

Allergic Asthma

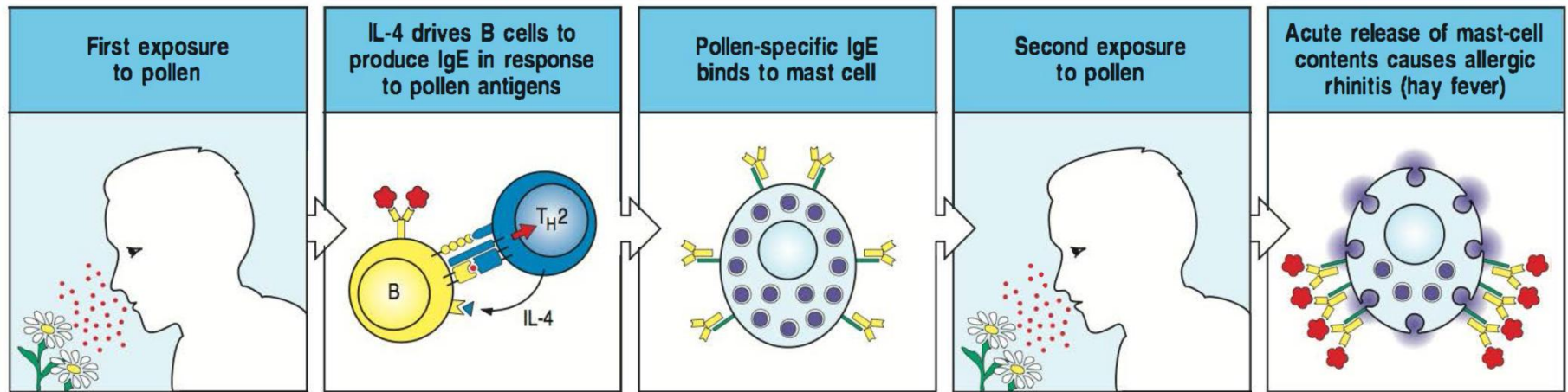
Case Study

Allergic Asthma

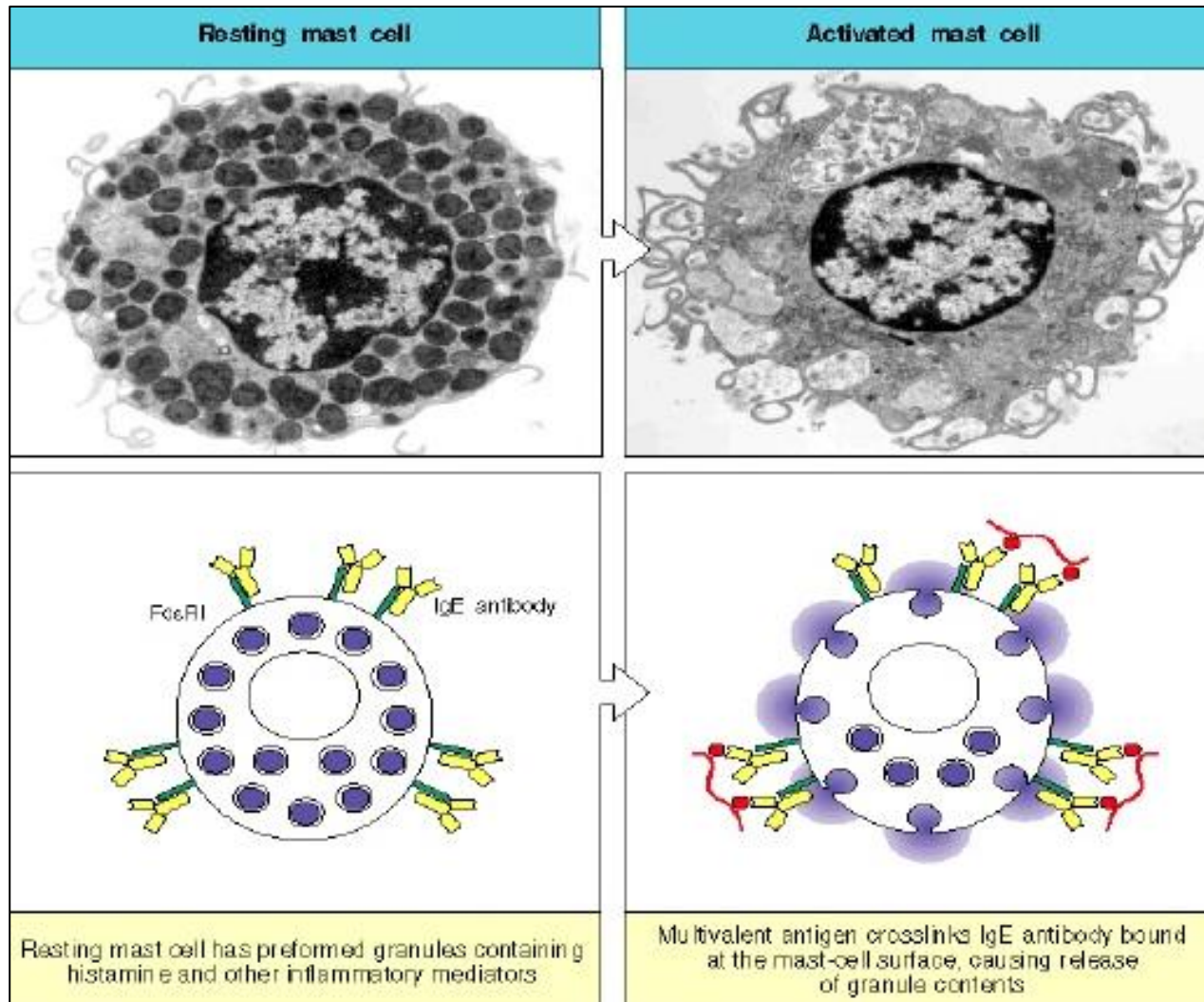
Type I IgE-mediated hypersensitivity reaction localized to respiratory tract but can be fatal.

Mediated by a Th2 response

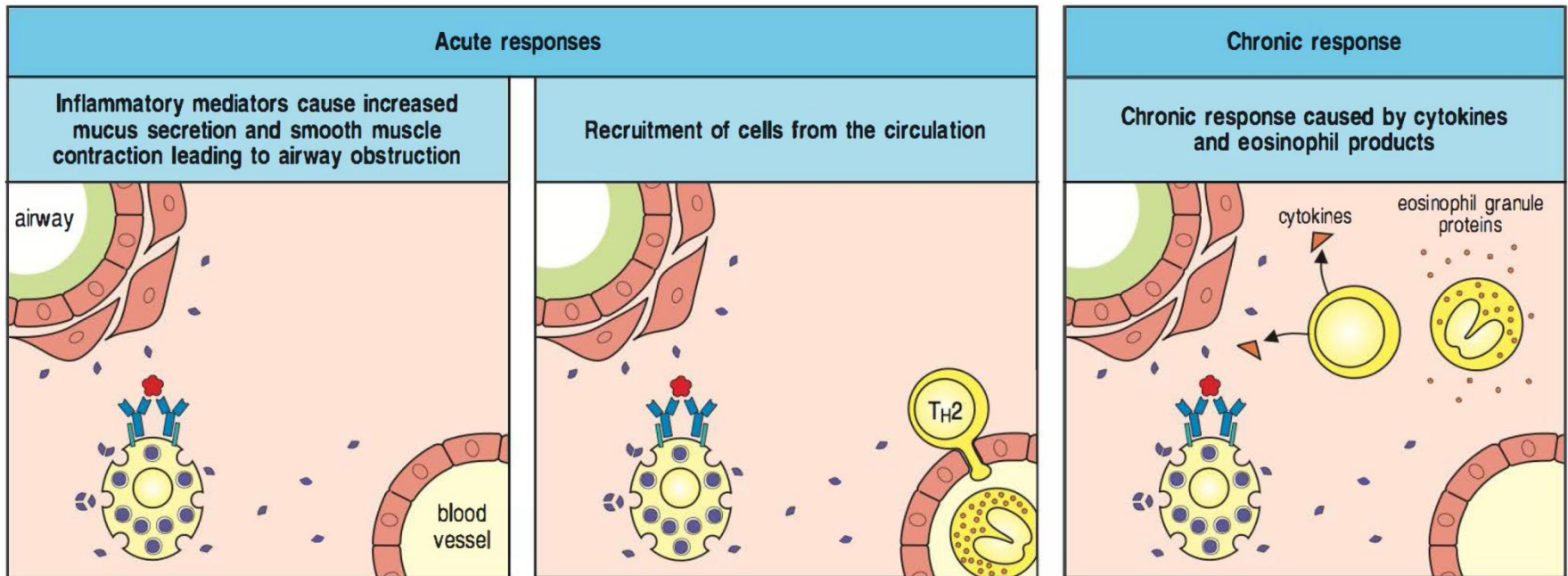
Allergic Reactions Require Prior Exposure to Allergen



Degranulation of Mast Cells



Acute Asthma causes chronic inflammation in airways



Molecules Released by Mast Cell Activation

Class of product	Examples	Biological effects
Enzyme	Tryptase, chymase, cathepsin G, carboxypeptidase	Remodel connective tissue matrix
Toxic mediator	Histamine, heparin	Toxic to parasites Increase vascular permeability Cause smooth muscle contraction Anticoagulation
Cytokine	IL-4, IL-13	Stimulate and amplify T _H 2-cell response
	IL-3, IL-5, GM-CSF	Promote eosinophil production and activation
	TNF- α (some stored preformed in granules)	Promotes inflammation, stimulates cytokine production by many cell types, activates endothelium
Chemokine	CCL3	Attracts monocytes, macrophages, and neutrophils
Lipid mediator	Prostaglandins D ₂ , E ₂ Leukotrienes C4, D4, E4	Smooth muscle contraction Chemotaxis of eosinophils, basophils, and T _H 2 cells Increase vascular permeability Stimulate mucus secretion Bronchoconstriction
	Platelet-activating factor	Attracts leukocytes Amplifies production of lipid mediators Activates neutrophils, eosinophils, and platelets

IgE-mediated allergic reactions			
Syndrome	Common allergens	Route of entry	Response
Systemic anaphylaxis	Drugs Serum Venoms	Intravenous (either directly or following oral absorption into the blood)	Edema Vasodilation Tracheal occlusion Circulatory collapse Death
Acute urticaria (wheal-and-flare)	Insect bites Allergy testing	Subcutaneous	Local increase in blood flow and vascular permeability
Allergic rhinitis (hay fever)	Pollens (ragweed, timothy, birch) Dust-mite feces	Inhaled	Edema of nasal mucosa Irritation of nasal mucosa
Allergic asthma	Danders (cat) Pollens Dust-mite feces	Inhaled	Bronchial constriction Increased mucus production Airway inflammation
Food allergy	Shellfish Milk Eggs Fish Wheat	Oral	Vomiting Diarrhea Pruritus itching Urticaria (hives) Anaphylaxis (rarely)

Case of Frank Morgan

14 year-old, wheezing for 2 weeks, history of wheezing and respiratory problems

Family History of asthma (Genetic causes)= Atopy

Normal CBC except for eosinophilia

Elevated serum IgE

Reduced peak flow rate (PFR), Reduced expiratory volume in the first second (FEV1)

Multiple treatments

Skin prick test 2 weeks later for inhalants.

Started on immunotherapy for pollens and dust mites.

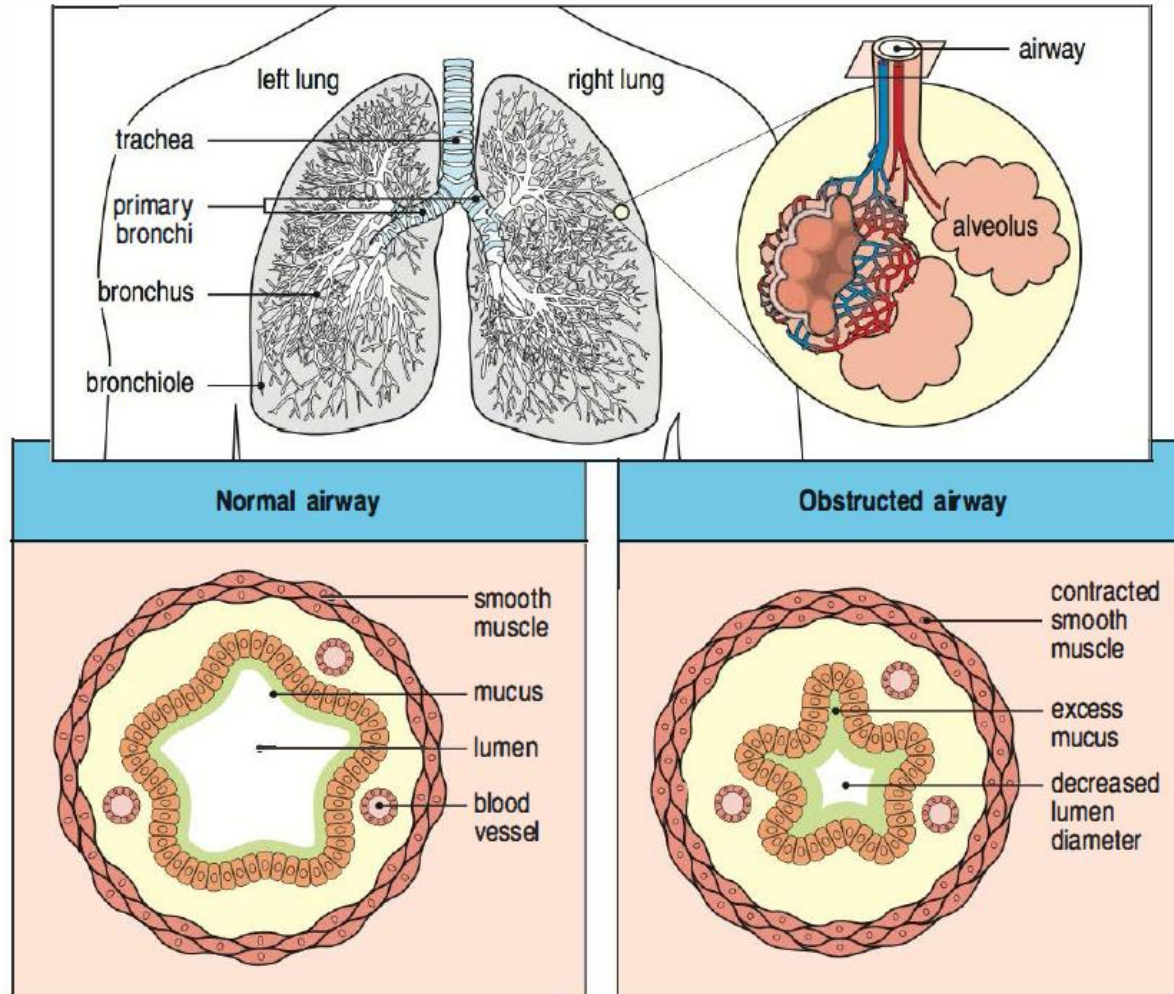


Ragweed

Saline

Histamine

Obstruction of Airways in Chronic Asthma



Treatment of Asthma

Three classes of drugs commonly used:

1- Disodium Cromoglycate: Reduced airway irritability by inhibiting the release of chemical mediators such as: Histamine. (Immediate and late phases)

2- β_2 agonists (Albuterol): binds to receptors on the surface of bronchial smooth muscle cells causing them to relax. (Immediate phase)

3- Corticosteroids ex: (Oral prednisone and inhaled beclomethasone)

Inhibit cells involved in airway inflammation (Late Phase)

Minimize exposure to allergens, Immunotherapy

Explain and Hyperinflation of lungs in X-rays and chest pain?

Narrowing of airways in asthma causes air to be trapped in lungs (Hyperinflation). Breathing at high residual lung volume is more work to muscles and increased energy expenditure= Chest tightness

Why didn't Frank's asthma improve with bronchodilators?

Chronic Allergic asthma is more due to inflammation than bronchoconstriction.

Several members of Frank's family are atopic, what's the basis for this familial predisposition?

Atopy maps to chromosome 5q in areas coding for IL-4, IL-5, and IL-9

How do we explain eosinophilia in blood and nasal/bronchial secretions of patients with allergic rhinitis and asthma?

IL-4, IL-5 production by Th2, eosinophil production by T cells and bronchial epithelial cells

24 hours after skin prick test, Frank called hospital worried that redness and swelling had recurred at several skin test sites, explain?

Late-phase response characterized by cellular infiltrates.

Frank wants to buy a rabbit as a pet and demands a skin-prick test for rabbits, should we go along with his idea?

No. Atopic people are prone to developing IgE Abs to numerous allergens. Skin prick result is irrelevant.

How can immunotherapy help alleviate Frank's allergies?

s.c. Injection of high doses of allergens is thought to favour antigen presentation of cells producing IL-12. Favours a Th1 response, IFN- γ production, and a skew towards IgG production.

IgG competes with IgE, and Th1 cytokine profile blocks further IgE production.

Why don't atopic children develop allergic reactions against immunization with protein antigens such as tetanus toxoid?

s.c. Injection of large doses of antigens favours a Th1 response.

Th2 responses usually arise from small, highly soluble protein molecules that are presented to the immune system via mucosal route at very low doses.