

## Biological Basis of the Allergic Response

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## Allergic reactions

- Also known as type I hypersensitivity reactions
- Requires prior exposure and sensitization (IgE)
- Atopy: familial disposition towards allergy
  - "He comes from an atopic family"
- Allergic sensitization
  - Production of IgE and arming of FcεRI-bearing cells but does not imply clinical disease

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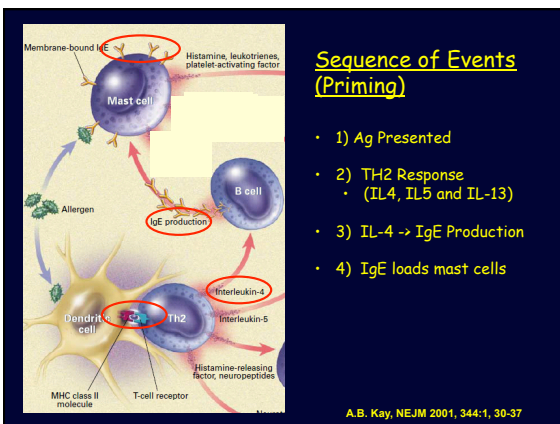
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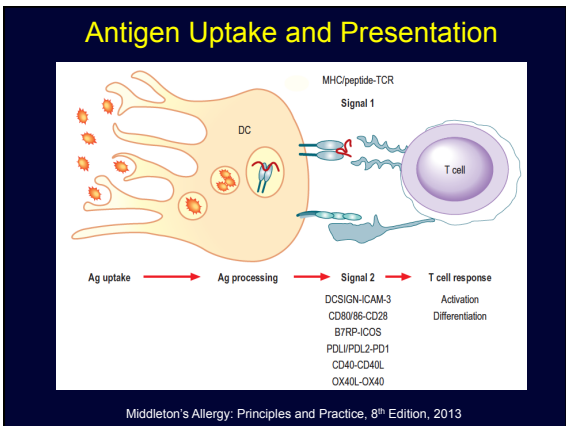
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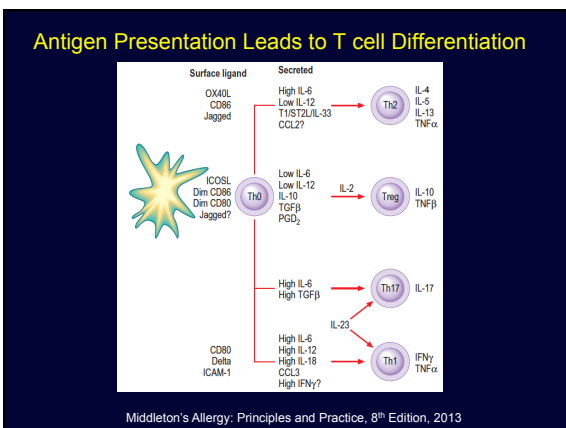
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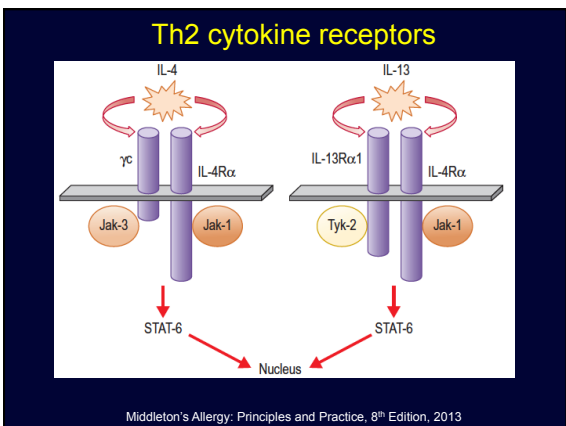
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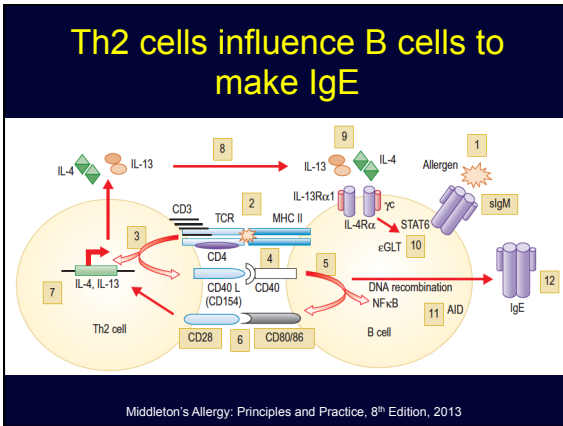
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- ### What Makes an Antigen IgE-Promoting ?
- Protein, not lipid; can rarely be carbohydrate
  - Mucosal exposure
  - Low concentration but must be multivalent
  - Stable, water soluble
  - Many have protease activity
    - Grass pollens
  - Some resemble helminthic parasite antigens
    - Filarial tropomyosin is similar to house dust mite, shellfish and cockroach proteins

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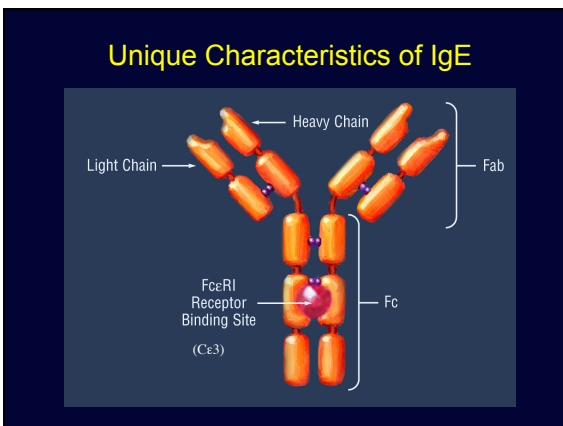
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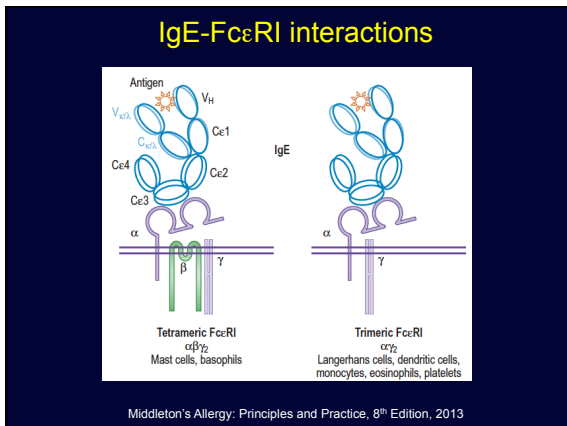
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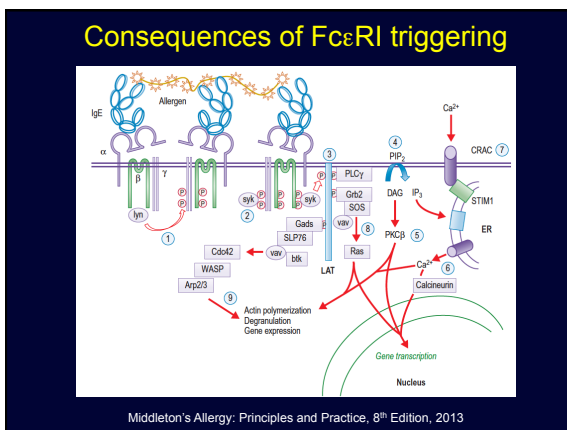
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### Mast cells and Basophils

Dvorak AM, J. Histochem Cytochem 53:1043, 2005

Mediator	MC	Baso
Histamine	+++	+
Tryptase	+++	+/-
LTs	+++	+
PG's	+++	-
IL-4	+/-	+++
IL-13	+	+++
Other cytokines	+++	+

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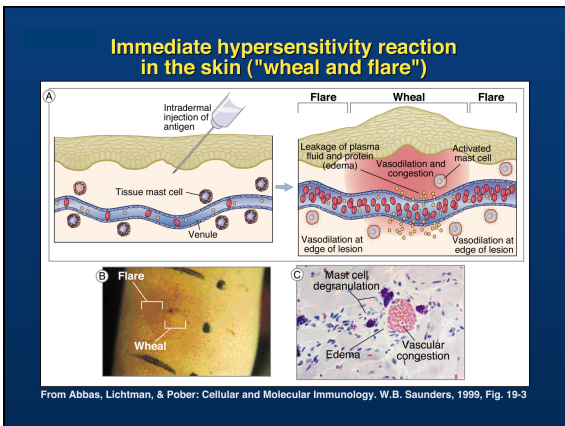
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### Detection of Specific IgE-Mediated Sensitivity

- Skin Testing: wheal and flare responses
- Laboratory measurement of serum specific IgE levels

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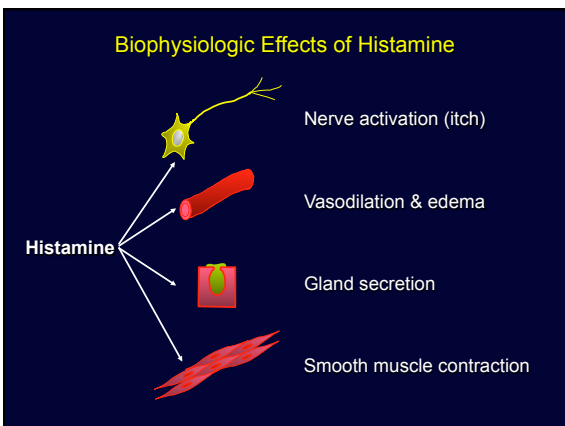
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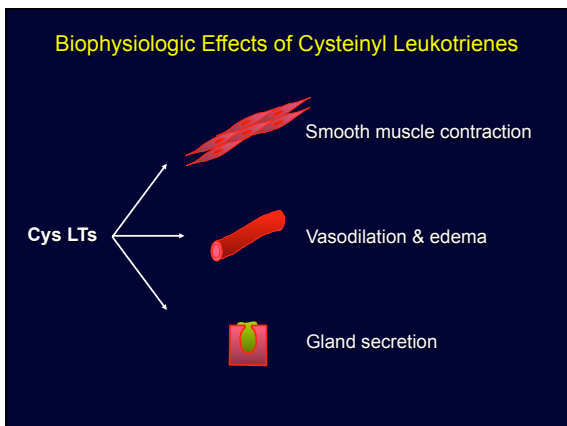
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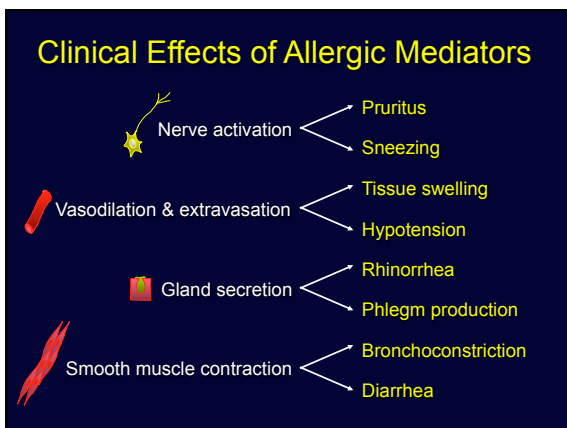
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### Definition and Diagnosis of Anaphylaxis

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

- 1** Sudden onset of an illness (minutes to several hours), with involvement of the skin, mucosal tissue, or both (e.g., generalized hives, itching or flushing, swollen lips-tongue-uvula) AND AT LEAST ONE OF THE FOLLOWING:
  - Sudden respiratory symptoms and signs (e.g., wheezing of breath, wheezing cough, stridor, hypoxemia)
  - Sudden reduced BP or symptoms of end-organ dysfunction (e.g., hypotonia, collapse, incontinence)
- 2** Two or more of the following that occur suddenly after exposure to a likely allergen or other trigger\* for that patient (minutes to several hours):
  - Sudden skin or mucosal symptoms and signs (e.g., generalized hives, itch, flush, swollen lips-tongue-uvula)
  - Sudden respiratory symptoms and signs (e.g., wheezing of breath, wheezing cough, stridor, hypoxemia)
  - Sudden reduced BP or symptoms of end-organ dysfunction (e.g., hypotonia, collapse, incontinence)
  - Sudden gastrointestinal symptoms (e.g., crampy abdominal pain, vomiting)
- 3** Reduced blood pressure (BP) after exposure to a known allergen\*\* for that patient (minutes to several hours):
  - Infants and children: low systolic BP (age-specific) or greater than 30% decrease in systolic BP\*
  - Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person's baseline

Simons et al., J Allergy Clin Immunol 127:587, 2011

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### Immunologic Causes of Anaphylaxis

Via IgE				
peanut	tree nuts	shellfish	fish	stinging insects
milk	egg	soybean	peach	sesame
Foods		Venoms		Medications*
Natural rubber latex	Occupational allergens	Seminal fluid	Aeroallergens	Radiocontrast media**
Not via IgE				
Radiocontrast media**	NSAIDs***	Dextrans (e.g. HMW***)	Biologic agents*	
<small>*Trigger anaphylaxis by more than one mechanism    **NSAIDs, non-steroidal anti-inflammatory drugs    ***HMW, high molecular weight</small>				

Simons et al., J Allergy Clin Immunol 127:587, 2011

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### Allergic responses are not just immediate

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### Chemokine receptors

Middleton's Allergy: Principles and Practice, 8<sup>th</sup> Edition, 2013

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**TABLE 7-3 Cellular Expression of Chemokine Receptors\***

Cell Type	Chemokine Receptor
Naïve T cells	CXCR4, CCR7
Th1 cells	CCR5, CXCR3
Th2 cells	CCR4, CCR8
Th17 cells	CCR6
Eosinophils	CCR3
Basophils	CCR3

Middleton's Allergy: Principles and Practice, 8<sup>th</sup> Edition, 2013

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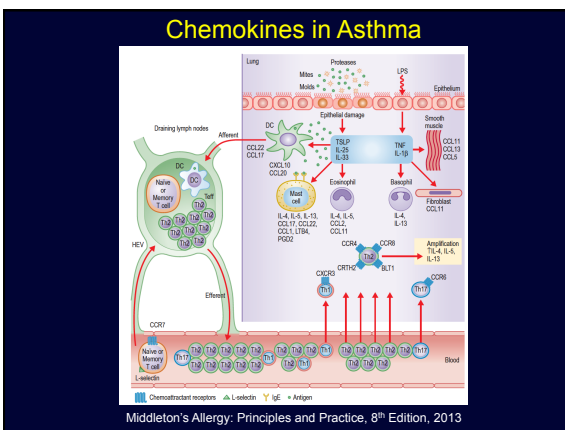
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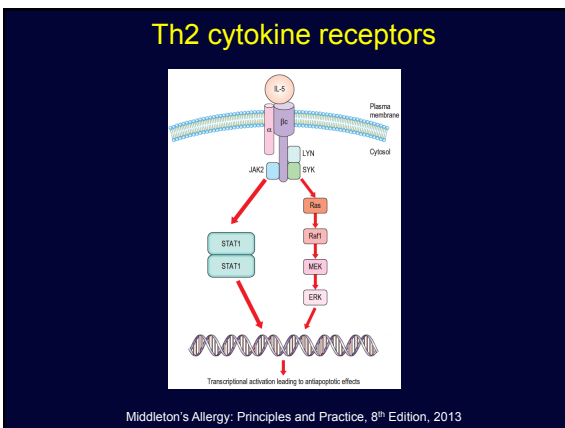
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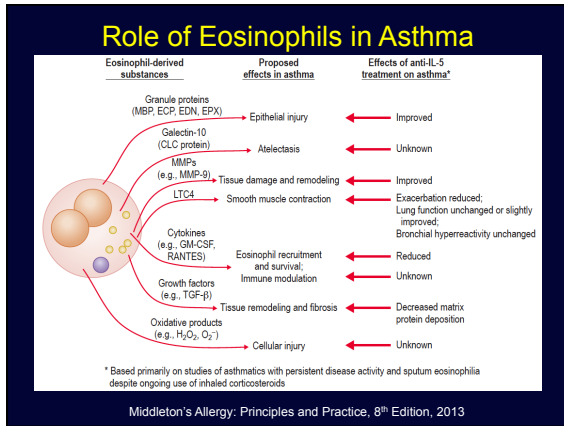
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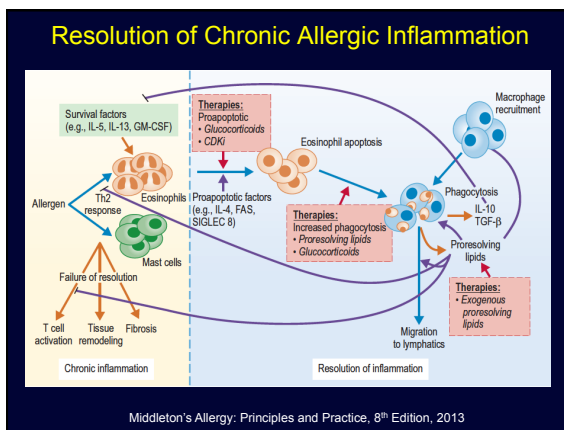
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### Key concepts

- Can't have allergies without IgE or FcεRI
- Mediators released during allergic reactions cause a characteristic pattern of signs and symptoms
- A myriad of preformed and newly synthesized biochemical and protein mediators, and their respective receptors, provide a range of therapeutic targets

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