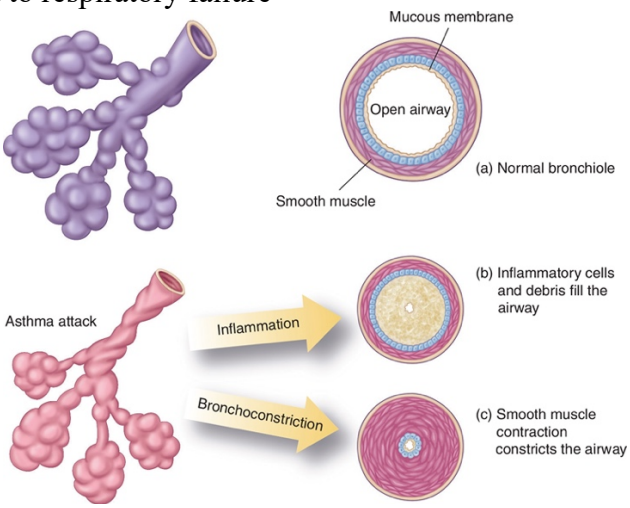
Pharmacotherapy of Asthma, Pulmonary Disorders, Vaccines, Inflammation

Physiology of the Lower Respiratory Tract

- The physiology of the respiratory system involves two main processes: perfusion and ventilation.
- Physiology of the Lower Respiratory Tract
  - Nervous system controls ventilation by changing diameter of bronchioles.
    - Sympathetic nervous system
      - Causes bronchiolar muscle to relax and bronchodilation to occur
    - Parasympathetic nervous system
      - Causes bronchiolar smooth muscle to contract, airway diameter to narrow, and bronchoconstriction to occur

Pathophysiology of Asthma

- Asthma is a chronic disease that has both inflammatory and bronchospasm components.
- Asthma
  - Chronic inflammation, resulting in:
    - Increase in airway edema
    - Increased mucous secretions
- Bronchospasm
  - Inflammatory condition in airway makes smooth muscle hyper-responsive to stimuli
    - Air pollutants &Allergens
    - Chemicals and food
    - Respiratory infections
    - Stress & Exercise
- Status asthmaticus
  - Emergency situation in which asthma unresponsive to drug treatment
  - May lead to respiratory failure



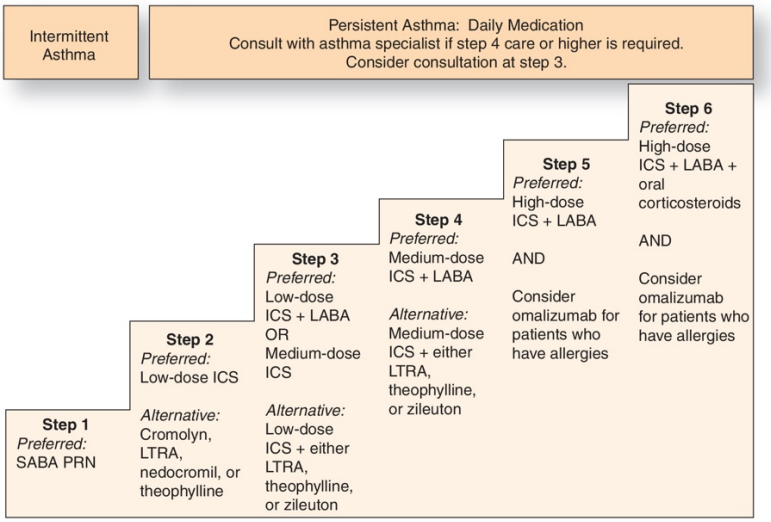
- Changes in the bronchioles during an asthma attack: (a) Normal open bronchiole. (b) Inflammation plugs the airway. (c) Bronchoconstriction narrows the airway.

Administration of Pulmonary Drugs via Inhalation

- Inhalation is a common route of administration for pulmonary drugs because it delivers drugs directly to their sites of action and have fewer side effects
- Advantage of aerosol therapy
  - Delivers drugs directly to site of action through particles suspended in a gas
- Delivery route
  - Metered-dose inhaler (MDI)
    - Use of spacer recommended
  - Dry powder inhaler (DPI)
  - Nebulizer (or small volume nebulizer)

Principles of Asthma Pharmacotherapy

- The goals of asthma pharmacotherapy are to terminate acute bronchospasms and to reduce the frequency of asthma attacks.
- National Asthma Education and Prevention Program (NAEPP) recommended three strategies of asthma management
  - Incorporate four components of care:
    - Medications
    - Patient education
    - Environmental control measures
    - Management of comorbidities
  - Use a step based therapy
    - Initiate therapy based on asthma severity
    - Adjust therapy based on asthma control
  - Two simple classes of asthma drugs
    - Quick-relief medications
    - Long-term control medications



Key: ICS, inhaled corticosteroid; LABA, long-acting inhaled beta$_2$-agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$ agonist

Stepwise approach for managing asthma in adults and patients 12 years and older. Adapted from Figure 4.5 in *Expert Panel Report 3 (EPR3): Guidelines for the Diagnosis and Management of Asthma* by the National Asthma Education Prevention Program, coordinated by the National Heart, Lung, and Blood Institute of the National Institutes of Health, 2007. Retrieved from http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm

Principles of Asthma Pharmacotherapy

Beta$_2$-adrenergic agonists

- are the most effective drugs for relieving acute bronchospasm. Use for acute attacks
- Beta$_2$-adrenergic agonists
  - Most frequently prescribed drugs for treatment of bronchoconstriction
  - Activate sympathetic nervous system, resulting in bronchodilation
  - Classified by duration of action
    - Short-acting beta agonists (SABAs)
      - Rapid onset of action, last 2 to 6 hours
      - Used for acute attacks
    - Long-acting beta agonists (LABAs)
      - Slow onset, lasts up to 12 hours
      - Public health advisory by FDA warned of danger of taking for acute episode.
  - Available in PO, inhaled, and parenteral formulations
- Prototype drug: *Albuterol* (Proventil HFA, Ventolin HFA, VoSpire ER)
  - Therapeutic classification
    - Bronchodilator
  - Pharmacologic classification
    - Beta$_2$-adrenergic agonist
  - Therapeutic effects and uses
    - Relieving and preventing bronchospasm of asthma
  - Mechanism of action
    - Selectively binds to beta$_2$-adrenergic receptors in bronchial smooth muscle to cause bronchodilation
  - Adverse effects
    - Palpitations and tachycardia
    - Headaches
    - Throat irritation
    - Tremor
    - Nervousness and restlessness
    - Insomnia
    - Dry mouth
  - Serious adverse effects
    - Chest pain
    - Paradoxical bronchospasm – opposite/paradoxical effect
    - Allergic reactions
    - Principles of Asthma Pharmacotherapy
  - Contraindications/precautions
    - Hypersensitivity to the drug
    - History of tachyarrhythmias
    - Prolonged QT interval
    - Coronary artery disease
    - Hypertension

- Drug interactions
  - Beta blockers
  - MAOIs
  - Thyroid hormone
    - Herbal/food: caffeine
- Pregnancy category C

Drugs similar to Albuterol (Proventil HFA, Ventolin HFA, VoSpire ER)

- *Arformoterol* (Brovana)
  - LABA (long term)
  - COPD, chronic bronchitis, and emphysema
- *Formoterol* (Foradil, Perforomist)
  - LABA (Long term)
  - Asthma, COPD
- *Indacaterol (*Arcapta Neohaler)
  - Maintenance bronchodilator for COPD, chronic bronchitis, emphysema
- *Levalbuterol* (Xopenex)
  - Isomer of albuterol
  - For acute bronchospasm
  - Pregnancy category C
- *Metaproterenol*
  - SABA available by oral route
  - Pregnancy category C
- *Olodaterol* (Striverdi Respimat)
  - LABA
  - COPD
  - Pregnancy category C
- *Salmeterol* (Serevent)
  - LABA
  - Bronchospasm of COPD
  - Pregnancy category C
- *Terbutaline*
  - Given PO
  - May take 30 or more minutes to act
  - Bronchospasm
  - Pregnancy category B

The inhaled anticholinergics are used for preventing bronchospasm.

- Inhaled anticholinergics
  - Cholinergic blockers or antagonists
  - Alternative bronchodilators
  - *Ipratropium* (Atrovent)
    - Short-acting drug
  - *Aclidinium* (Tudorza Pressair)
  - *Umeclidinium* (Incruse Ellipta)

- *Tiotropium* (Spiriva)
  - Newer, long-acting anticholinergics
- Inhaled anticholinergics
  - Similar actions to those of beta-adrenergic agonists
    - Drugs from two classes may be combined to produce greater and more prolonged bronchodilation
    - Pharmaceutical companies developed inhalants that combine an anticholinergic and a beta agonist into a single canister.

Prototype drug: *Ipratropium* (Atrovent)

- Therapeutic classification
  - Bronchodilator
- Pharmacologic classification
  - Anticholinergic
- Therapeutic effects and uses
  - Relieving and preventing bronchospasm of asthma and COPD
- Mechanism of action
  - Blocks cholinergic receptors in bronchial smooth muscle
- Adverse effects
  - Dry mouth
  - Nausea
  - GI distress
  - Irritation of upper respiratory tract
  - Bitter taste
- Serious adverse effects
  - Paradoxical acute bronchospasm
  - Can worsen glaucoma
- Contraindications/precautions
  - Hypersensitivity to ipratropium, soya lecithin, soybeans, peanuts
  - Closed-angle glaucoma
  - Urinary tract obstruction
- Drug interactions
  - Other anticholinergics
- Pregnancy category B
- Treatment of overdose
  - Unlikely because very little of the drug is absorbed

Corticosteroids

- Inhaled corticosteroids are the most effective drugs for the long-term control of asthma.
- Corticosteroids
  - Most potent natural anti-inflammatory substances known
  - Inhaled corticosteroids
    - First-line drugs for prevention of asthmatic attacks and management of chronic asthma
  - Oral corticosteroids

        - Short-term management of acute asthma attacks
- Prototype drug: *Beclomethasone* (Beconase AQ, Qvar)
    - Therapeutic classification
        - Anti-inflammatory
    - Pharmacologic classification
        - Corticosteroid
    - Therapeutic effects and uses
        - Asthma
        - Allergic rhinitis
    - Mechanism of action
        - Reduces inflammation and immune response, thus decreasing frequency of asthma attacks
    - Adverse effects
        - Hoarseness
        - Dry mouth
        - Changes in taste
    - Serious adverse effects
        - Development of cataracts (long-term therapy)
        - Corticosteroid toxicity
        - Growth inhibition in children
    - Contraindications/Precautions
        - Hypersensitivity to the drug
    - Drug interactions
        - No clinically significant drug interactions
    - Pregnancy category C

- Drugs similar to Beclomethasone (Beconase AQ, Qvar)
    - B*udesonide* (Pulmicort)
        - Intranasal (allergic rhinitis)
        - Nebulizer (asthma)
        - PO capsule (Crohn's disease)
        - Pregnancy category B

Mast cell stabilizers

- are used for the prophylaxis of asthma and act by preventing the release of histamine.
- Mast cell stabilizers
    - Serve limited but important role in prophylaxis of asthma and COPD
    - Prevent release of histamine and other inflammatory mediators in airways
    - Cromolyn is the only mast cell stabilizer approved for respiratory indications
- Prototype drug: *Cromolyn*
    - Therapeutic classification
        - Anti-inflammatory
        - for Asthma and COPD
    - Pharmacologic classification
        - Mast cell stabilizer

    - Therapeutic effects and uses
        - Preventing inflammation in COPD and asthma
    - Mechanism of action
        - Stabilizes mast cells, thus preventing inflammatory response
    - Adverse effects
        - Bronchospasm
        - Cough
        - Pharyngeal irritation
        - Local burning and stinging
    - Contraindications/precautions
        - Hypersensitivity to the drug
        - Discontinue if eosinophilia develops
    - Drug interactions
        - None known
    - Pregnancy category B

The leukotriene modifiers,

- which are primarily used for asthma prophylaxis, act by reducing the inflammatory component of asthma.
- Leukotriene modifiers
    - One of newest classes of asthma management drugs
    - Reduce inflammation by either blocking enzyme that controls leukotriene synthesis or by blocking leukotriene receptors
    - Delayed onset
        - Not for acute attacks
    - Not considered bronchodilators, though they do reduce constriction indirectly
    - Available by PO route only
- Prototype drug: *Montelukast* (Singulair)
    - Therapeutic classification
        - Agent for asthma prophylaxis and allergic rhinitis
    - Pharmacologic classification
        - Leukotriene modifier
    - Therapeutic effects and uses
        - Long-term control of asthma symptoms
        - Not for relief of acute asthma attack
        - Relief of symptoms for allergic and seasonal rhinitis
    - Mechanism of action
        - Blocks leukotriene receptors in airways, which prevents airway edema and inflammation
    - Adverse effects
        - Headache
        - Rhinitis
        - Influenza
        - Abdominal pain
    - Severe adverse effects

        - Aggression
        - Anxiety
        - Depression
        - Suicidal ideation
        - Memory impairment
    - Principles of Asthma Pharmacotherapy
    - Contraindications/precautions
        - Potential to interact with substrates that inhibit this enzyme
            - Carbamazepine
            - Erythromycin
            - Azole antifungals
        - Herbal/food: St. John's wort may decrease the effectiveness of theophylline.
    - Pregnancy category B
    - Treatment of overdose
        - Supportive
    - Nursing responsibilities
        - Refer to Nursing Practice Application for Patients Receiving Pharmacotherapy for Asthma and COPD
        - Principles of Asthma Pharmacotherapy

Drugs similar to Montelukast (Singulair)

- *Roflumilast* (Daliresp)
    - Chronic management of COPD
    - Not for acute bronchospasms
    - Pregnancy category C
- *Zafirlukast* (Accolate)
    - Prophylaxis of persistent, chronic asthma
    - Pregnancy category B
- *Zileuton* (Zyflo CR)
    - PO drug
    - Alternate drug in prophylaxis of persistent, chronic asthma
    - Pregnancy category C

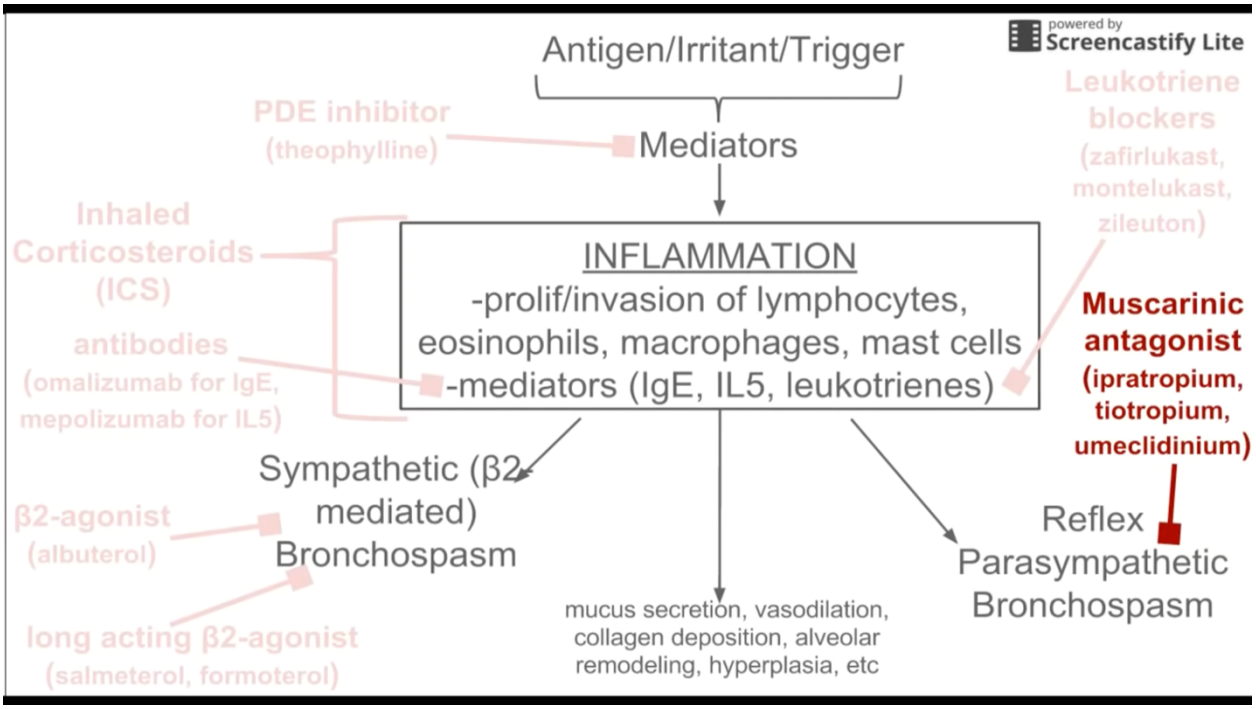
Methylxanthines

- were once the mainstay of asthma pharmacotherapy but are now rarely prescribed for that disorder.
- Methylxanthines
    - Use reserved for long-term management of persistent asthma that is unresponsive to beta agonists or inhaled corticosteroids
    - Risk of toxicity
    - Significant interactions with other drugs
    - Modest bronchodilators
    - Chemically related to caffeine
        - Share stimulant effect

  - Not available for inhalation
- Prototype drug: *Theophylline*
  - Therapeutic classification
    - Bronchodilator
  - Pharmacologic classification
    - Methylxanthine
    - Principles of Asthma Pharmacotherapy

Monoclonal antibodies

- are a newer form of therapy for the prevention of asthma symptoms.
- Monoclonal antibodies
  - *Omalizumab* (Xolair), a monoclonal antibody, is first biologic therapy for asthma.
    - Approved in 2003 for treatment of allergic rhinitis and moderate to severe persistent asthma that cannot be controlled with inhaled corticosteroids
    - Prevents inflammation and dampens response to allergens
    - Available only by subcutaneous route
    - Black box warning regarding potential for anaphylaxis
    - Pregnancy category has not been established
  - *Reslizumab* (Cinqair)
    - Binds to interleukin-5 (IL-5)
    - Reserved for severe, persistent asthma in patients ages 18 years and older who have eosinophilic phenotype
    - Black box warning regarding potential for anaphylaxis



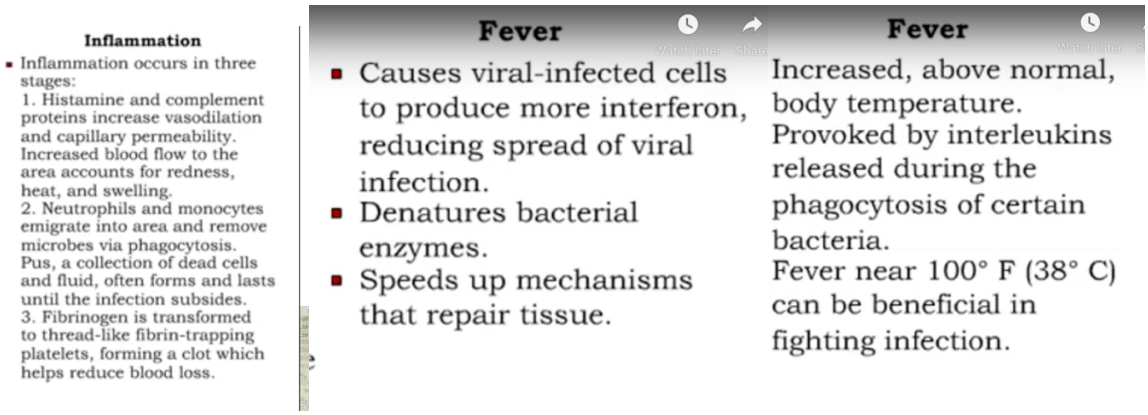
Nursing Interventions for Asthma and Other Pulmonary Disorders

Best treatment of fevers and colds in children

For treatment of fever or pain in children, consider giving your child infants' or children's over-the-counter fever and pain medications such as **acetaminophen (Tylenol, others)** or ibuprofen (Advil, Motrin, others). These are safer alternatives to aspirin.

Clear out mucus, Add moisture (Humidifier, saline spray), Give fluids (Pedialyte), treat fever and pain (if older than 6mo Tylenol or ibuprofen, do not give aspirin if under 16 years old, do not use cough medications for children under 6, raise head of the bed to relieve congestion, avoid irritants.

Inflammation provides early protection by keeping infection at site of pathogen or trauma



Asthma medication – contraindications and dietary factors

High fat intake and low fiber intake have been associated with airway inflammation and worsened lung function in asthmatic patients.

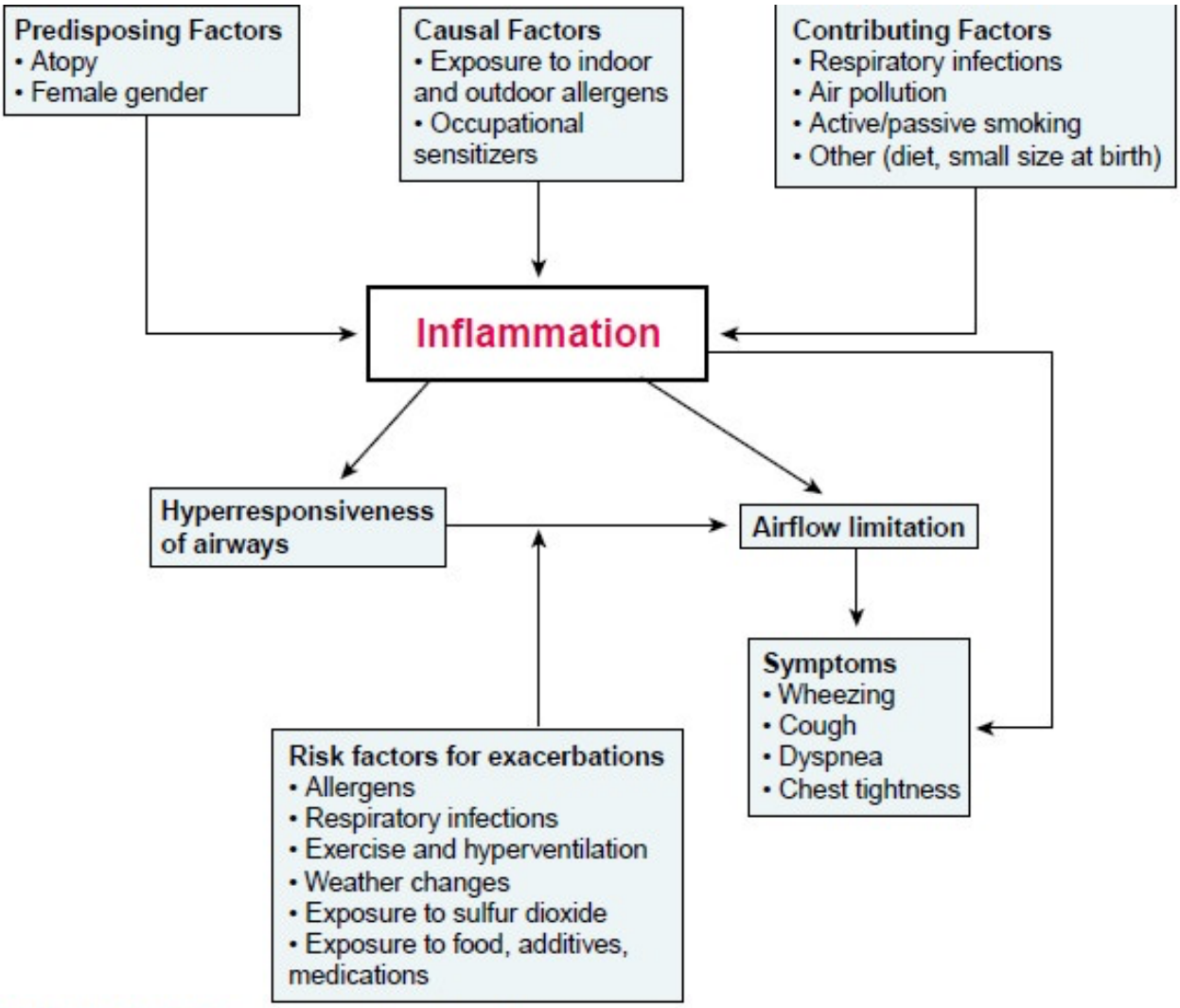


FIGURE 24-6 Pathophysiology of asthma. Adapted from materials developed for the Global Initiative for Asthma (GINA): Global Strategy for Asthma Management and Prevention, National Institutes of Health–National Heart, Lung, and Blood Institute, revised 2002.

Aspirin components and actions.

Aspirin causes several different effects in the body, mainly the reduction of inflammation, analgesia (relief of pain), **the prevention of clotting**, and the reduction of fever. Much of this is believed to be due to decreased production of prostaglandins and TXA2. Aspirin induced asthma is a side effect

Vaccines

How they work: Influenza vaccine trigger a immune response by mimicking an immune infection usually use a inactive viral components (NA and HA), given by IM injection. In blood stream they meet immune response (B-cells, macrophages, t-cells). Mechanism of action: Phagocytosis, break it into smaller components. T-cells now recognize the foreign antigen. T-cells activated and become cytotoxic t-cells, suppressor t-cells, or helper t-cells. Helper t-cells express HA receptors to help antibody generation and memory b-cell activation. B-cells ingest hemagglutinin (HA) and then present it on their surface. When helper T-cells interact with these b-cells they secrete lymphokines. They trigger activated b-cell proliferation which become memory b-cells (aid in future immune response) or plasma cells (produce hemagglutinin antibodies specific to virus in the vaccine). When exposed to the live virus this hemagglutinin later blocks viral attachment of live virus to host epithelial cells.

Immunizations and types of vaccines

1. Birth -hepatitis B
2. 2-6mo: pediatrix, diptheria, tetanus, pertussis, polio, hepatitis, prevar, HIB
3. 6mo + influenza
4. 12 months: MMRV, Measles, mumps, rubella, hepatitis A, Prevanar, Varicella, chicken pox
5. 15mo: [Depheria, tetnus, pertussis (Booster)],
6. 18mo: Hepatitis A
7. 4-6 years: [Depheria, tetnus, pertussis], Second MMR, Last polio
8. 9 years: HPV