Biological Basis of the Allergic Response

Bruce S. Bochner, M.D.
Samuel M. Feinberg Professor of Medicine
Northwestern University Feinberg School of Medicine
Division of Allergy-Immunology
bruce.bochner@northwestern.edu

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

Sequence of Events (Priming)

- 1) Ag Presented
- 2) Th2 Response
  - (IL4, IL5 and IL-13)
- 3) IL-4 → IgE Production
- 4) IgE loads mast cells

Antigen Uptake and Presentation

Antigen Presentation Leads to T cell Differentiation

Th2 cytokine receptors
Th2 cells influence B cells to make IgE

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

Unique Characteristics of IgE
IgE-FcεRI interactions

Consequences of FcεRI triggering

Mast cells and Basophils

<table>
<thead>
<tr>
<th>Mediator</th>
<th>MC</th>
<th>Baso</th>
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<tbody>
<tr>
<td>Histamine</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Tryptase</td>
<td>+++</td>
<td>+/-</td>
</tr>
<tr>
<td>LTBs</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>PG's</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>IL-4</td>
<td>+/-</td>
<td>+++</td>
</tr>
<tr>
<td>IL-13</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Other cytokines</td>
<td>+++</td>
<td>+</td>
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</tbody>
</table>
Skin Testing: wheal and flare responses

Laboratory measurement of serum specific IgE levels

Detection of Specific IgE-Mediated Sensitivity

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

Biophysiologic Effects of Histamine

- Nerve activation (itch)
- Vasodilation & edema
- Gland secretion
- Smooth muscle contraction
Biophysical Effects of Cysteinyl Leukotrienes

- Smooth muscle contraction
- Vasodilation & edema
- Gland secretion

Clinical Effects of Allergic Mediators

- Nerve activation
  - Pruritus
  - Sneezing
- Vasodilation & extravasation
  - Tissue swelling
  - Hypotension
  - Rhinorrhea
  - Phlegm production
  - Bronchoconstriction
  - Diarrhea

Definition and Diagnosis of Anaphylaxis

Immunologic Causes of Anaphylaxis

Via IgE

Not via IgE

Allergic responses are not just immediate

Chemokine receptors


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Chemokines in Asthma

Th2 cytokine receptors
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