Treatment of Bronchial Asthma

Definition of Asthma

- ***Chronic inflammatory disorder with intermittent narrowing of the airways.***
- **Or a *condition characterized by wide variations, over short periods of time, in the resistance to flow in the intrapulmonary airways.***

Factors in the Treatment Strategy

- Asthma is a ***chronic*** condition
- The goal of therapy is ***normal function***
- The Condition is ***heterogeneous*** in terms of:
  - Cause or trigger mechanism.
  - Extent of bronchoconstriction *and*
  - Degree of inflammation.
- The course is ***unpredictable.***
- Therapy must be ***individualized.***

Risk of Not Treating Asthma

- Poor or no control of the patient's asthma.
- Accelerated decline in the function of the patient's lungs
- Increased number of attacks of asthma.
- Poorer response to therapy if started late.
- Increased mortality from asthma.

Goals of Therapy in Asthma

- Minimal symptoms even during sleep.
- No, or infrequent, acute episodes.
- No ED visits or missed days in school or work.
- Rare need for beta-agonist inhaler therapy.
- No limitation of activities – even sports.
- Peak flow rate variability less than 20%.
- No or minimal adverse effects from drugs.

Pathogenesis

- **Early Asthmatic Response:**

Allergens can provoke IgE production.

The tendency to produce IgE is genetically determined.

Re-exposure to the allergen causes antigen-antibody interaction on the surface of the mast cells leading to:

Release of stored mediators.

Synthesis of other mediators.

Also, activation of neural pathways

Prevented by bronchodilators.

Pathogenesis

- **Late Asthmatic Response:**

4-5 hours later.

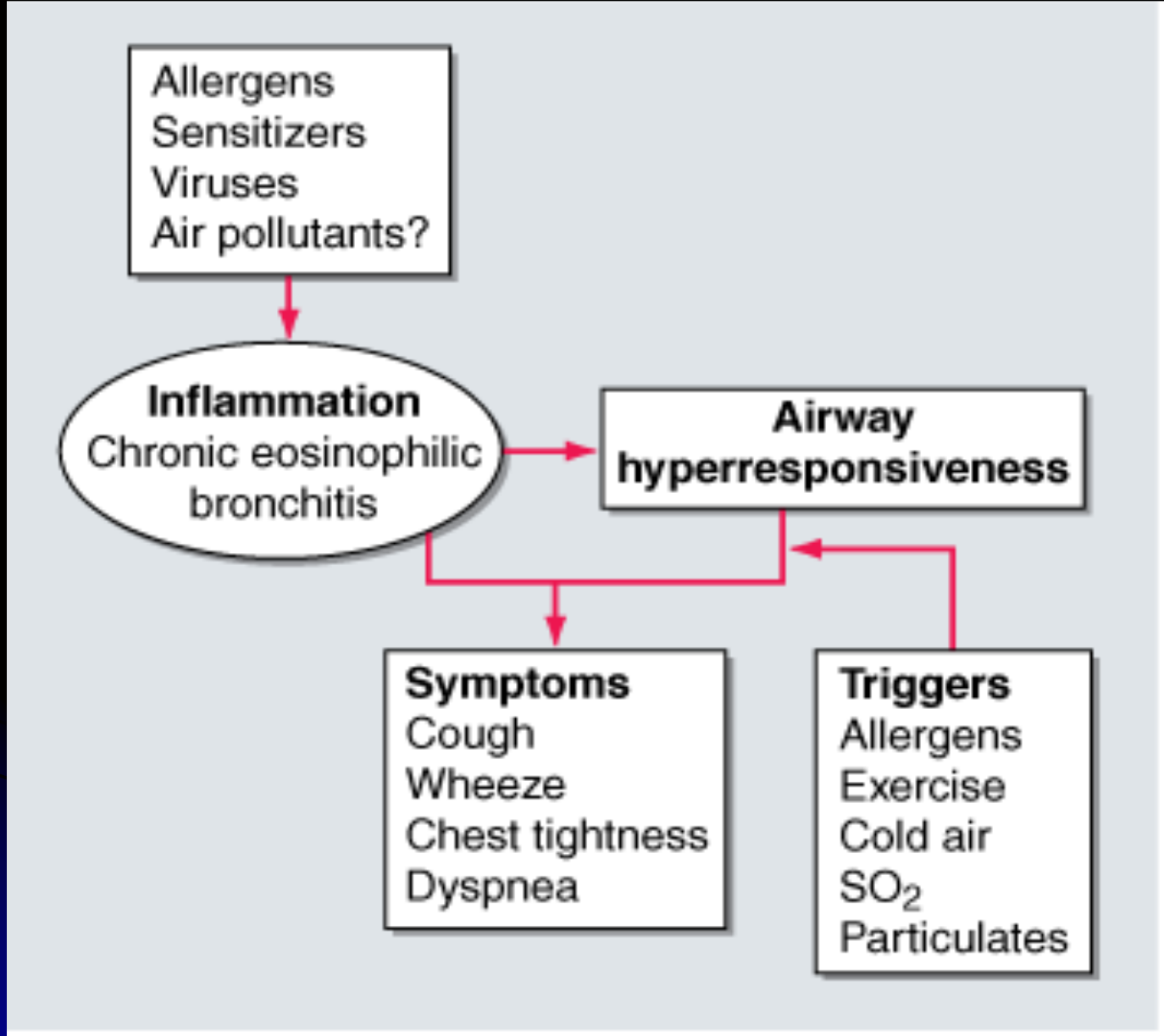
More sustained phase of bronchoconstriction.

Influx of inflammatory cells and an increase in bronchial responsiveness.

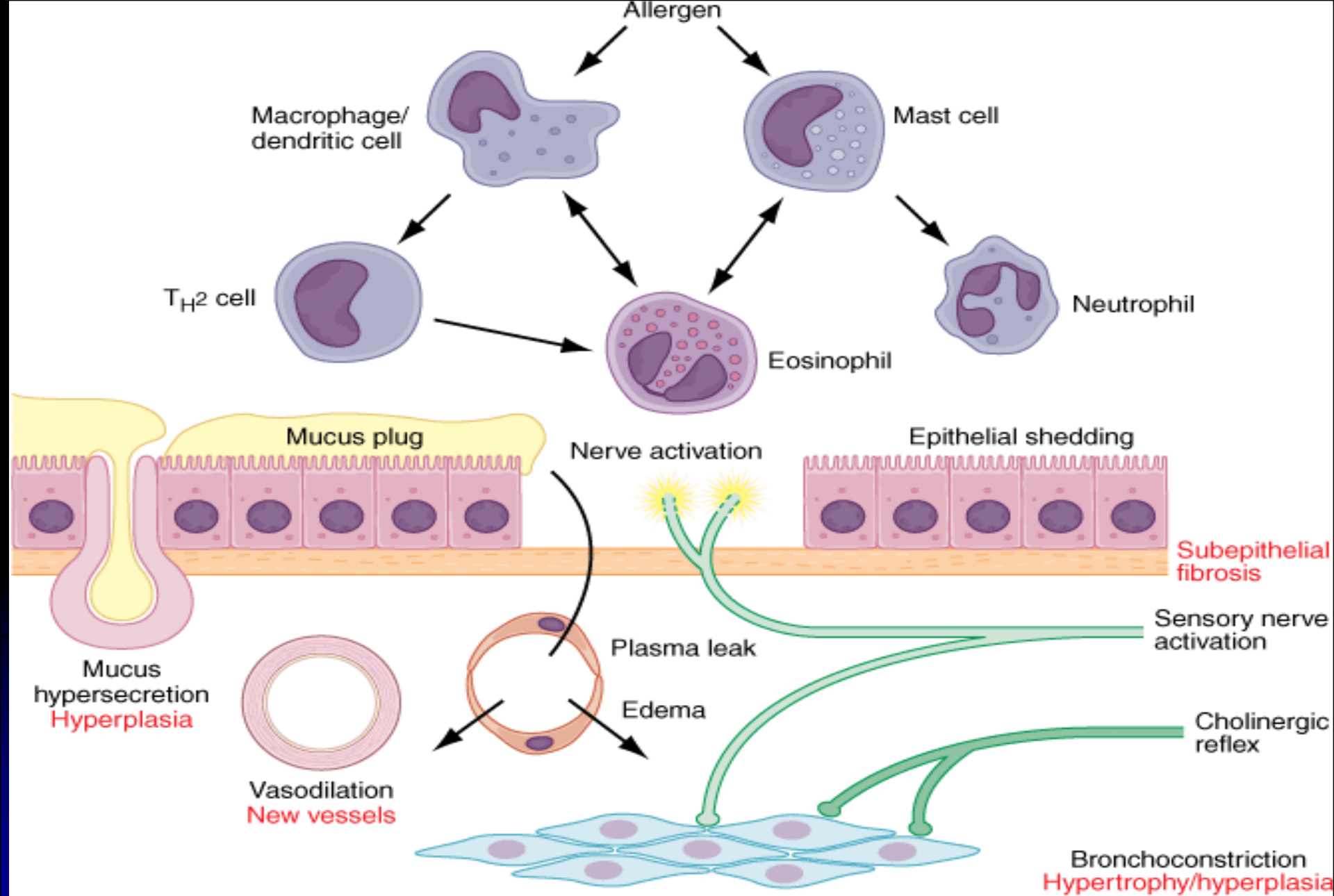
The mediators here are cytokines produced by TH2 lymphocytes, especially interleukins 5, 9, and 13.

These will stimulate IgE production by B lymphocytes, and directly stimulate mucus production.

Prevented by corticosteroids.



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J
Harrison's Principles of Internal Medicine, 17th Edition: http://www.accessmedicine.com



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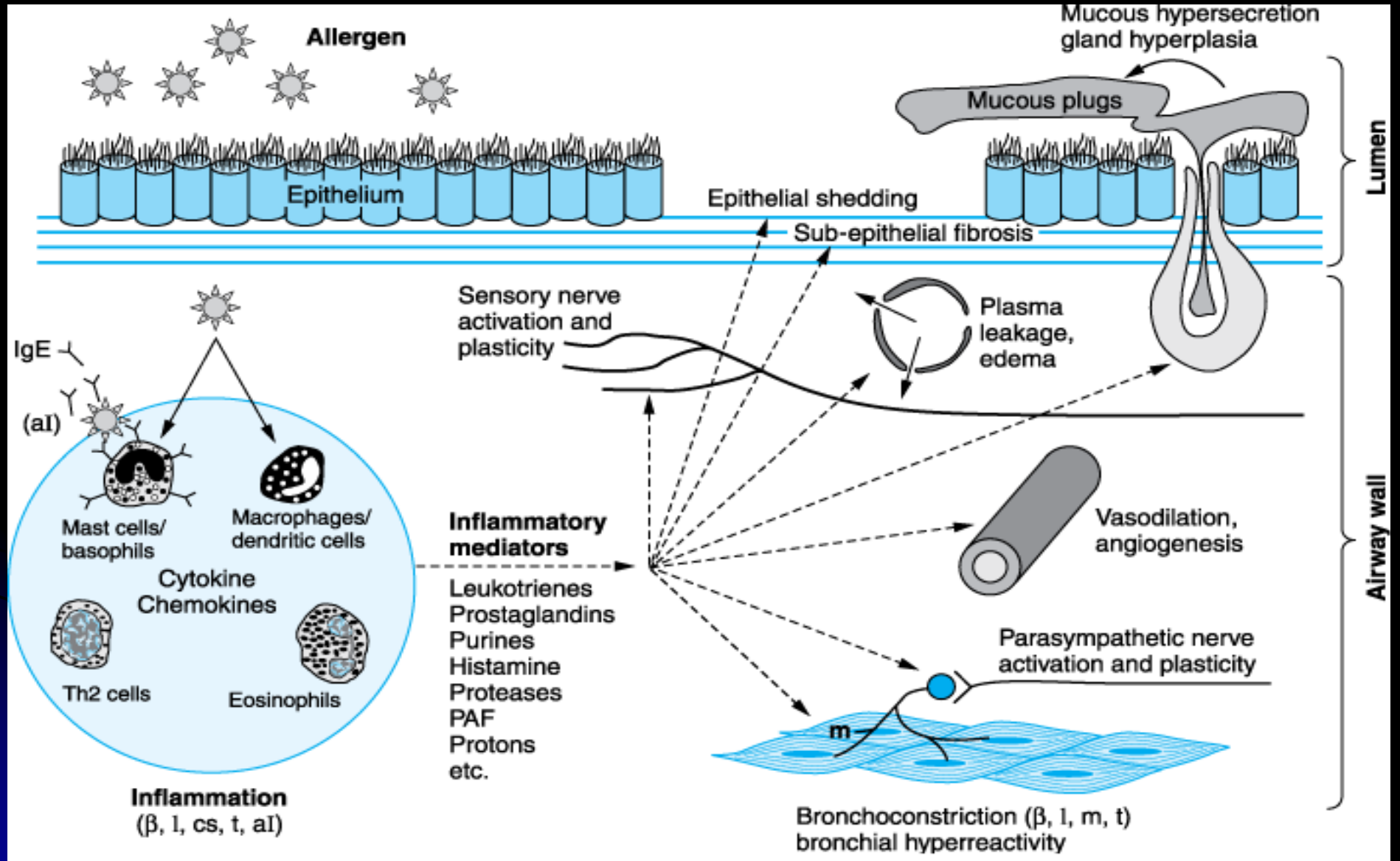
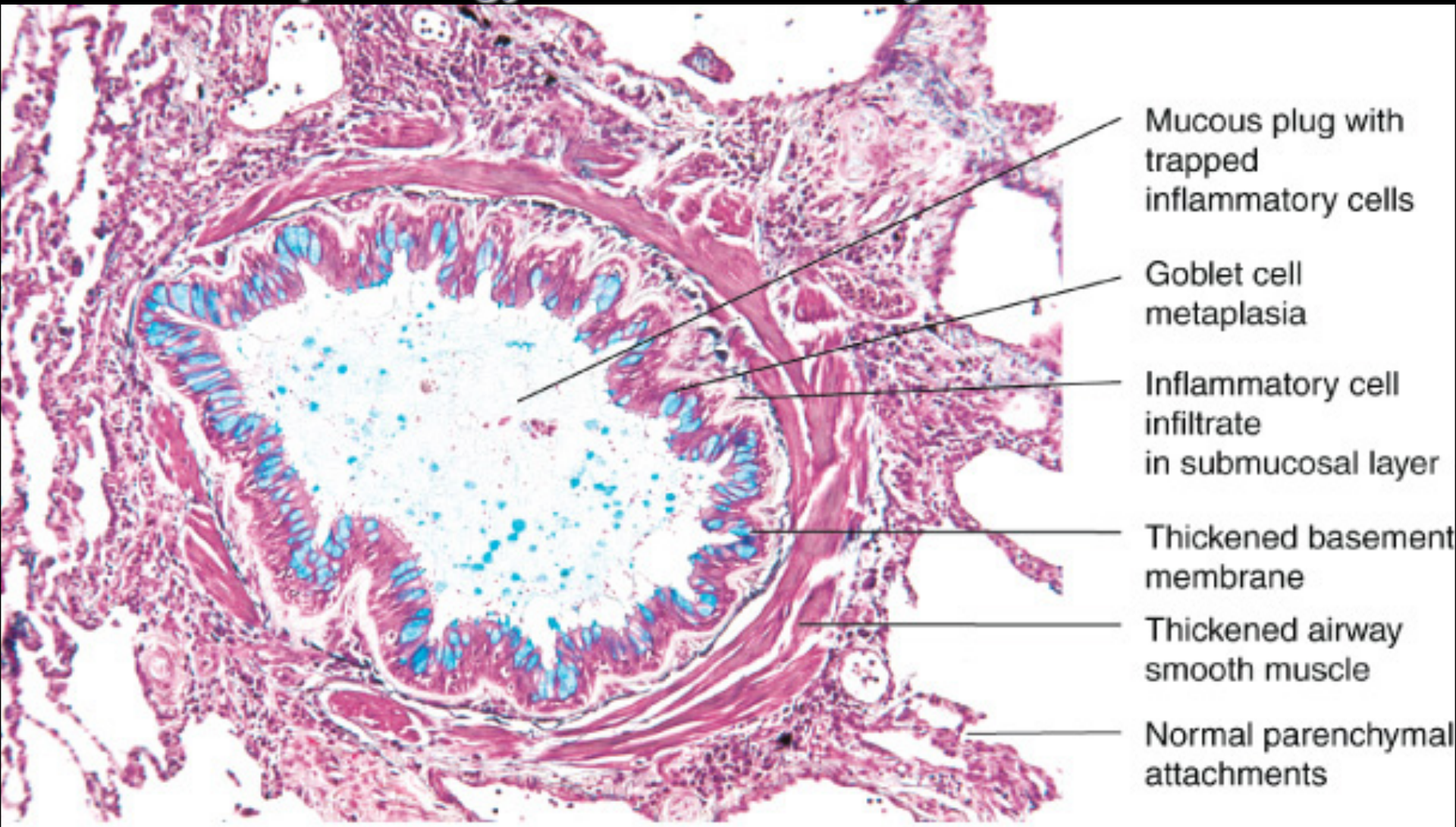
Simplified view of allergic inflammation in the airways.



Histopathology of a small airway in fatal asthma



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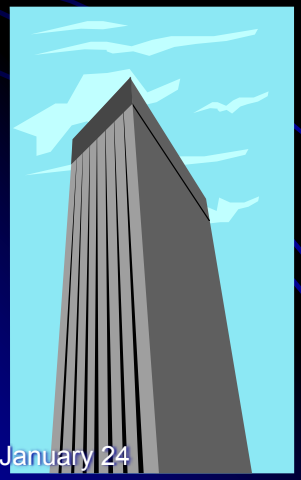
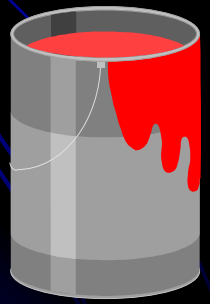
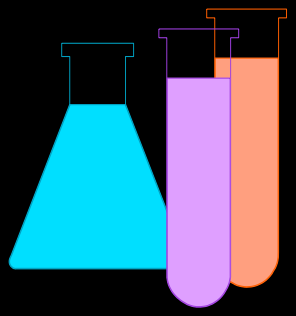
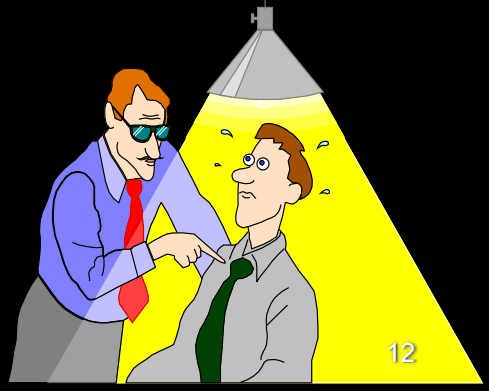
Asthma Triggers









Asthma Triggers

- Exercise / cold air
- Cigarette smoke
- Stress / anxiety situations
- Animal dander's (cats, dogs etc..)
- Allergens (grass, trees, molds, cockroach)
- Pollutants (sulfur dioxide, ozone, etc…)
- Fumes/toxic substances
- Medications (ASA, NSAID’s, others)

Diagnosis of Asthma - Subjective

- ✓ **Cough** - usually in spasms and to the point of vomiting - nighttime worse than daytime.
- ✓ **Cough** may follow exposure to cold air, exercise, a URI (common cold), or allergen
- ✓ **Dyspnea** > cough or wheezing > sputum.
- ✓ **Past history** of bronchiolitis as a child
- ✓ **Family history** of asthma is common

Diagnosis of Asthma - Objective

- Diminished Peak Expiratory Flow Rate (PEFR)
- Reduced mean and Forced Expiratory Flow Rate (FEFR)
- Reversibility with Bronchodilators
- Heightened response to Methacholine Test.
- Increase in expired Nitric Oxide
- Increase in Inflammatory Mediators and their metabolic products in body fluids

Myths and Misconceptions

- ✓ Patient and physician "Steroid-o-phobia".
- ✓ Asthma is an emotional illness.
- ✓ Asthma is an acute disease.
- ✓ Asthma medications are addictive.
- ✓ Asthma medications become ineffective if they are used regularly.
- ✓ Asthma is not a fatal illness / It does not kill.

Survey of the changing therapy of asthma by decade

1960's

Aminophylline, Epinephrine, Ephedrine

1970's

Beta-agonists, Theophyllines, Beclomethasone, Cromolyn, Ipratropium

Survey of the changing therapy of asthma by decade

1980's

Beta-agonists, Inhaled Corticosteroids, Cromolyn, Ipratropium

1990's

Inhaled Corticosteroids, Beta-agonists, Theophylline, Leukotriene Inhibitors

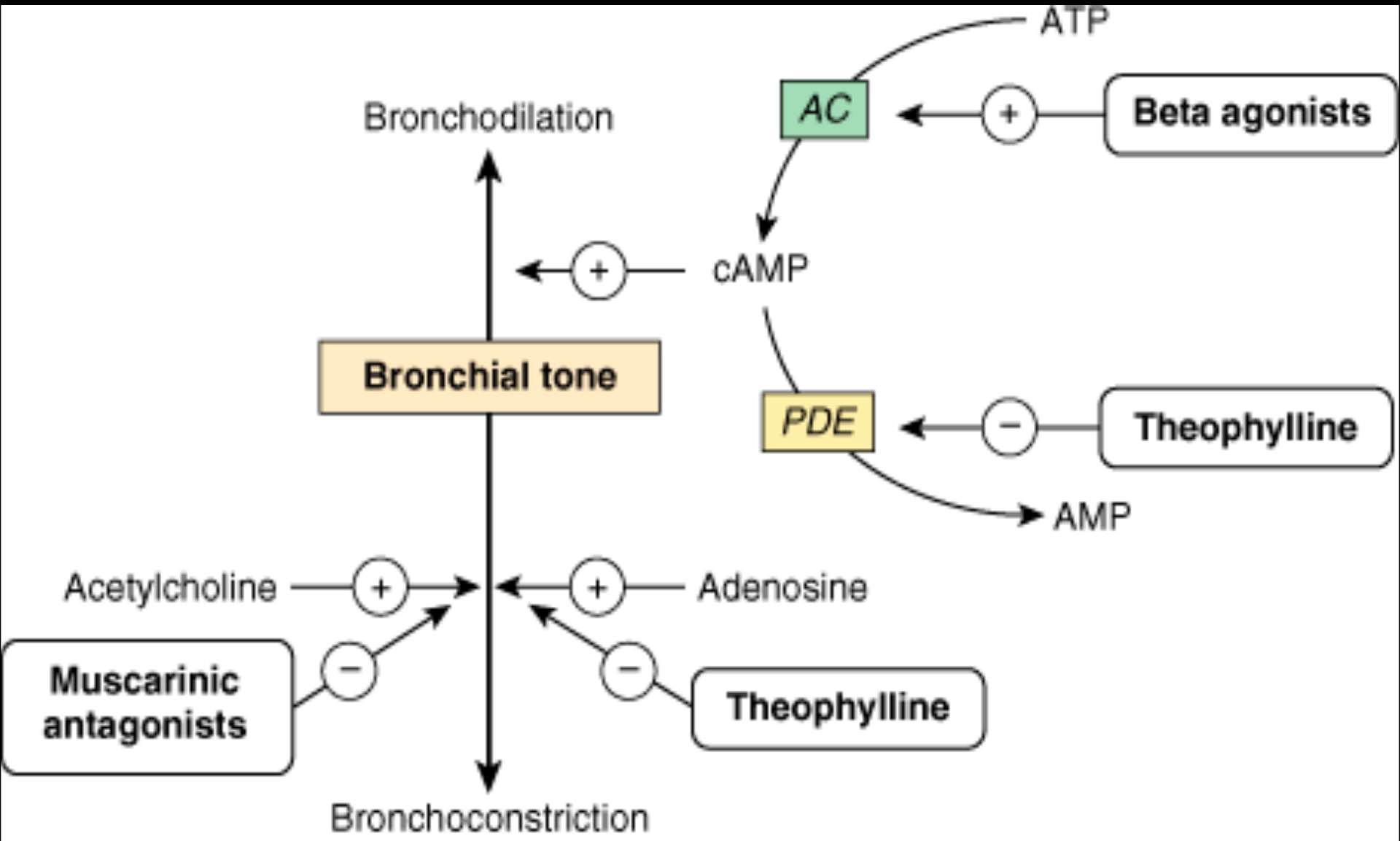
Survey of the changing therapy of asthma by decade

2000's

Corticosteroids + LABA, LTRAs, Theophylline, Cromolyn, Ipratropium, Tiotropium

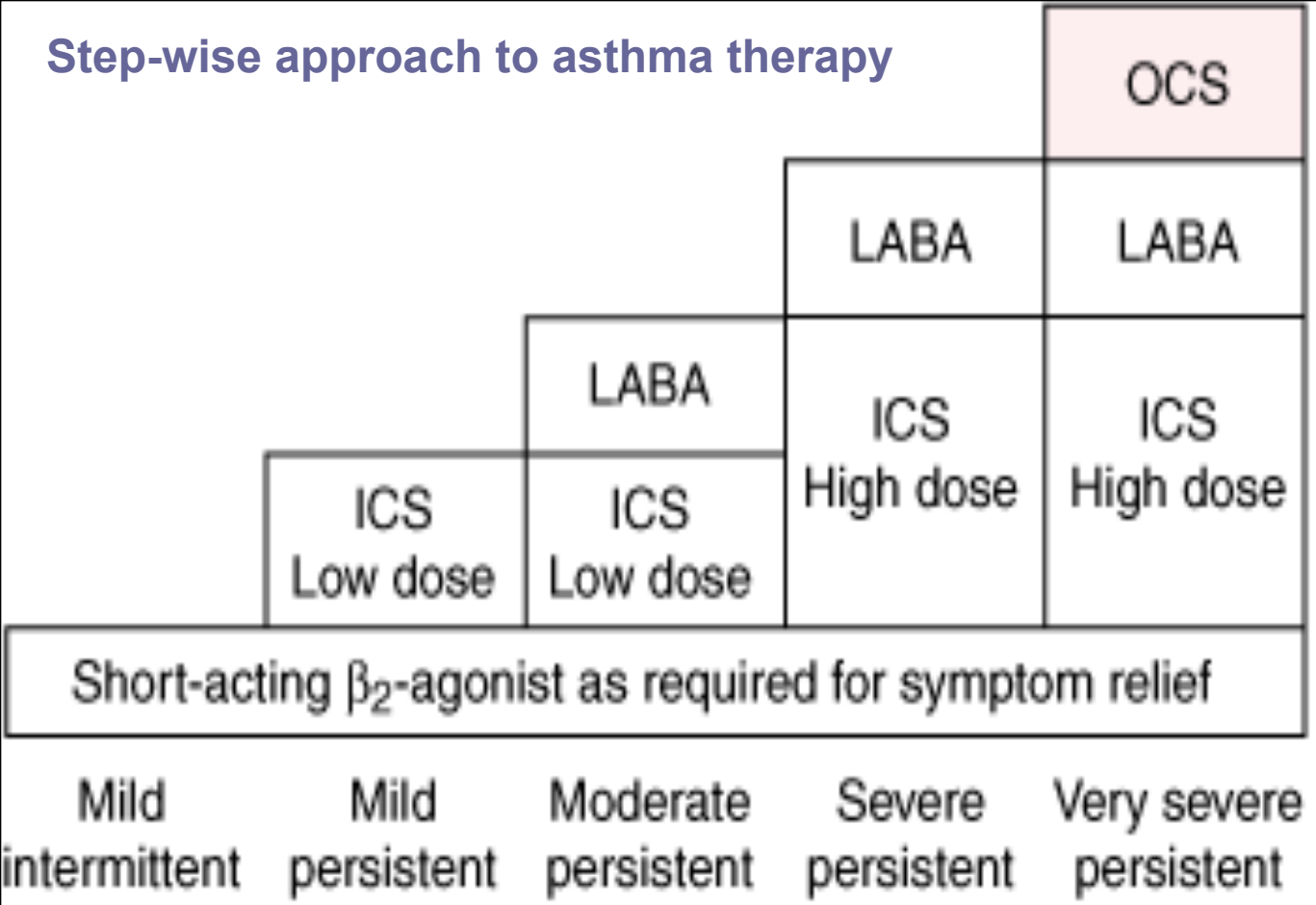
2010's

Prevention including gene therapy.



Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 11th Edition*: http://www.accessmedicine.com

Step-wise approach to asthma therapy



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Inhaled Long-acting Beta-2 Agonists (LABA)
Inhaled Corticosteroids(ICS)
(OCS) oral Corticosteroids

Relievers / Controllers

- **Quick relief medications:**
  - Inhaled Short acting Beta-2 Agonists
  - Inhaled Anticholinergics
  - Systemic Corticosteroids
- **Long-term control medications:**
  - Topical (inhaled) Corticosteroids
  - Inhaled Cromolyn Na and Nedocromil
  - Oral Methylxanthines (Theophyllines)
  - Inhaled Long-acting Beta-2 Agonists (LABA)
  - Oral Leukotriene modifiers (LTRA)