

Hypersensitivity Reactions

IgE-Mediated (Type I) Hypersensitivity

Blue Bear

*When Blue Bear had a trip to the world, He had so much fun, making many new friends.**



Hypersensitivity Reactions

Hypersensitivity: Although the word hypersensitivity implies an increased response, the response is not always heightened but may, instead, be an inappropriate immune response to an antigen. Hypersensitive reactions may develop in the course of either humoral or cell-mediated responses.

Anaphylaxis: Term loosely translated from Greek to mean the opposite of prophylaxis.

Hypersensitivity Reactions

Atopy: a hereditary predisposition to the of immediate hypersensitivity reactions against common environmental antigens.

The abnormal IgE response of atopic individuals is at least partly genetic—it often runs in families.

Atopic individuals have:

1. abnormally high levels of circulating IgE
2. & more than normal numbers of circulating eosinophils.

Allergen: refers specifically to non parasitic antigens capable of stimulating type I hypersensitive responses in allergic individuals.

GENETIC PREDISPOSITION

It appears that allergenicity is a consequence of a complex series of interactions involving:

- The allergen.
- Dose.
- The sensitizing route.
- The genetic constitution of the recipient.

ALLERGIC REACTIONS

Skin Contact

Injection

Ingestion

Inhalation



poison plants



animal scratches



pollen



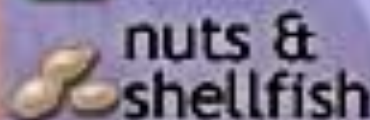
latex



bee sting



medication



nuts & shellfish



pollen



dust



mold & mildew



animal dander

Common allergens:

Components of allergic reactions

1. Sensitization

- production of T_H2 CD4 T cells and IgE
- Binding of IgE to Fc ϵ RI on mast cells and basophils

2. Effector phase

- Acute (immediate reaction)
 - Mast cell/basophil degranulation
- Late phase reaction - chronic
 - Influx of eosinophils and eosinophil degranulation
 - Influx of TH2 CD4 T cells

IgE-Mediated (Type I) Hypersensitivity

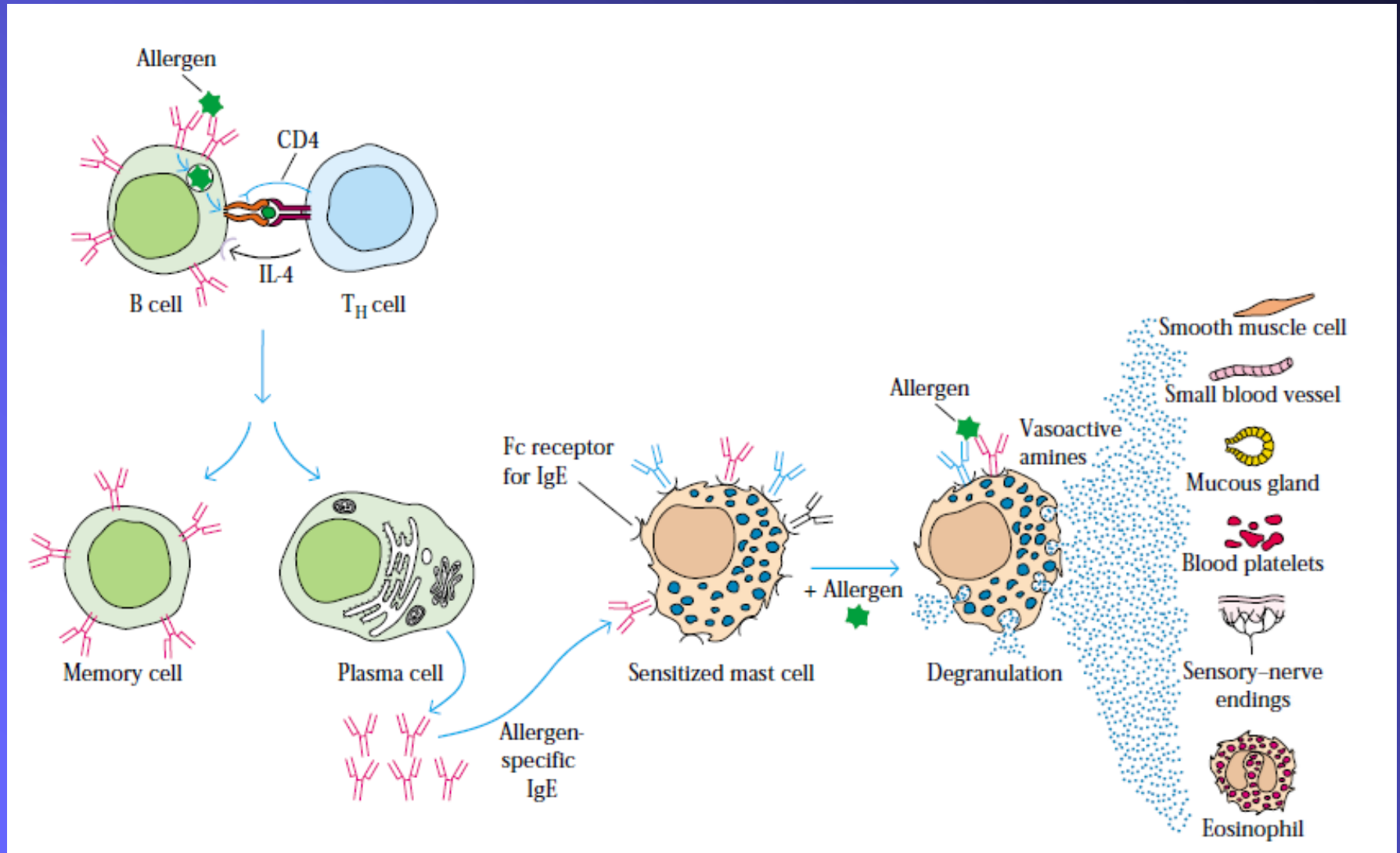


TABLE 16-3

Principal mediators involved in type I hypersensitivity

Mediator	Effects
PRIMARY	
Histamine, heparin Serotonin Eosinophil chemotactic factor (ECF-A) Neutrophil chemotactic factor (NCF-A) Proteases	Increased vascular permeability; smooth-muscle contraction Increased vascular permeability; smooth-muscle contraction Eosinophil chemotaxis Neutrophil chemotaxis Bronchial mucus secretion; degradation of blood-vessel basement membrane; generation of complement split products
SECONDARY	
Platelet-activating factor Leukotrienes (slow reactive substance of anaphylaxis, SRS-A) Prostaglandins Bradykinin Cytokines IL-1 and TNF- α IL-2, IL-3, IL-4, IL-5, IL-6, TGF- β , and GM-CSF	Platelet aggregation and degranulation; contraction of pulmonary smooth muscles Increased vascular permeability; contraction of pulmonary smooth muscles Vasodilation; contraction of pulmonary smooth muscles; platelet aggregation Increased vascular permeability; smooth-muscle contraction Systemic anaphylaxis; increased expression of CAMs on venular endothelial cells Various effects (see Table 12-1)

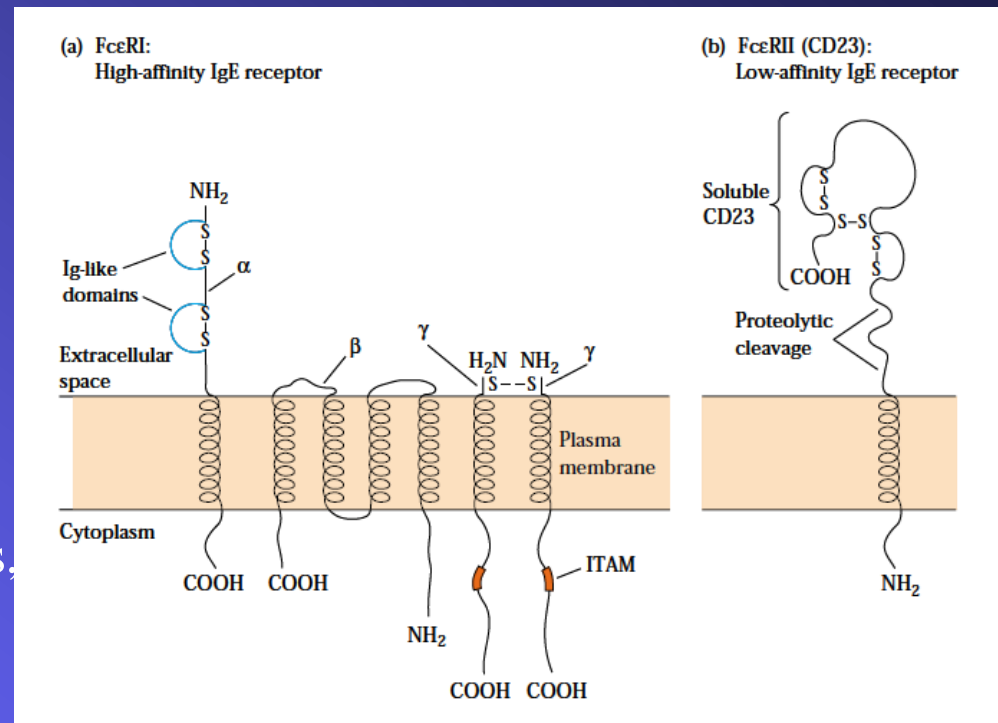
IgE-BINDING Fc RECEPTORS

HIGH-AFFINITY RECEPTOR (FcRI):

Mast cells and basophils express FcRI, which binds IgE with a high affinity.

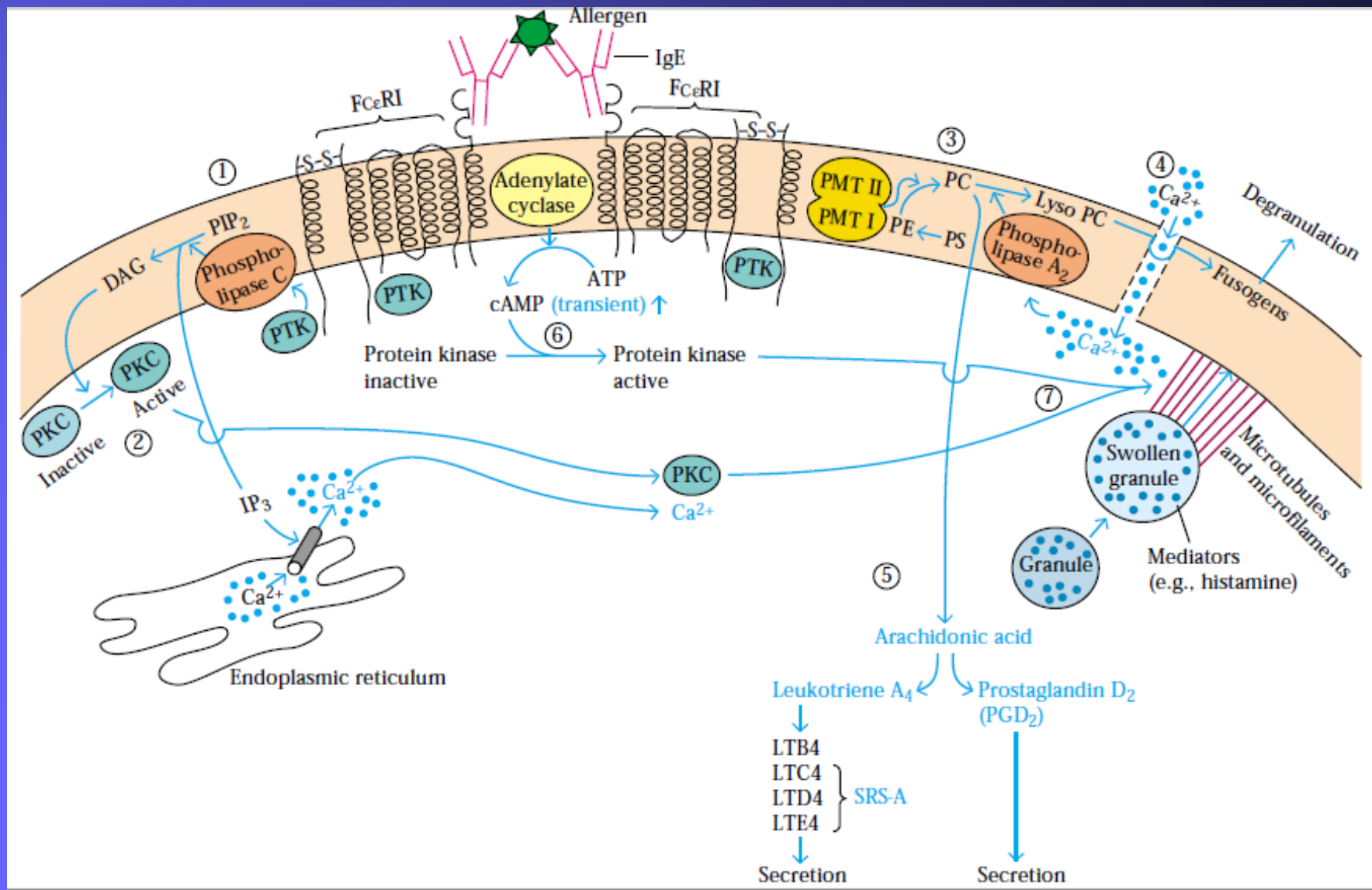
LOW-AFFINITY RECEPTOR (FcRII):

FcRII has been shown to activate B cells, Alveolar macrophages, & eosinophils.



ITAM = immunoreceptor tyrosine-based activation motif

Intracellular Events Regulate Mast-Cell Degranulation



Systemic vs. Localized Type I Reactions

- Systemic Anaphylaxis:
- Initiated by direct delivery of allergen into the circulatory system.
- Usually fatal within minutes.

- Localized Anaphylaxis = Atopy:
- Delivery of allergen to specific tissue/organ.
- 20% of the population afflicted with a strong genetic component.
- Usually initiated on epithelial surfaces-gastrointestinal, respiratory, skin .

Systemic anaphylaxis:

- Systemic anaphylaxis is a shock-like and often fatal state whose onset occurs within minutes of a type I hypersensitive reaction.
- Usually initiated by an allergen introduced directly into blood stream or absorbed from the gut or skin.
- Symptoms include urticaria, flushing of skin over whole body, difficulty in breathing, nausea & diarrhea.
- Acute hypotension, loss of consciousness and death follow.



Causes:

- This kind of anaphylaxis can be associated with antibiotics, heterologous serum treatment (anti-snakevenom), insect stings.



Shellfish



Peanuts and nuts



Medications



Atopic disorder

ALLERGIC RHINITIS

- Commonly known as hay fever.
- Reaction to pollen or molds
- Targets respiratory membranes
- Symptoms
 - Nasal congestion
 - Sneezing
 - Coughing
 - Mucous secretions
 - Itchy, red and teary eyes
 - Mild bronchoconstriction



Atopic Disorders

Allergic Asthma: caused by airborne or blood-borne allergens

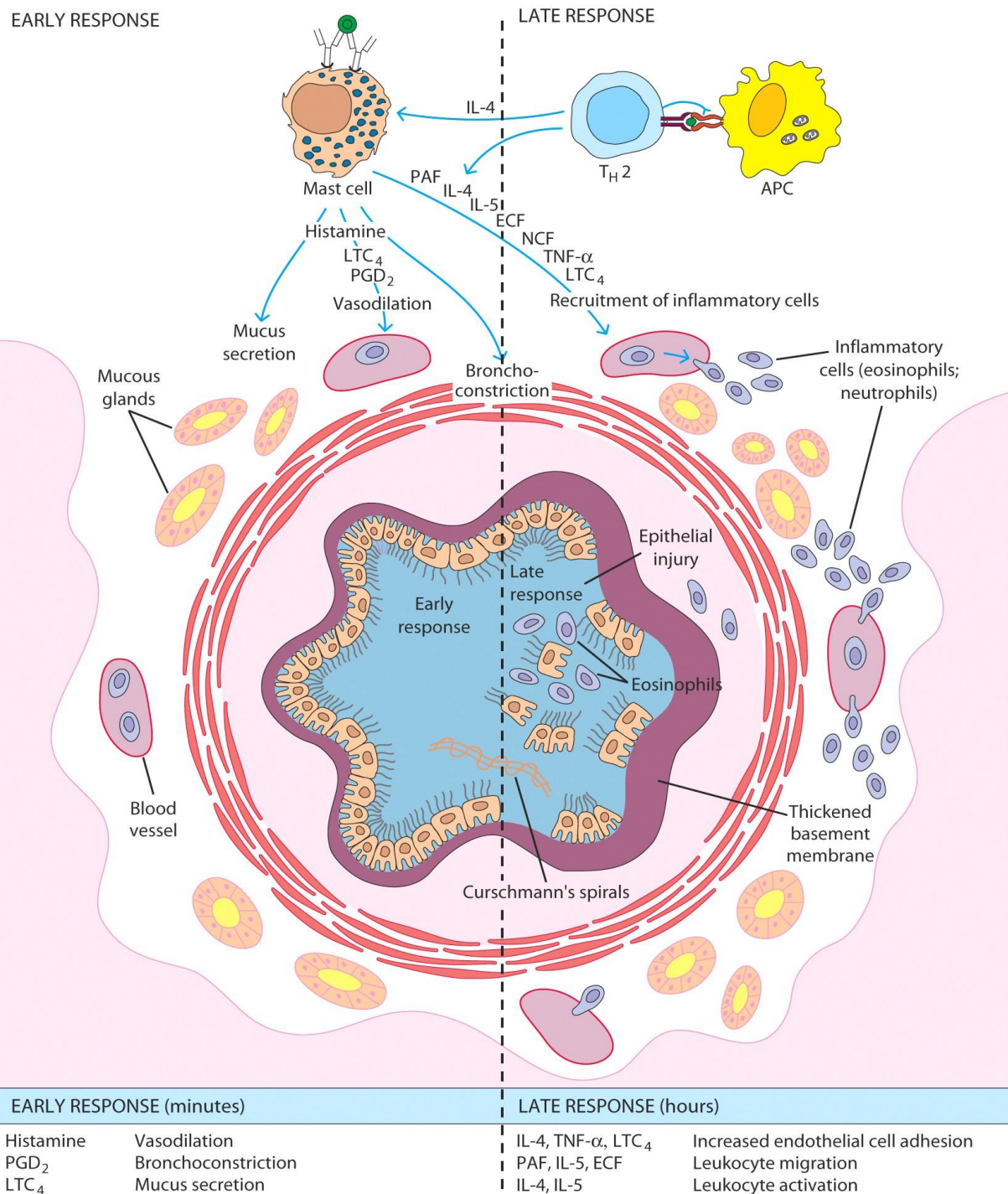
Intrinsic Asthma: Independent of allergen- exercise or cold weather

Initiated in the lower respiratory tract

Early phase- within minutes; bronchoconstriction, vasodilation and increased mucus production

Late phase- hours later; recruitment of neutrophils and eosinophils

Asthma



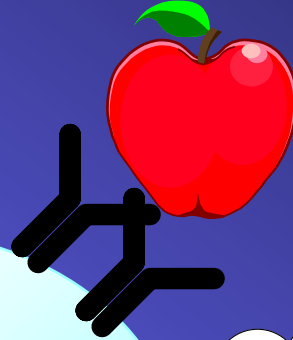
- Severe bronchoconstriction
- Symptoms
 - Shortness of breath to suffocation
 - Wheezing
 - Cough
 - Inflamed respiratory tract

Exercise-induced anaphylaxis

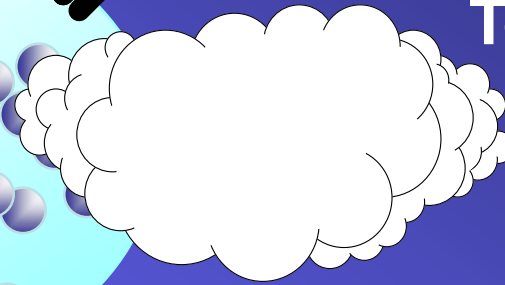
Exercise



Food



Temperature



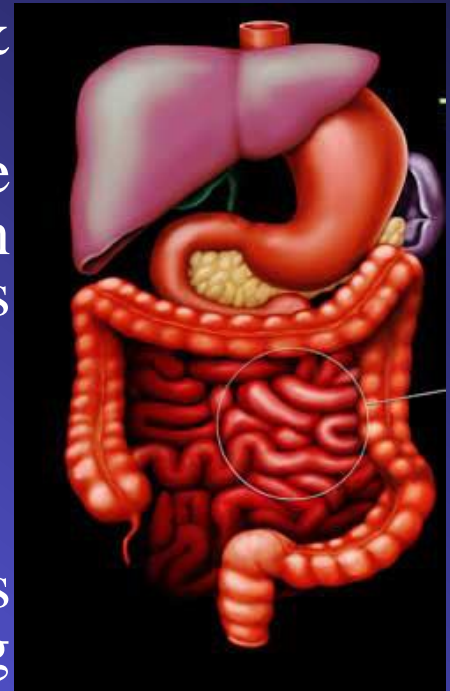
Mediator release

- Histamine
- Others (LTD4, PAF, etc)

ANAPHYLAXIS

FOOD ALLERGIES

- Allergen crosslinking of IgE on mast cells along the upper or lower gastrointestinal tract can induce localized smooth-muscle contraction & vasodilation \Rightarrow vomiting or diarrhea.
- Mast-cell degranulation along the gut can \uparrow the permeability of mucous membranes \Rightarrow allergen enters the bloodstream. Various symptoms depending on where the allergen is deposited.
- For example,
 - asthmatic attacks after ingesting certain foods.
 - atopic urticaria (hives) when a food allergen is carried to sensitized mast cells in the skin, causing swollen (edematous) red (erythematous) eruptions; this is the wheal and flare response.



ATOPIC DERMATITIS

- Atopic dermatitis (allergic eczema).
- an inflammatory disease of skin that is frequently associated with a family history of atopy.
- The disease is observed most frequently in young children, often developing during infancy.
- The allergic individual develops skin eruptions that are erythematous and filled with pus.
- Unlike a delayed-type hypersensitive reaction, which involves TH1 cells, the skin lesions in atopic dermatitis have TH2 cells and an increased number of eosinophils.



Assays to Detect Type I Hypersensitivity Reactions

Skin Tests (P-K test)-
Individual is inoculated with
allergen by scraping or
injection

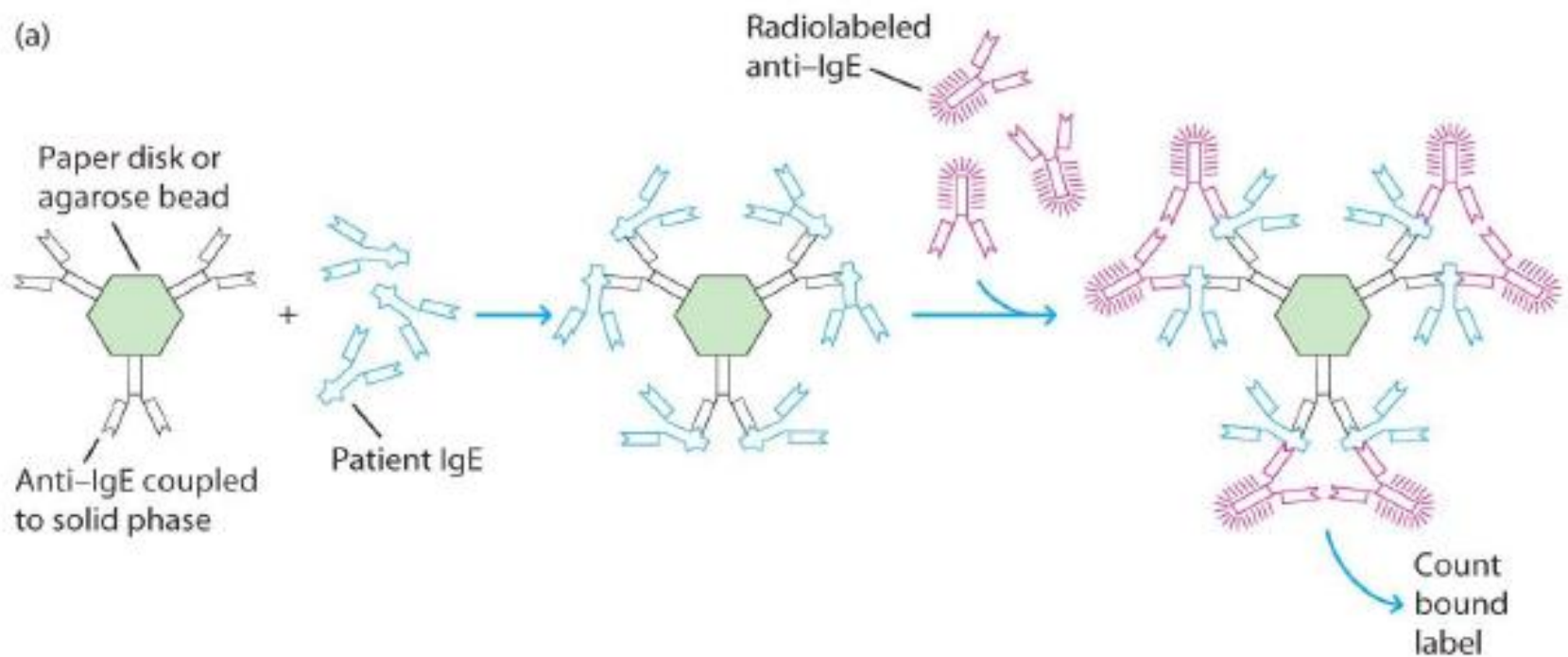
Fast: results within 30'



Assays to Detect Type I Hypersensitivity Reactions

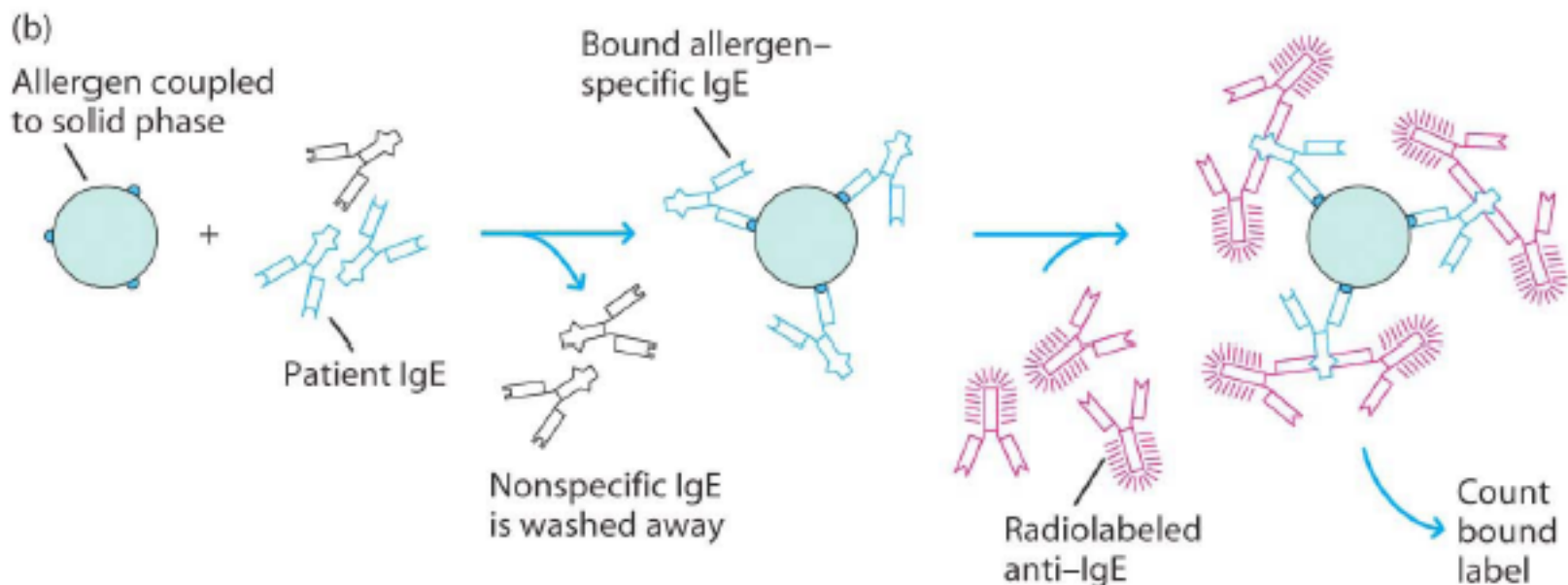
Radioimmunosorbent Tests (RIST)- measures levels of IgE in patient's serum

(a)



Assays to Detect Type I Hypersensitivity Reactions

Radioallergosorbent Tests (RAST)- measures levels of IgE in patient's serum that are specific for an allergen



Treatment of allergic reactions

1. Avoidance

- Foods
- Pets
- Dust

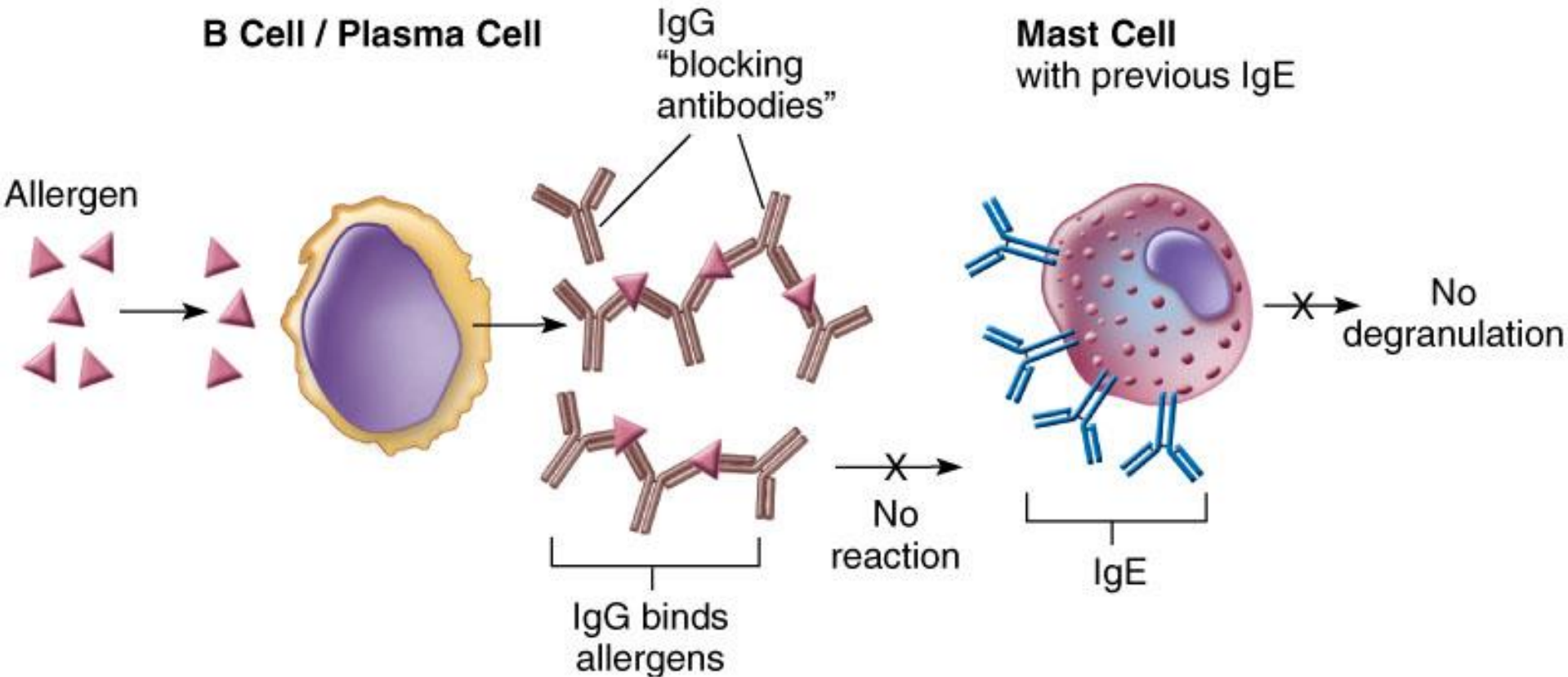
2. Desensitization

- Increasing doses of allergen via subcutaneous injection
- Shift response to T_H1 .
- Risk: induce/enhance allergy or type III hypersensitivity.

3. Drugs

The method of desensitization.

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The blocking antibody theory for allergic desensitization.

TABLE 16-4

Mechanism of action of some drugs used to treat type I hypersensitivity

Drug	Action
Antihistamines	Block H ₁ and H ₂ receptors on target cells
Cromolyn sodium	Blocks Ca ²⁺ influx into mast cells
Theophylline	Prolongs high cAMP levels in mast cells by inhibiting phosphodiesterase, which cleaves cAMP to 5'-AMP*
Epinephrine (adrenalin)	Stimulates cAMP production by binding to β-adrenergic receptors on mast cells*
Cortisone	Reduces histamine levels by blocking conversion of histidine to histamine and stimulates mast-cell production of cAMP*

*Although cAMP rises transiently during mast-cell activation, degranulation is prevented if cAMP levels remain high.

Thank You

