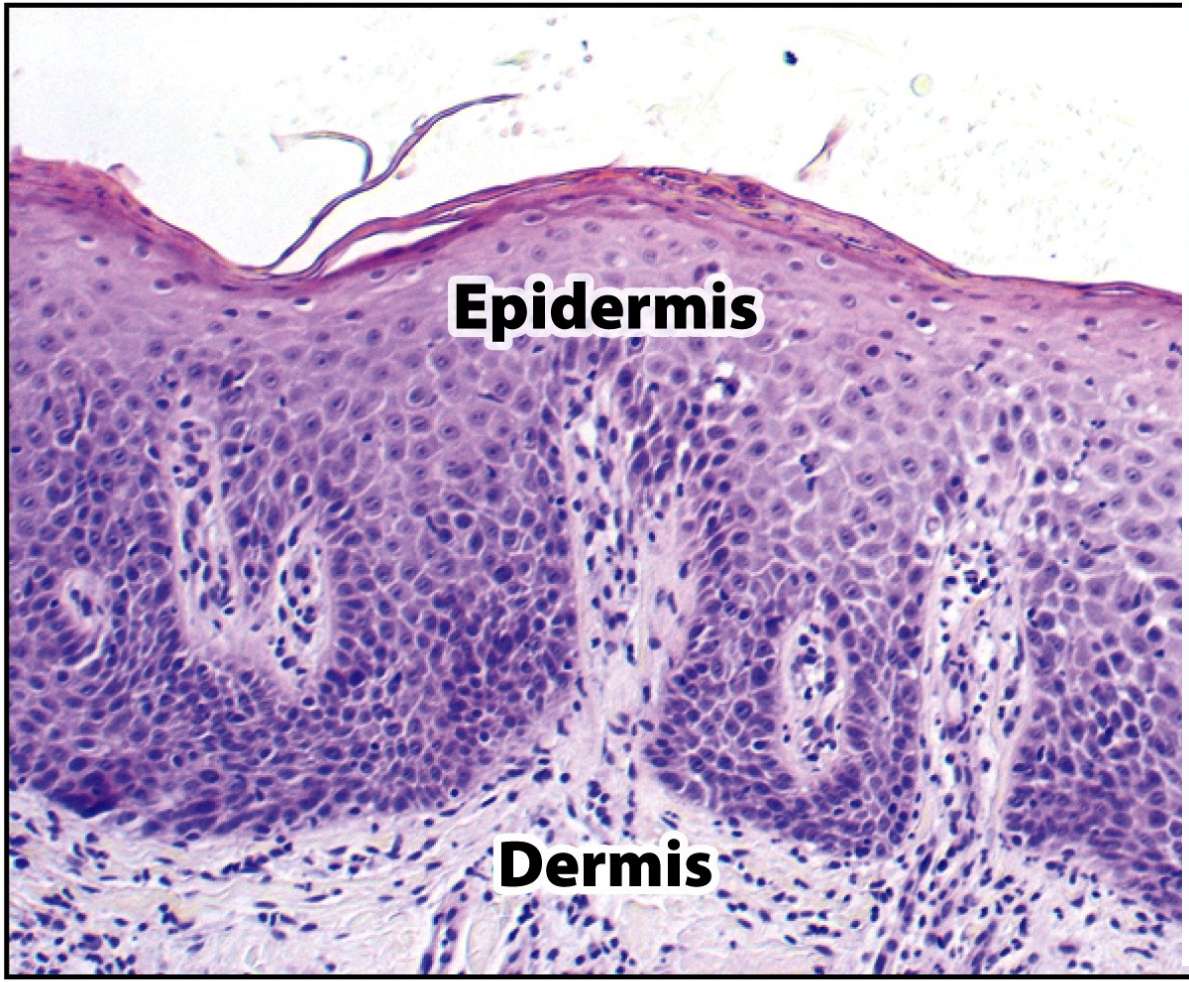
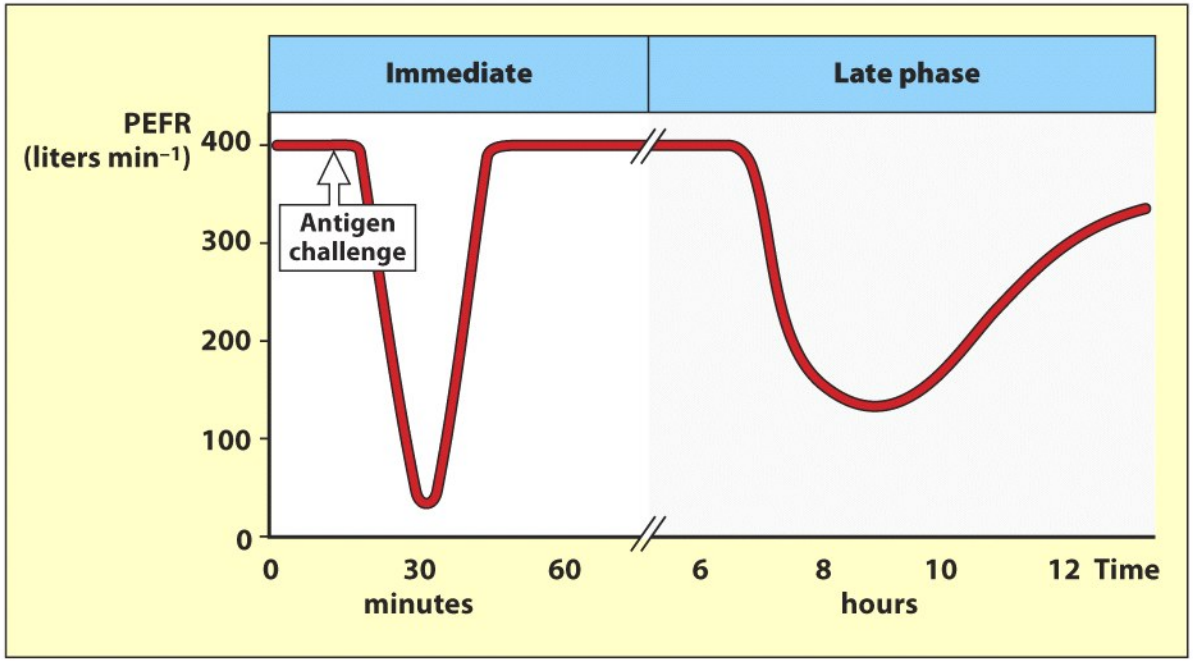


Figure 14.6 part 2 of 2 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Figure 14.26 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Timing of Allergic Response



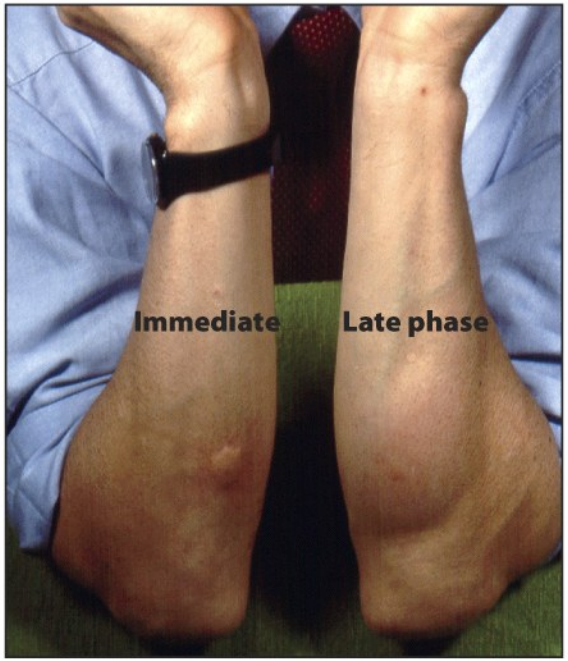


Figure 14.13 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Anaphylaxis

Table 1. Diagnostic Criteria for Anaphylaxis.*

Anaphylaxis is highly likely when any one of the following three criteria is fulfilled

Criterion 1

Onset of an illness within minutes to several hours after possible exposure to an allergen, with involvement of the skin, mucosal tissue, or both (e.g., generalized hives, pruritus or flushing, or swollen lips, tongue, or uvula) and at least one of the following signs or symptoms:

- Respiratory compromise (e.g., dyspnea, wheeze or bronchospasm, stridor, reduced peak expiratory flow, or hypoxemia)
- Reduced blood pressure or associated symptoms of end-organ dysfunction (e.g., hypotonia or collapse, syncope, or incontinence)

Criterion 2

Two or more of the following signs or symptoms that occur rapidly (within minutes to several hours) after exposure to a likely allergen:

- Involvement of the skin or mucosal tissue (e.g., generalized hives, itching or flushing, or swollen lips, tongue, or uvula)
- Respiratory compromise (e.g., dyspnea, wheeze or bronchospasm, stridor, reduced peak expiratory flow, or hypoxemia)
- Reduced blood pressure or associated symptoms of hypotension (e.g., hypotonia or collapse, syncope, or incontinence)
- Persistent gastrointestinal symptoms (e.g., crampy abdominal pain or vomiting)

Criterion 3

Reduced blood pressure within minutes to several hours after exposure to a known allergen:

- Infants and children: low systolic blood pressure (age-specific) or >30% decrease in systolic blood pressure
- Adults: systolic blood pressure of <90 mm Hg or >30% decrease from the person's baseline blood pressure

* Data are from Berin.[10]

Jones, Stacie M., and A. Wesley Burks. "Food allergy." *New England Journal of Medicine* 377.12 (2017): 1168-1176.

Clinical Diagnosis of Allergies

- Medical History and Physical Exam
- Skin Prick Tests
- IgE quantification
- Oral food challenge
- Elimination Diet

Treatments for Allergy

Treatments for allergic disease		
Target step	**Mechanism of treatment**	**Specific approach**
In clinical use		
Mediator action	Inhibit effects of mediators on specific receptors Inhibit synthesis of specific mediators	Antihistamines, β-blockers Lipoxygenase inhibitors
Chronic inflammatory reactions	General anti-inflammatory effects	Corticosteroids
T_H2 response	Induction of regulatory T cells	Desensitization therapy by injections of specific antigen
IgE binding to mast cell	Bind to IgE Fc region and prevent IgE binding to Fc receptors on mast cells	Anti-IgE antibodies (omalizumab)

Figure 14.19 part 1 of 2 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Treatments for Allergy

Treatments for allergic disease		
Target step	**Mechanism of treatment**	**Specific approach**
Proposed or under investigation		
T_H2 activation	Induction of regulatory T cells	Injection of specific antigen peptides Administration of cytokines, e.g., IFN-γ, IL-10, IL-12, TGF-β Use of adjuvants such as CpG oligodeoxynucleotides to stimulate T_H1 response
Activation of B cell to produce IgE	Block co-stimulation Inhibit T_H2 cytokines	Inhibit CD40L Inhibit IL-4 or IL-13
Mast-cell activation	Inhibit effects of IgE binding to mast cell	Blockade of IgE receptor
Eosinophil-dependent inflammation	Block cytokine and chemokine receptors that mediate eosinophil recruitment and activation	Inhibit IL-5 Block CCR3

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