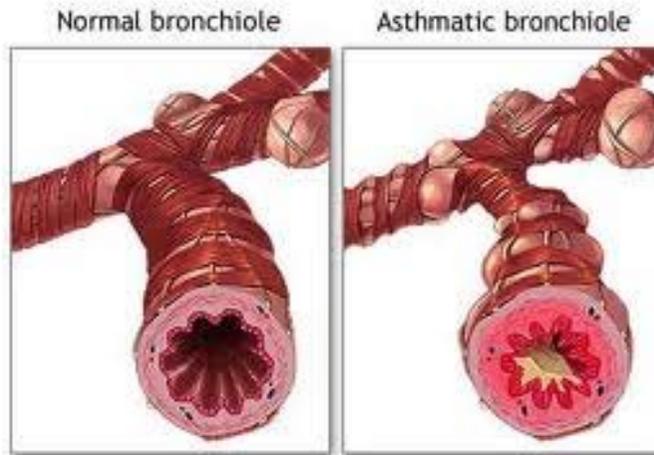
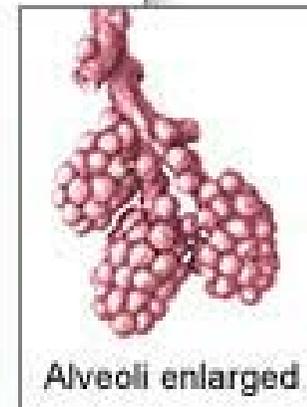
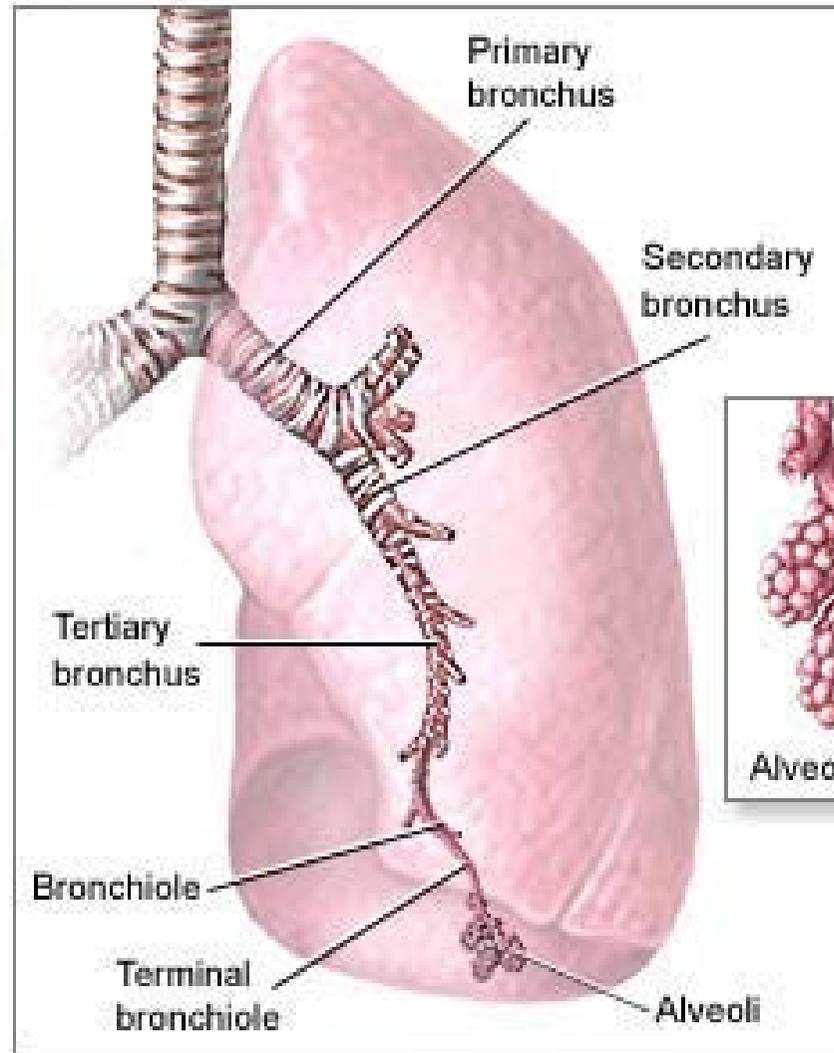
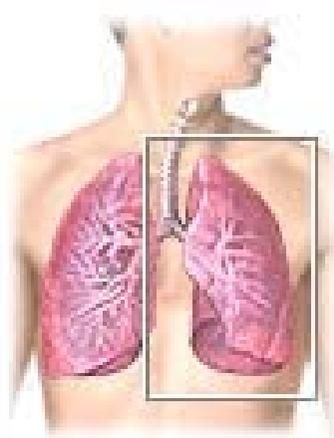


Bronchial Asthma



Sections

- Epidemiology
- Pathophysiology
- Diagnosis
- Medications
- Approach to Management
- Treatment Steps
- Special Situations
- Acute Asthma



What is Asthma....Definition (GINA)

- A **chronic inflammatory disorder** of the airways in which many cells and cellular elements play a role.
- The chronic inflammation is associated with **airway hyper-responsiveness** that leads to **recurrent episodes of wheezing , breathlessness, chest tightness** and coughing particularly at night or early morning.
- These episodes are usually associated with widespread, but **variable airflow obstruction** within the lung that is **often reversible** either spontaneously or with treatment

Asthma classification

- Child-onset asthma(extrinsic asthma)
 - Associated with **atopy**
 - **IgE** directed against common **environmental antigens** (house-dust mites, animal proteins, fungi)
 - **Viral wheezing** Infants/children, allergy/allergy history associated with **continuing asthma** through childhood

- **Adult-onset asthma**

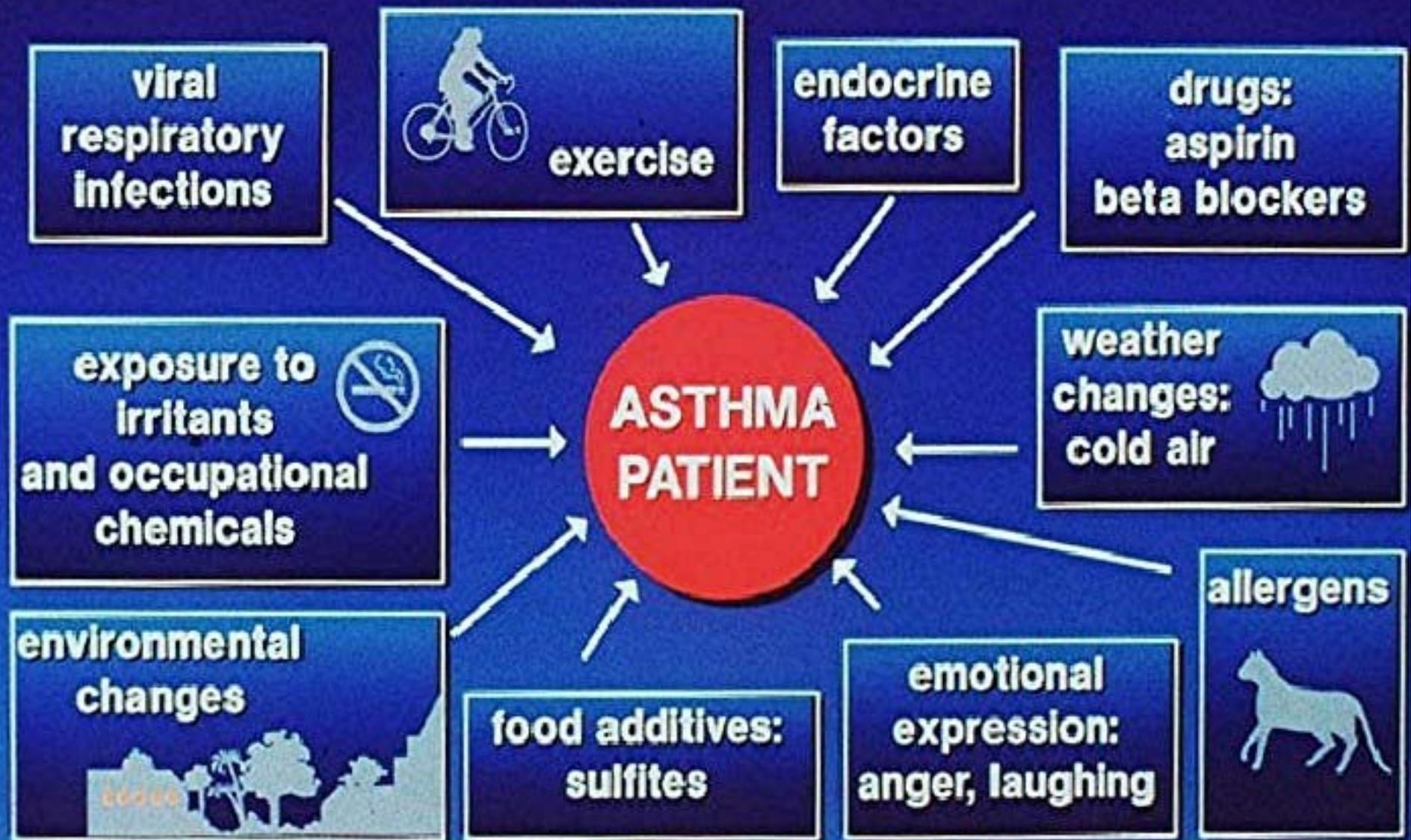
- Many situations
- Allergens important
- Non-IgE asthma have nasal polyps, sinusitis, aspirin sensitivity or NSAID sensitivity
- Idiosyncratic asthma less understood

- Adult-onset asthma
 - Occupational exposure
 - animal products, biological enzymes, plastic resin, wood dusts, metal
 - removal from workplace may improve symptoms although symptoms persist in some

Prevalence

- Most common chronic disease currently affecting appx. 300 million people worldwide.
- 10- 12% of adults
- 15 % of children
- Most have periodic wheezing attacks separated by symptom-free period.
- attacks can last minutes to days, and can become dangerous if the airflow becomes severely restricted.

PRECIPITATING OR AGGRAVATING FACTORS



Epidemiology

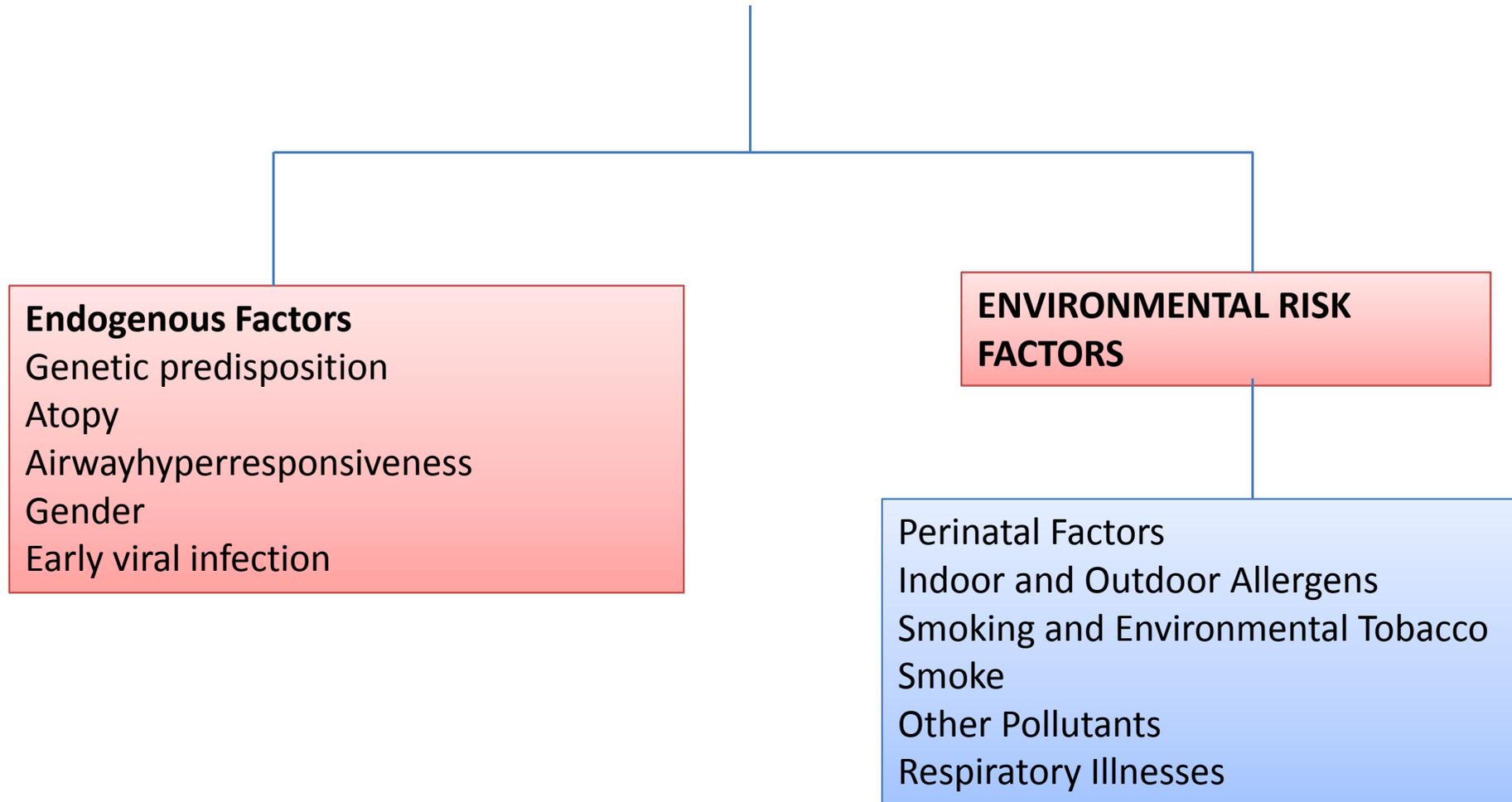
- Age –any (peak age 3 yrs)
- Current asthma prevalence is higher among
 - children than adults
 - boys than girls(2:1)
 - women than men
 - Children grow out of their asthma
- Asthma morbidity and mortality is higher among
 - African Americans than Caucasians

Risk Factors for Developing Asthma: Genetic Characteristics

Atopy

- Major risk factor
- The body's predisposition to develop an antibody (IgE) in response to exposure to environmental allergens
- Can be measured in the blood
- Includes allergic rhinitis, asthma, hay fever, and eczema

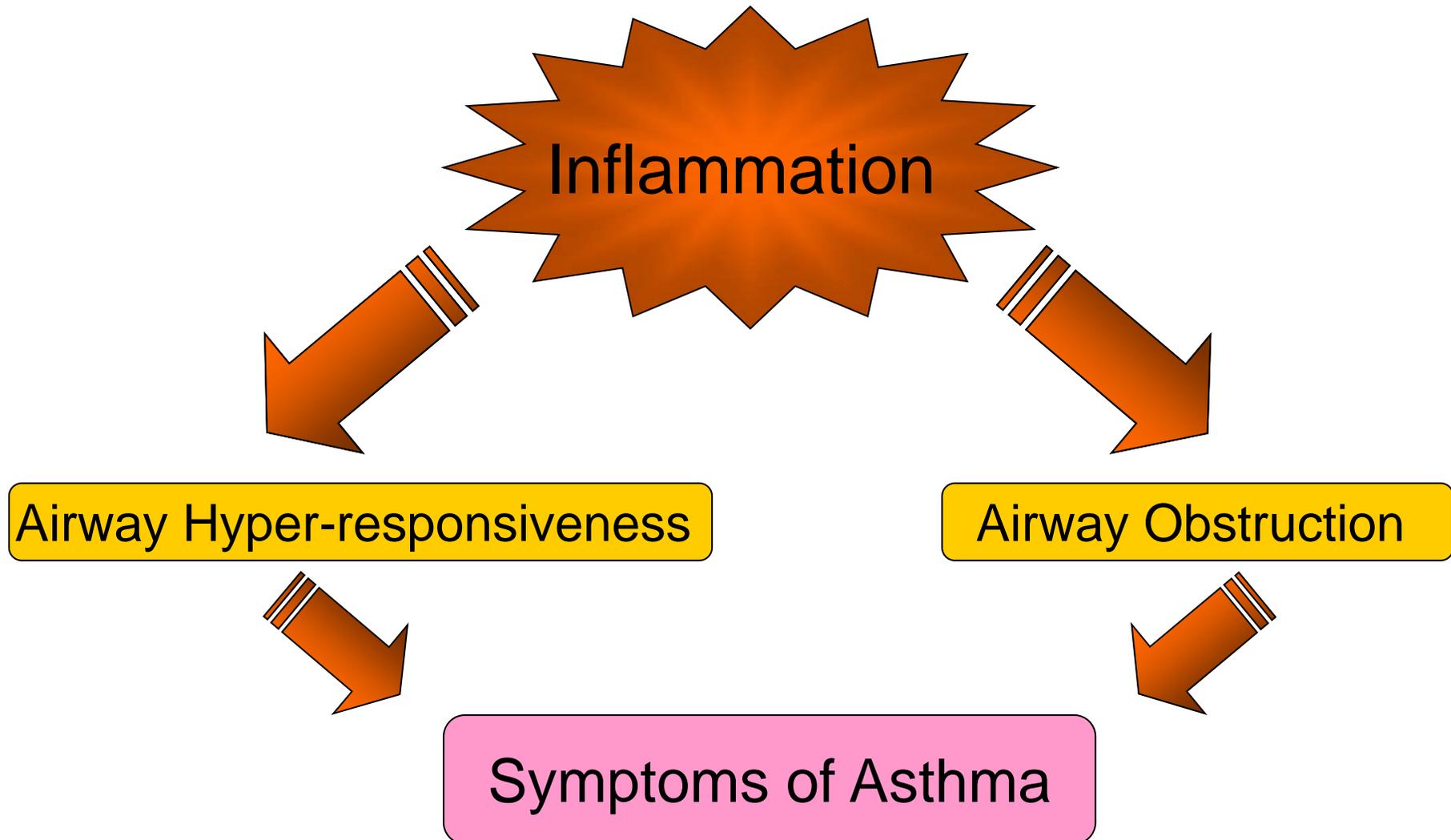
Causes/ Risk factors



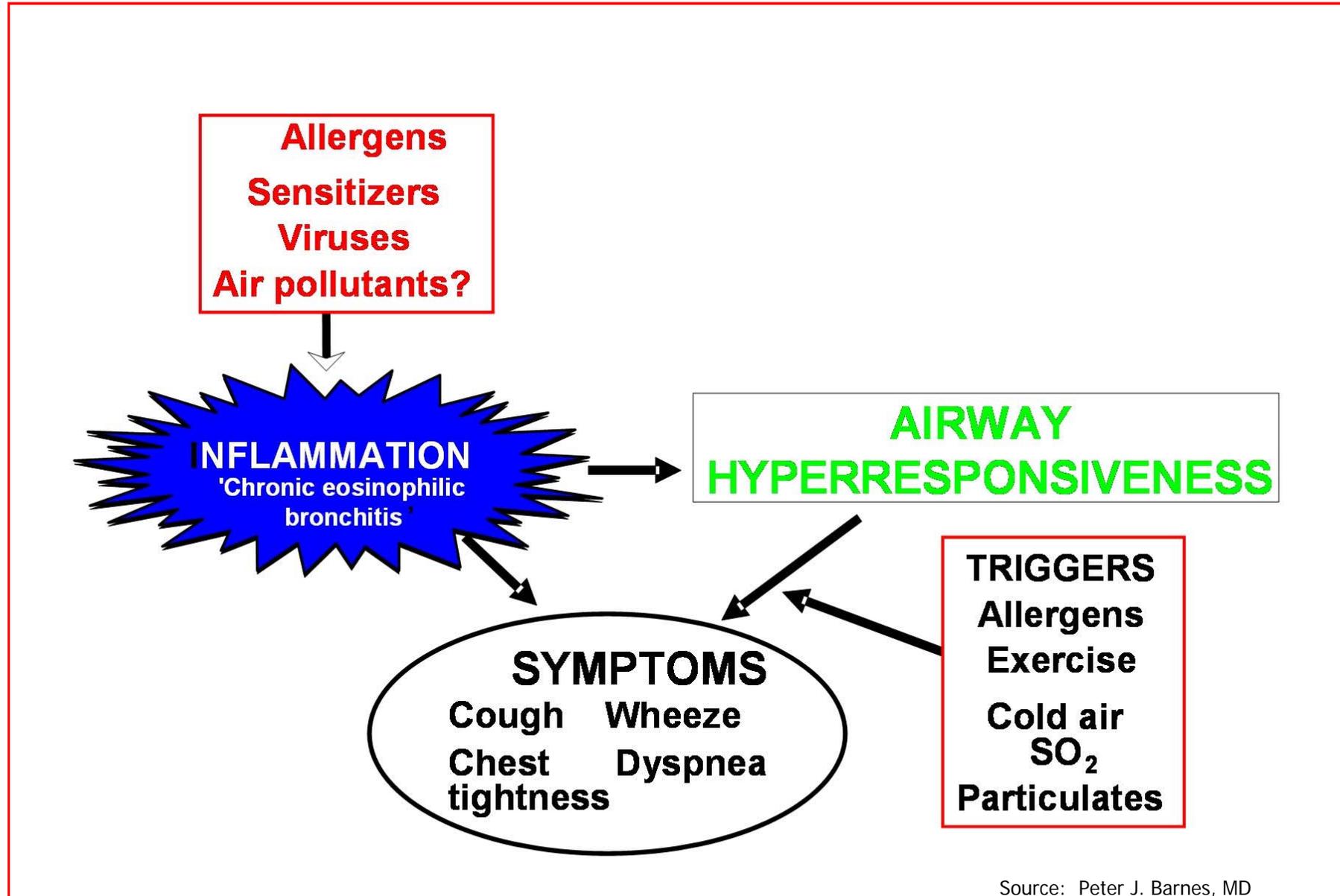
Triggers

- Allergens
- URI
- Exercise and hyperventilation
- Cold air
- Sulphur dioxide and irritant gases
- Drugs(β -blocker, aspirin)
- Stress
- Irritants (household sprays, paintfumes)

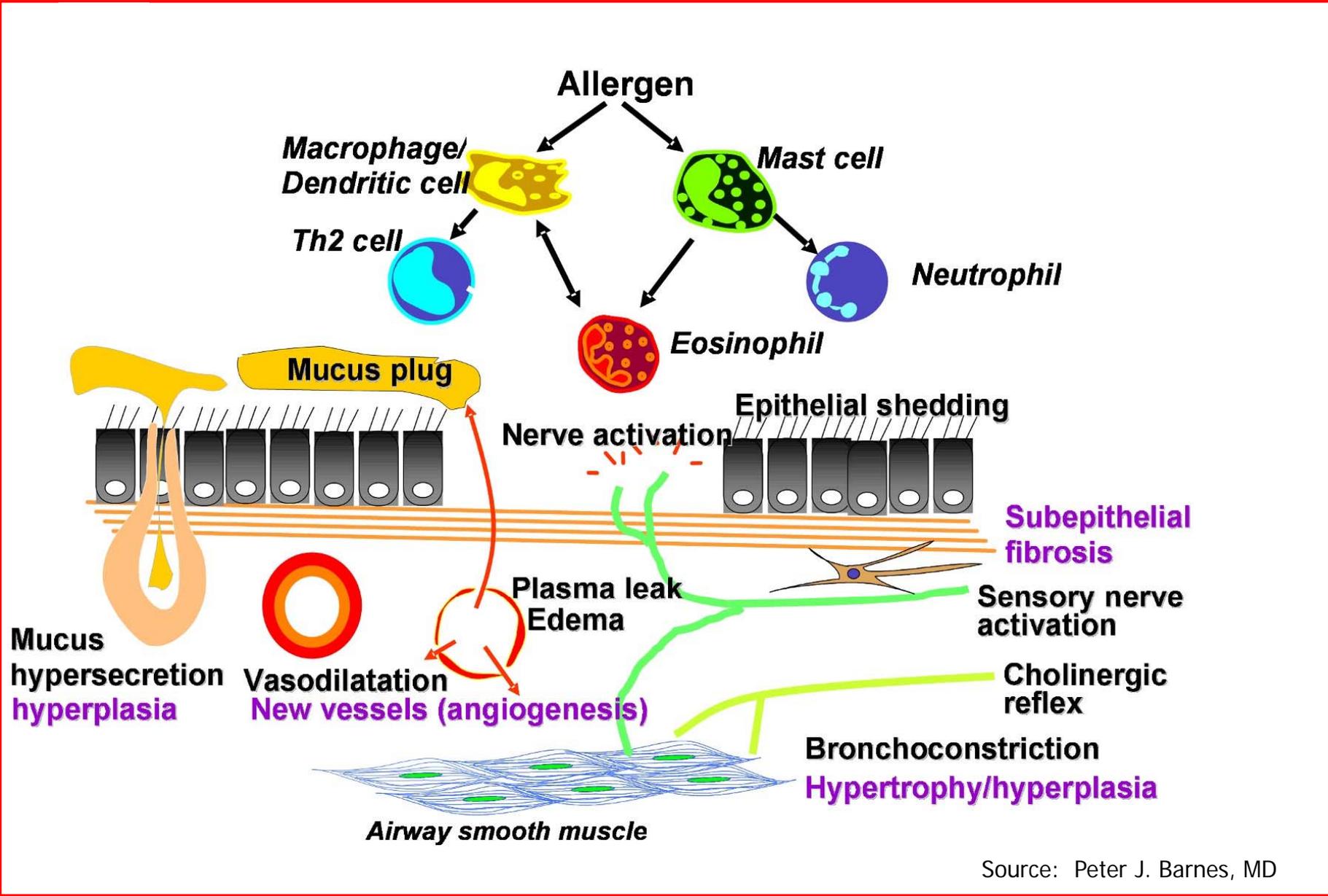
Pathology of Asthma



Mechanisms: Asthma Inflammation

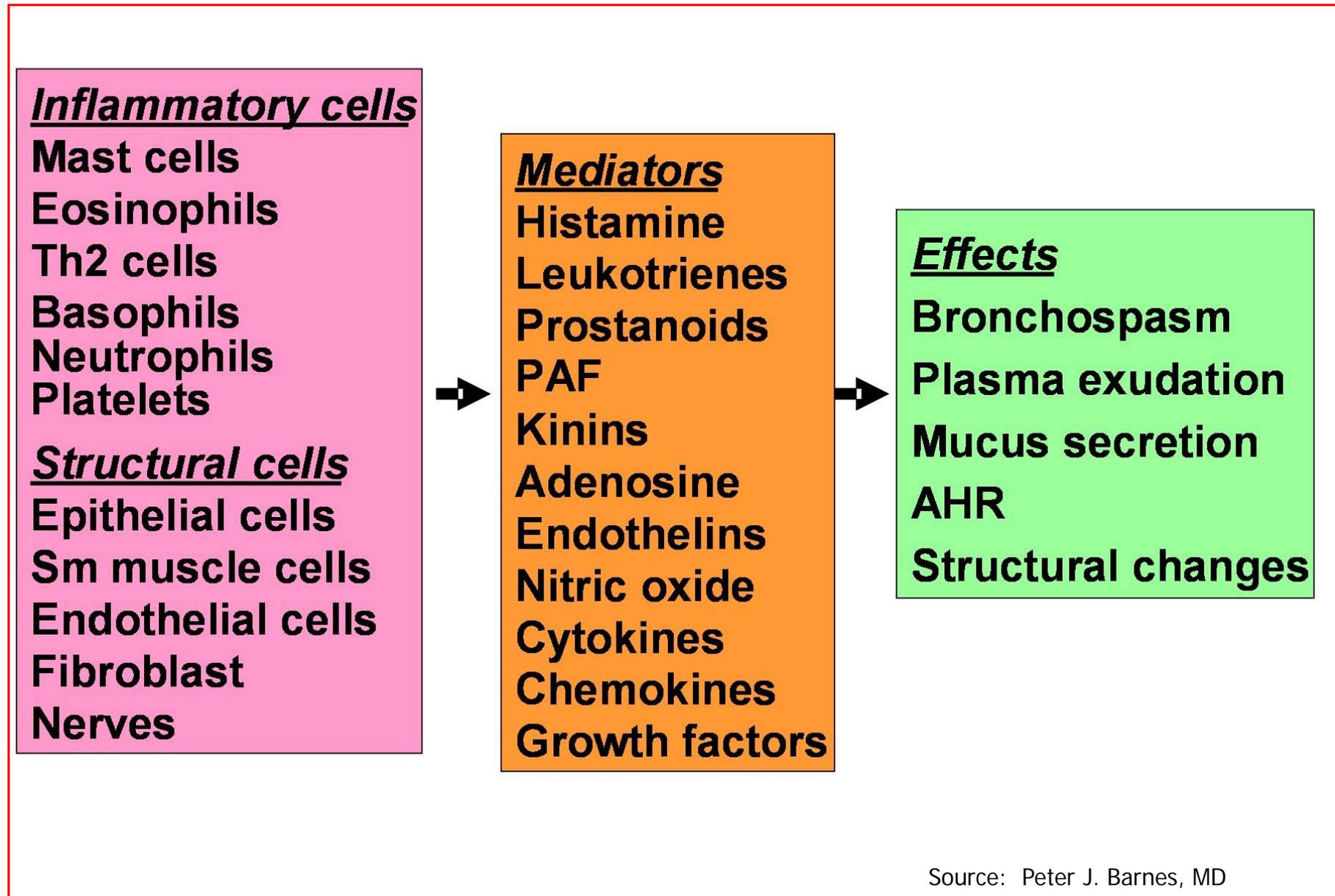


Asthma Inflammation: Cells and Mediators

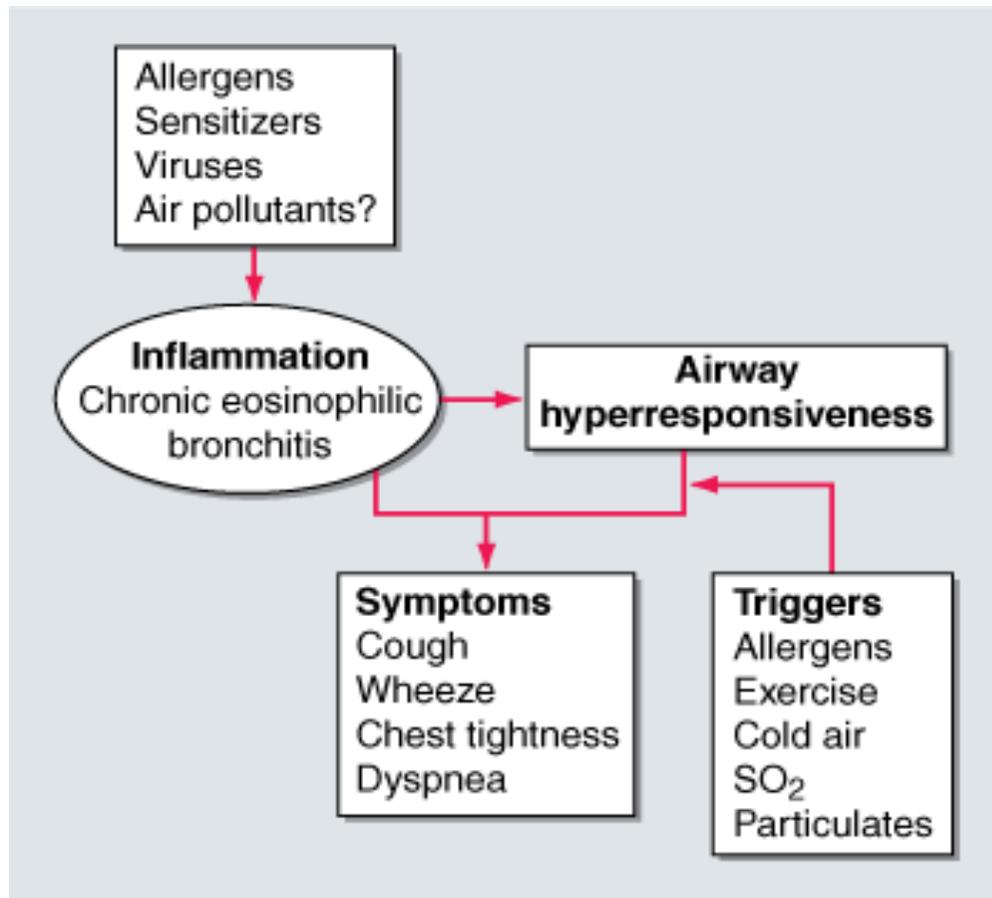


Source: Peter J. Barnes, MD

Asthma Inflammation: Cells and Mediators



Pathophysiology



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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Pathophysiology

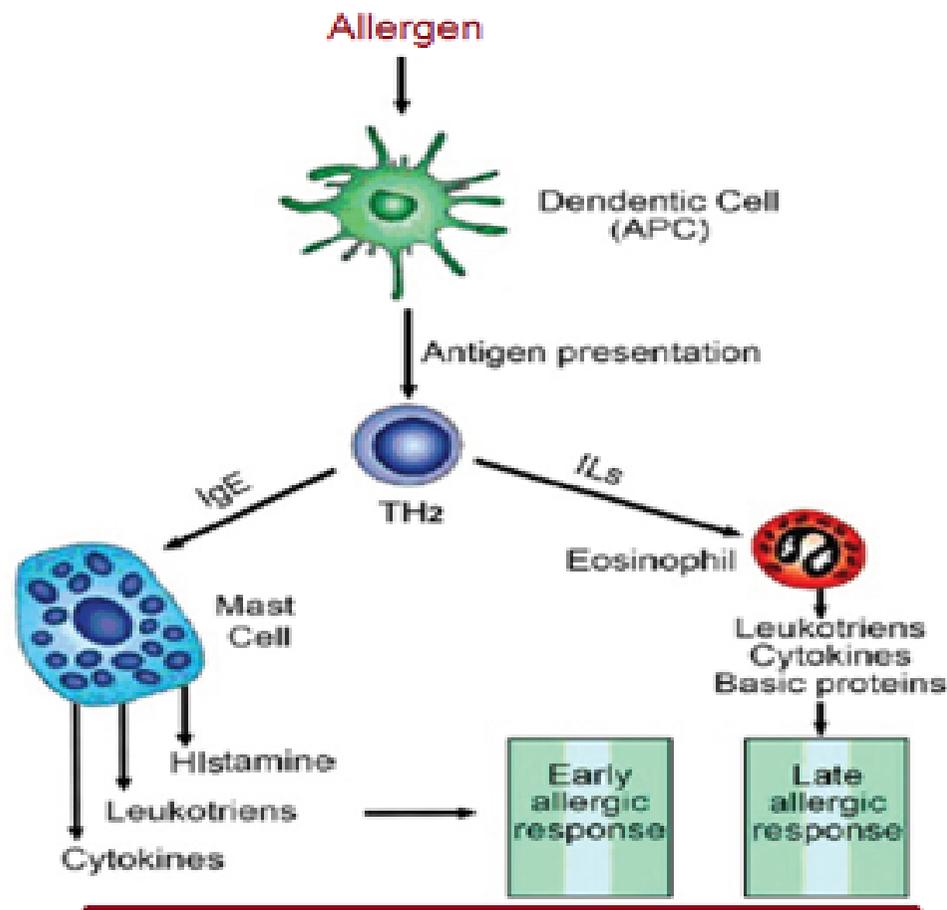
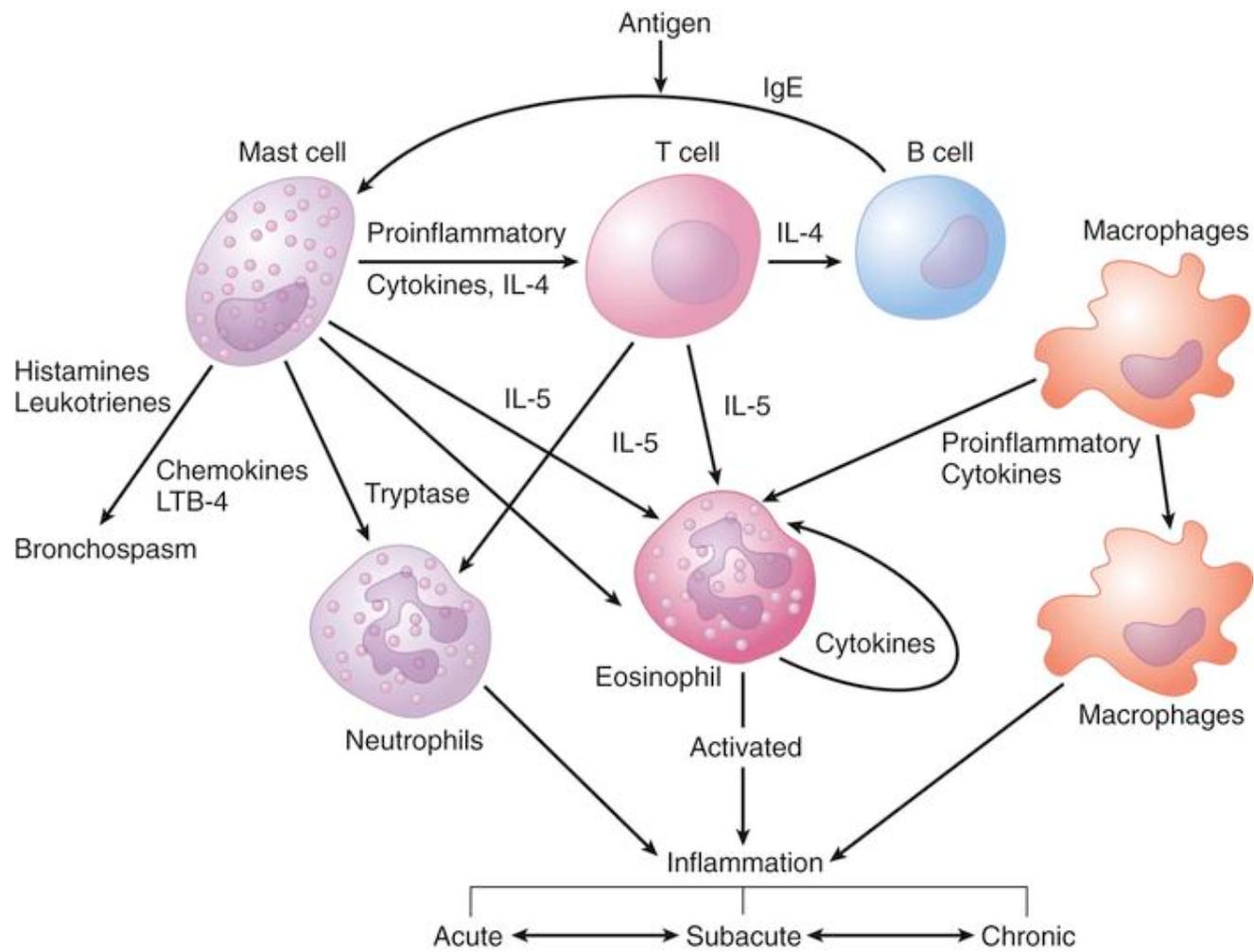


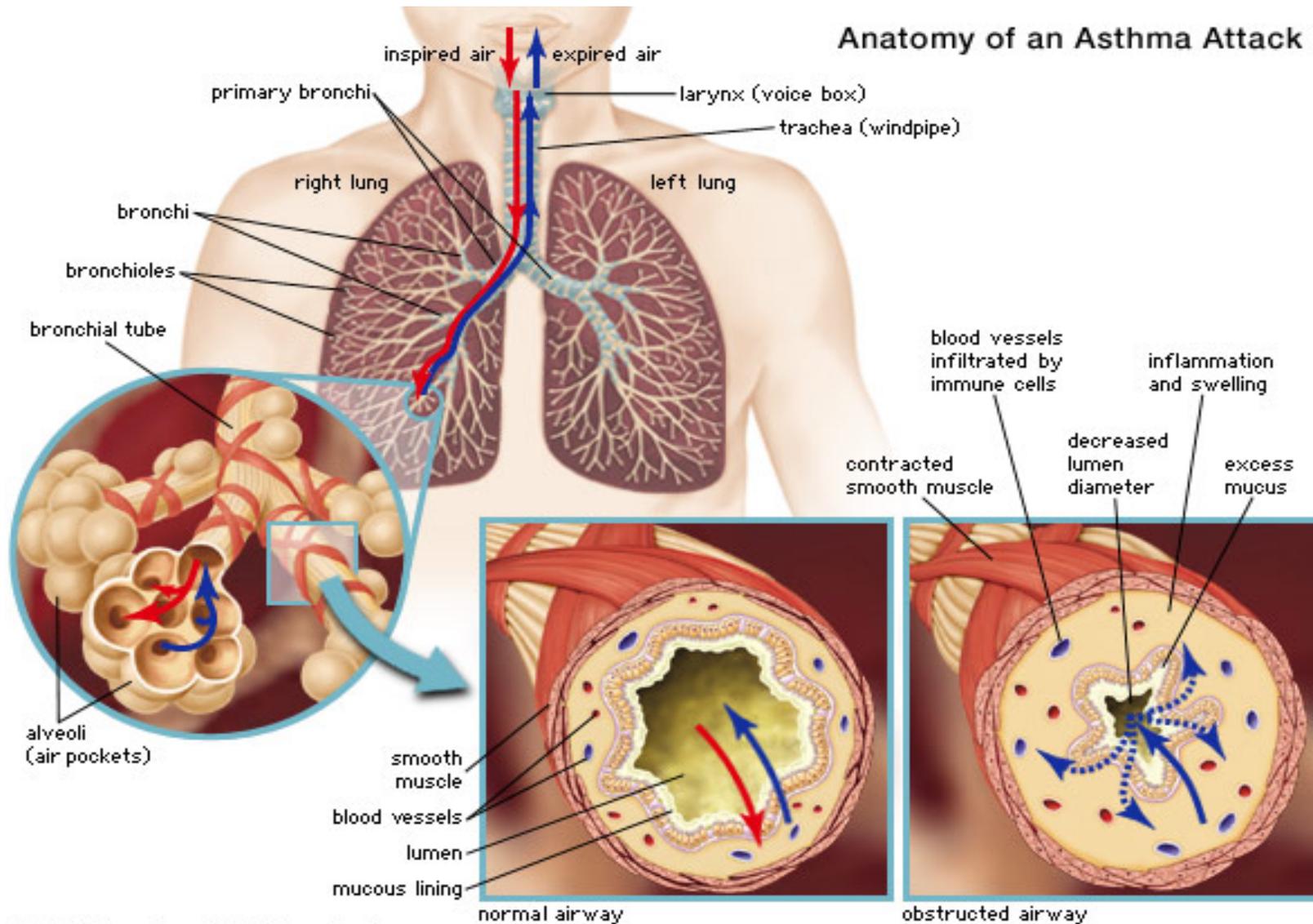
Fig. 1 : Pathophysiology of asthma
APC = Antigen presenting cell
ILs = Interleukins
TH2 = T-lymphocyte Helper cell 2

Inflammation → Remodeling

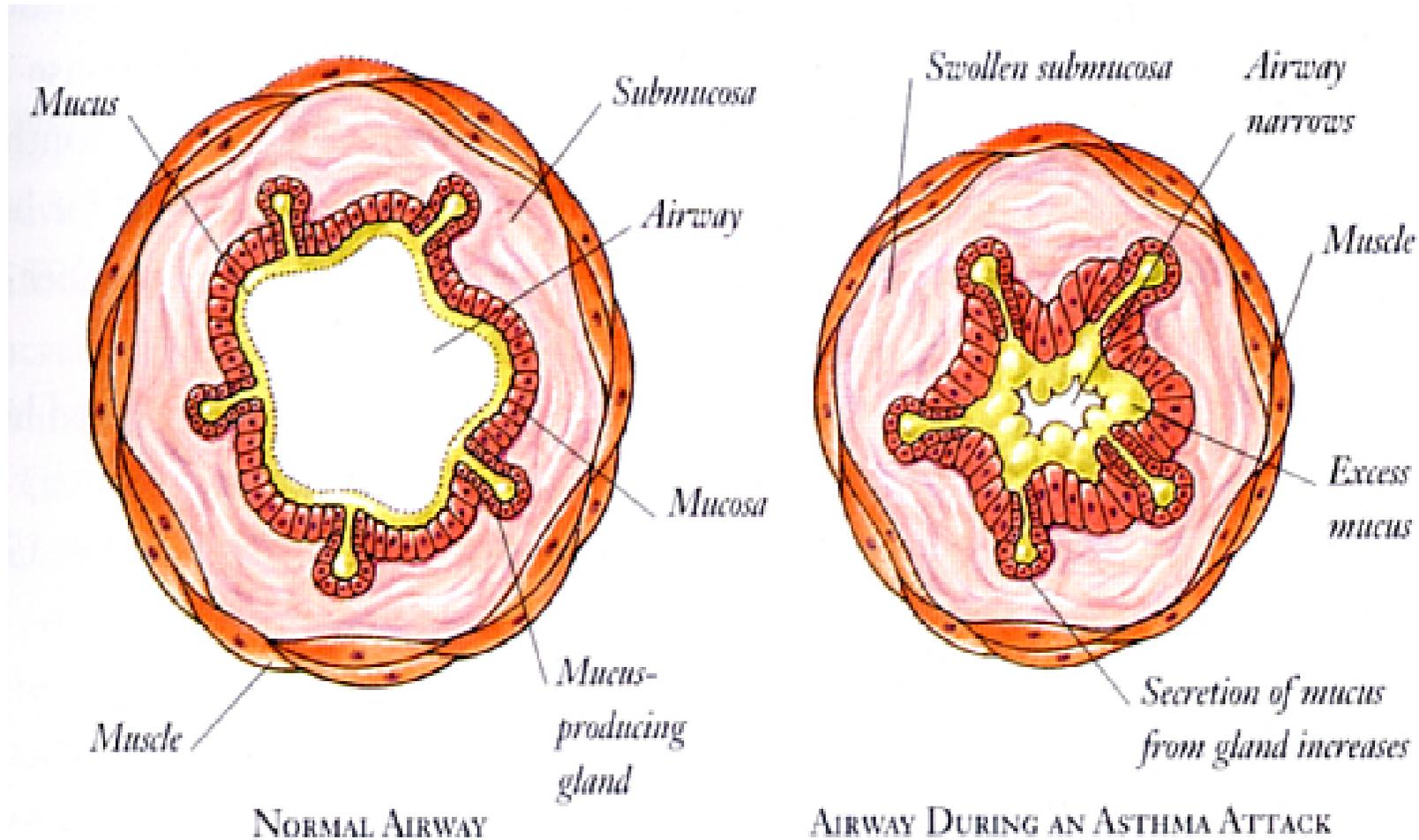
- Inflammation
- Airway Hypersecretion
- Subepithelial fibrosis
- Angiogenesis



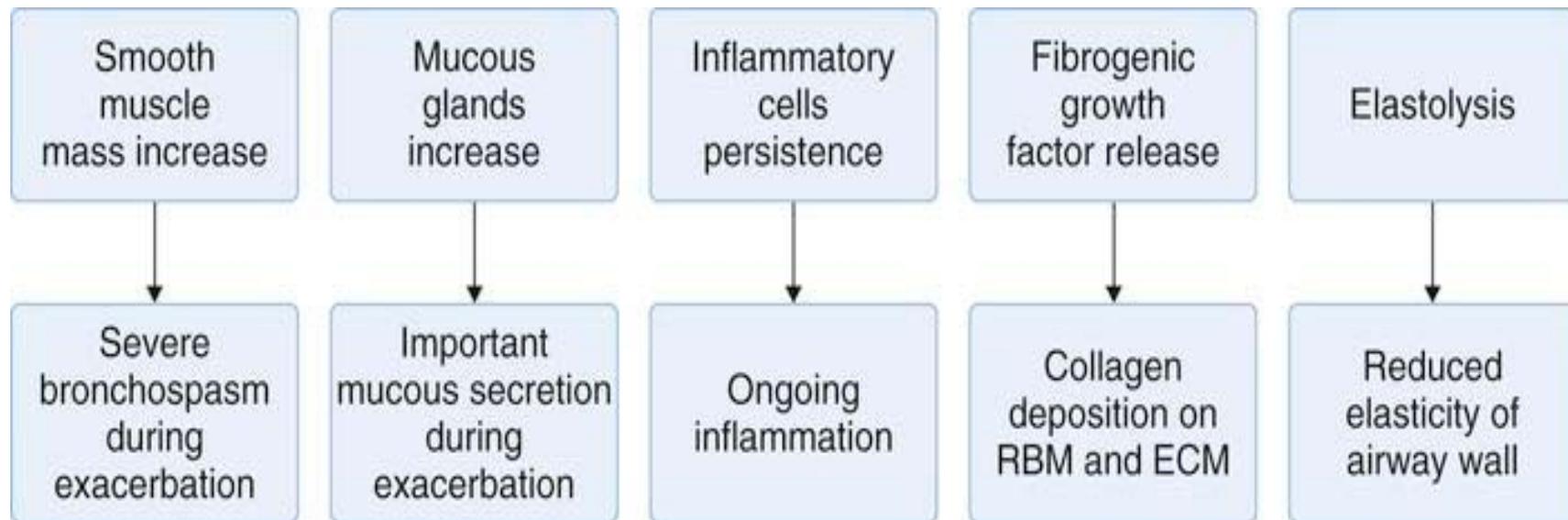
PATHOLOGY



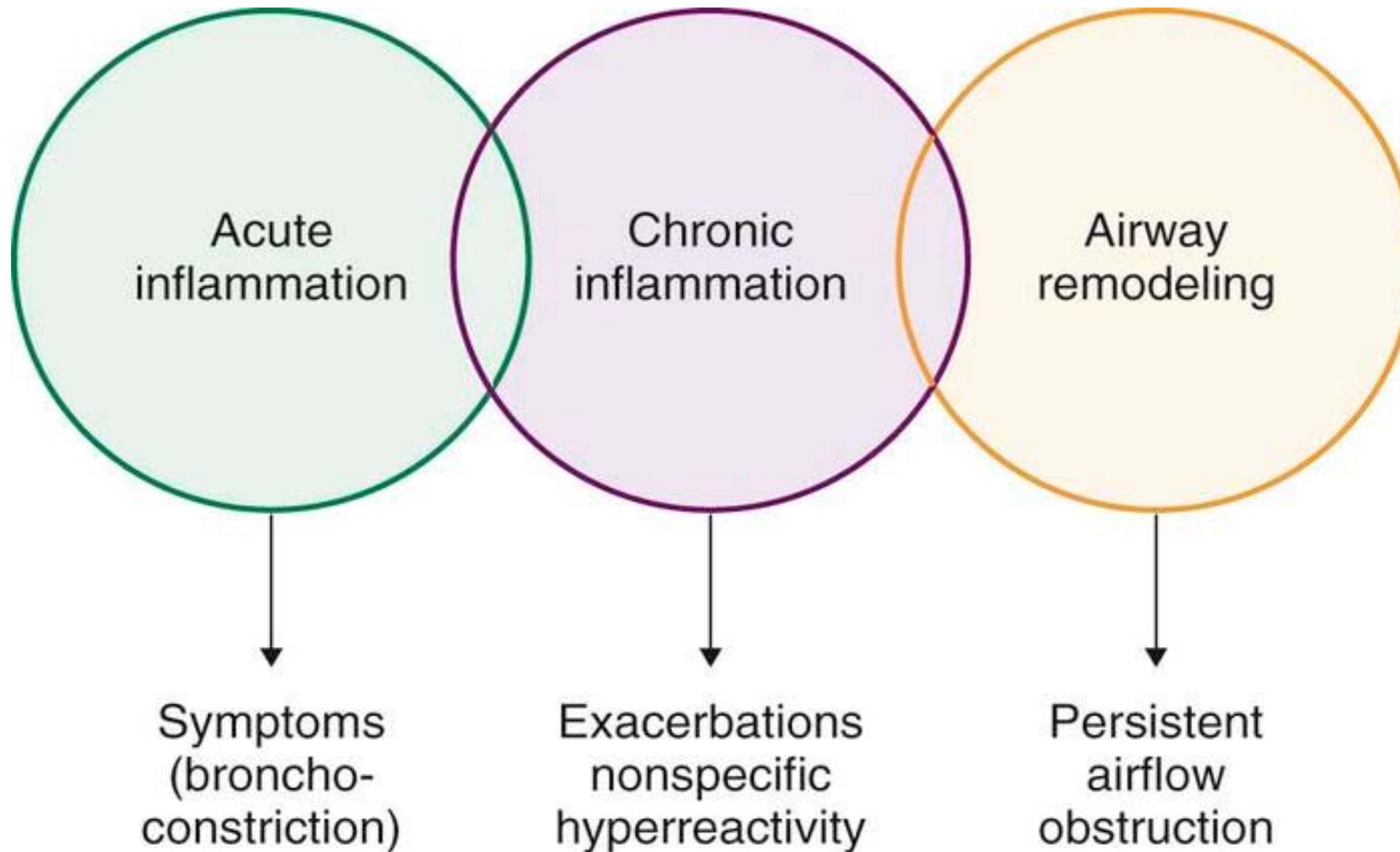
Asthma: Pathological changes



Pathology and consequences



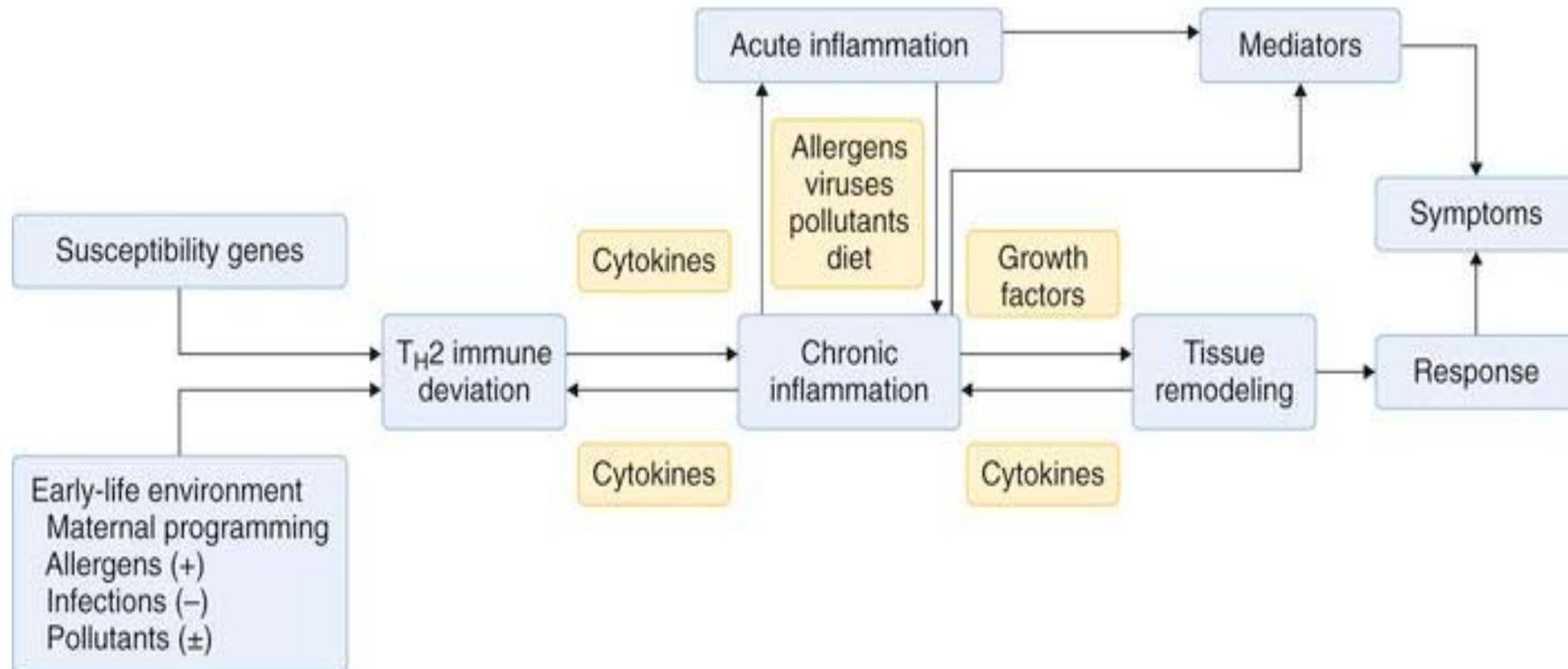
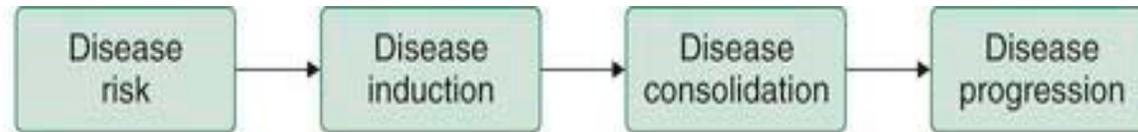
ASTHMA - PATHOPHYSIOLOGY



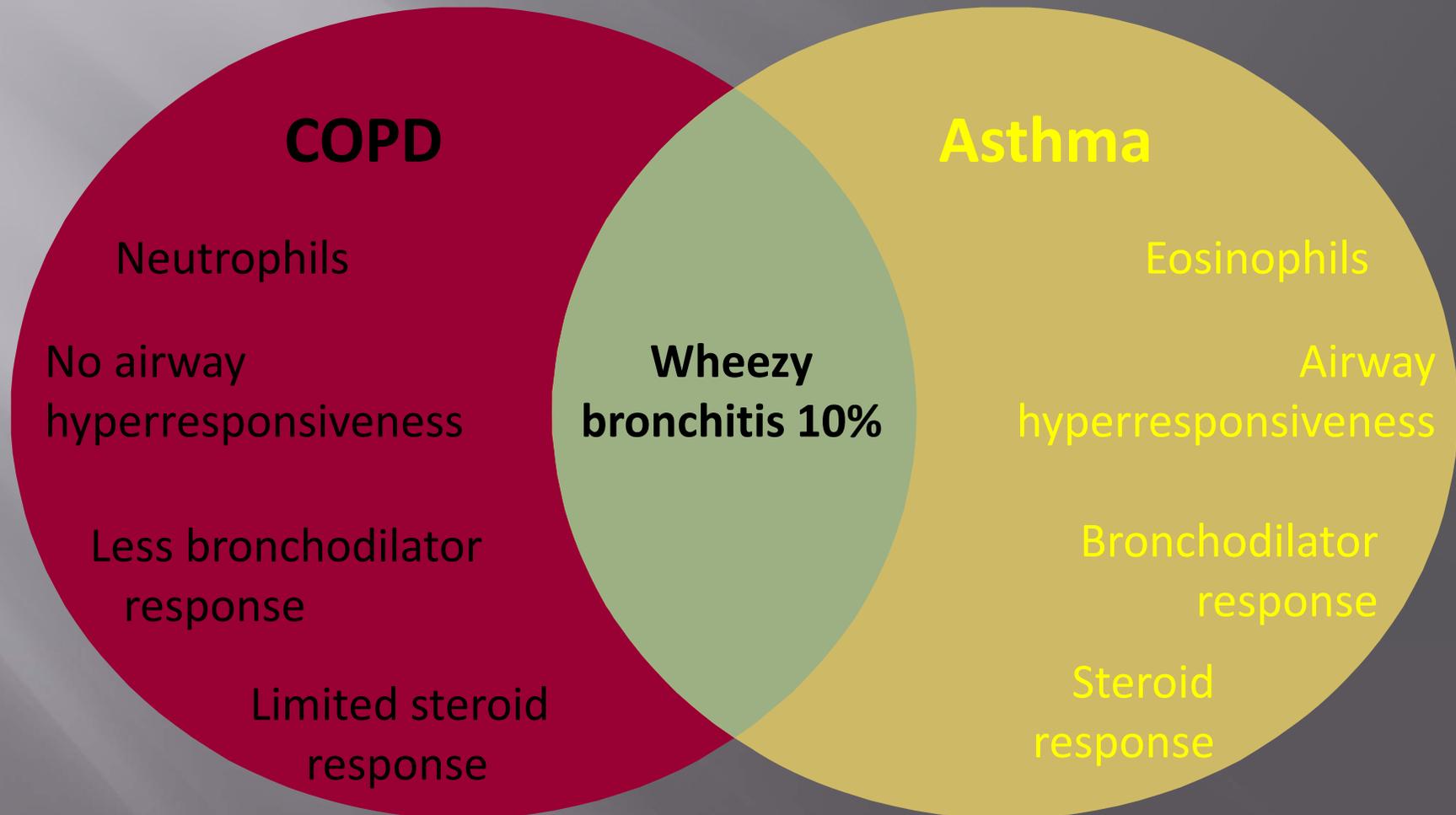
Genetic predisposition
Intrinsic vulnerability
Atopy/allergy

Inflammation underlies disease processes
Phenotype varies by individual and over time

Clinical symptoms also vary by individual and over time



Difference and overlap



Asthma
Sensitizing agent



Asthmatic airway inflammation
CD4+ T-lymphocytes
Eosinophils



Completely
reversible

**Airflow
limitation**

COPD
Noxious agent



COPD airway inflammation
CD8+ T-lymphocytes
Macrophages
Neutrophils



Completely
irreversible

Physiologic Differences

Asthma

- Normal DLCO
- Normal lung volume
- Normal elastic recoil
- Flow dominant BD response

COPD

- Abnormal DLCO
- Hyperinflation
- Decreased elastic recoil
- Volume dominant BD response

Disease Pathology

Asthma

COPD

Reversible airflow obstruction

+ ++

+

Airway inflammation

+ + +

+ +

Mucus hypersecretion

+

+ + +

Goblet cell metaplasia

+

+ +

Impaired mucus clearance

+ +

+ +

Epithelial damage

++

—

Alveolar destruction

—

++

Smooth muscle hypertrophy

+ +

—

Basement membrane thickening

+++

—

Asthma-Classic presentation

- Episodic wheeze, dyspnea, chest tightness, or cough often triggered by allergens or sinusitis/rhinitis.
- Physical examination: wheezing, prolonged end-expiration, and decreased air movement. However, the examination can be normal.
- Uncontrolled symptoms in spite of aggressive therapy warrant evaluation to rule out other etiologies of the patient's symptoms and assess whether there are any triggers that can be controlled



Is it Asthma?

- Recurrent episodes of wheezing
- Troublesome cough at night
- Cough or wheeze after exercise
- Cough, wheeze or chest tightness after exposure to airborne allergens or pollutants
- Colds “go to the chest” or take more than 10 days to clear

How Does Asthma present ??

Clinical Presentations

Episodic Attack

Status Asthamatics

Chronic Asthma

Always Describe diseases in following manner

- ✓ Patient Symptoms
- ✓ Clinical features
 - ✓ Inspection
 - ✓ Palpation/percussion
 - ✓ Auscultation



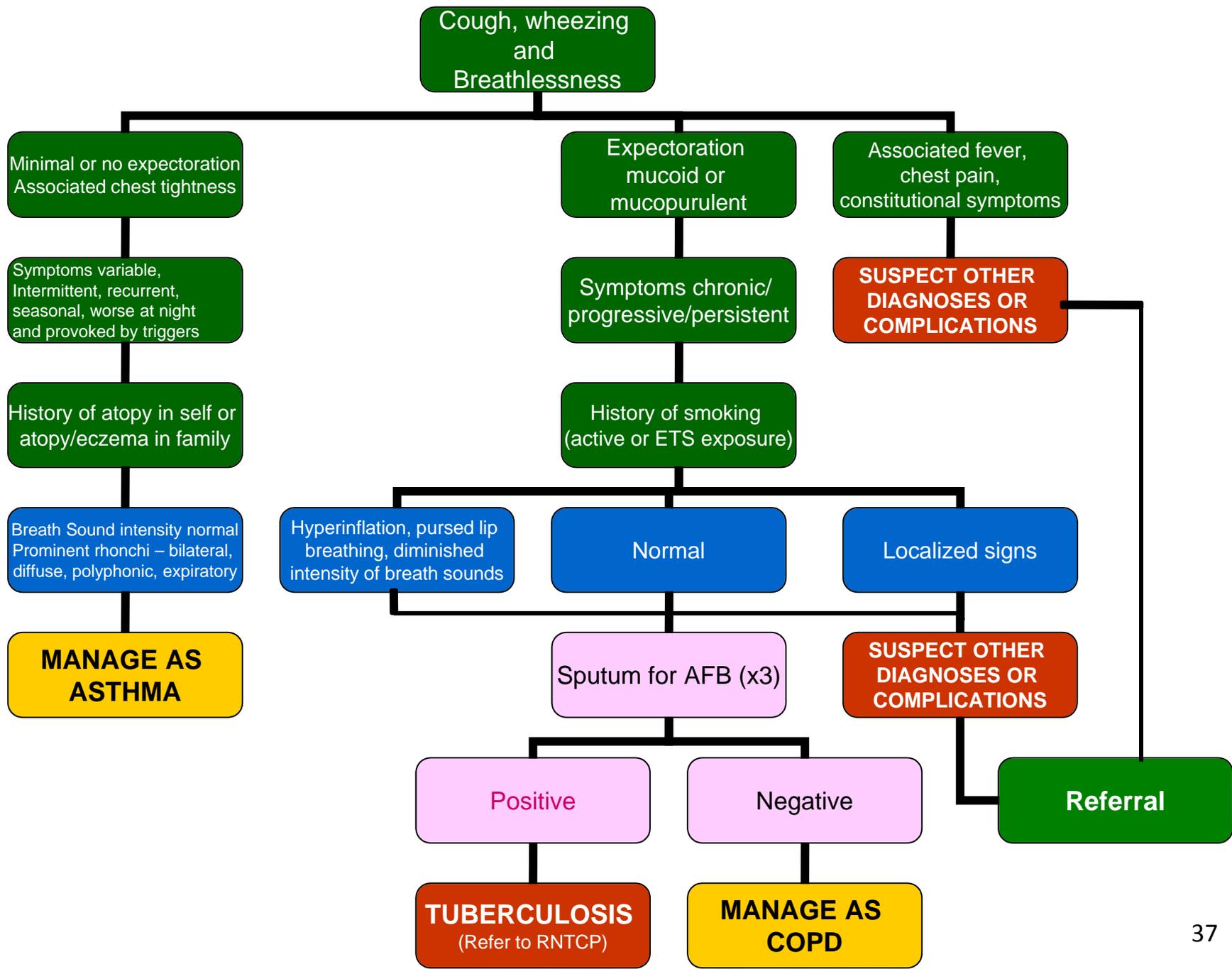
Extrinsic vs intrinsic asthma

Points	Early Onset	Late Onset
Age	Early	Late
Atopy	Yes	No
Allergen involvement	Yes	No
Family history	Yes	No
IgE in Serum	Increased levels	Normal levels
Skin Hypersensitivity test	Positive	Negative
Provocation test result	Positive	Negative

Differential diagnosis

Category	Examples
Diseases causing recurrent episodic dyspnea	Chronic obstructive pulmonary disease, coronary artery disease, congestive heart failure, pulmonary emboli, recurrent gastroesophageal reflux with aspiration, recurrent anaphylaxis, systemic mastocytosis, carcinoid syndrome
Common diseases causing cough	Rhinitis, sinusitis, otitis, bronchitis (chronic or postviral), bronchiectasis, cystic fibrosis, pneumonia, diffuse pulmonary fibrosis
Common diseases causing airflow obstruction	Chronic obstructive bronchitis and emphysema, bronchiolitis obliterans, cystic fibrosis, organic or functional laryngeal narrowing, extrinsic or intrinsic narrowing of trachea or major bronchus.

DIAGNOSIS



Key indicators for considering a diagnosis of asthma

- Typical history
- Intermittent symptoms (reversible)
- Association of symptoms to weather changes, dust, smoke, exercise, viral infection, animals with fur or feathers, house-dust mites, mold, pollen, strong emotional expression (laughing or crying hard), airborne chemicals or dust
- Diurnal variation
- Family history
- Presence of atopy, allergic rhinitis, skin allergies

Routine Investigations

- Hemogram including eosinophil count
- Blood gas analysis
- X-ray chest
- ECG
- Serum electrolytes (Mg, Na, K)
- spirometry

Spirometry

- Spirometry measurements (FEV_1 , FVC, FEV_1/FVC) before and after bronchodilator helps determine whether there is airflow obstruction and whether it is reversible over the short term
- **(12% in increase in FEV1 and absolute increase in 200ml after 200ug of salbutamol inhalation)**

Spirometry

- Spirometry should be done
 - at the time of initial assessment
 - after treatment is initiated and symptoms and peak expiratory flow (PEF) have been stabilized
 - at least every 1 to 2 years to assess the maintenance of airway function



Classification of Severity

CLASSIFY SEVERITY Clinical Features Before Treatment		
Continuous Limited physical activity	Frequent	$\leq 60\%$ predicted Variability $> 30\%$
Daily Attacks affect activity	> 1 time week	60 - 80% predicted Variability $> 30\%$
> 1 time a week but < 1 time a day	> 2 times a month	$\geq 80\%$ predicted Variability 20 - 30%
< 1 time a week Asymptomatic and normal PEF between attacks	≤ 2 times a month	$\geq 80\%$ predicted Variability $< 20\%$

The presence of one feature of severity is sufficient to place patient in that category.

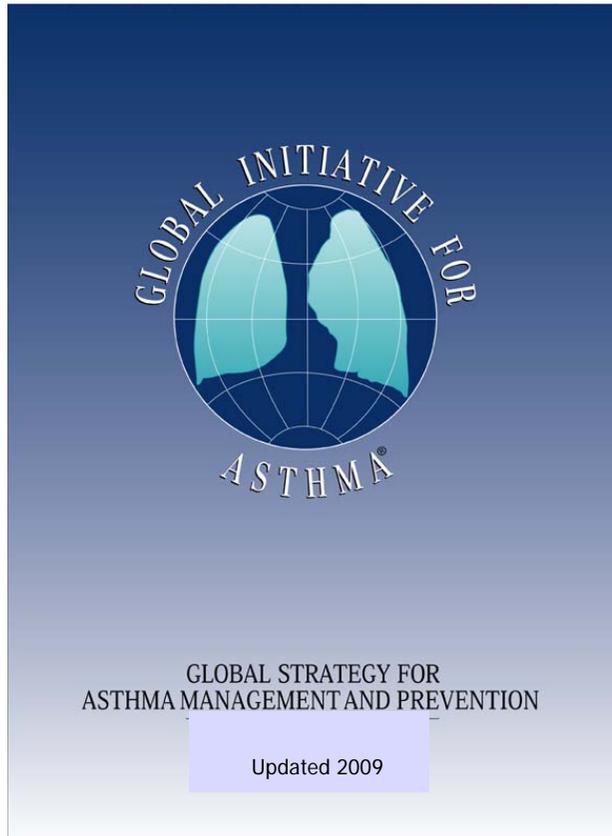
TREATMENT

Goals of Asthma Therapy

- Prevent recurrent exacerbations and minimize the need for emergency department visits or hospitalizations
- Maintain (near-) “normal” pulmonary function
- Maintain normal activity levels (including exercise and other physical activity)
- Provide optimal pharmacotherapy with minimal or no adverse effects
- Prevent asthma mortality



Asthma Management and Prevention Five Components



1. Develop Patient/Doctor Partnership
2. Identify and Reduce Exposure to Risk Factors
3. Assess, Treat and Monitor Asthma
4. Manage Asthma Exacerbations
5. Special Considerations



Asthma Management and Prevention Program

- Asthma can be effectively controlled in most patients by intervening to suppress and reverse inflammation as well as treating bronchoconstriction and related symptoms
- Early intervention to stop exposure to the risk factors that sensitized the airway may help improve the control of asthma and reduce medication needs.



Asthma Management and Prevention Program

- Although there is no cure for asthma, appropriate management that includes a partnership between the physician and the patient/family most often results in the achievement of control



Component 1: Develop Patient/Doctor Partnership

- Educate continually
- Include the family
- Provide information about asthma
- Provide training on self-management skills
- Emphasize a partnership among health care providers, the patient, and the patient's family



Component 1: Develop Patient/Doctor Partnership

Key factors to facilitate communication:

- ✓ Friendly demeanor
- ✓ Interactive dialogue
- ✓ Encouragement and praise
- ✓ Provide appropriate information
- ✓ Feedback and review



Factors Involved in Non-Adherence

Medication Usage

- Difficulties associated with inhalers
- Complicated regimens
- Fears about, or actual side effects
- Cost
- Distance to pharmacies

Non-Medication Factors

- Misunderstanding/lack of information
- Fears about side-effects
- Inappropriate expectations
- Underestimation of severity
- Attitudes toward ill health
- Cultural factors
- Poor communication



Component 2: Identify and Reduce Exposure to Risk Factors

- Measures to prevent the development of asthma, and asthma exacerbations by avoiding or reducing exposure to risk factors should be implemented wherever possible.
- Asthma exacerbations may be caused by a variety of risk factors – allergens, viral infections, pollutants and drugs.
- Reducing exposure to some categories of risk factors improves the control of asthma and reduces medications needs.



Component 2: Identify and Reduce Exposure to Risk Factors

- Reduce exposure to indoor allergens
- Avoid tobacco smoke
- Avoid vehicle emission
- Identify irritants in the workplace
- Explore role of infections on asthma development, especially in children and young infants



Influenza Vaccination

- Influenza vaccination should be provided to patients with asthma when vaccination of the general population is advised



Component 3: Assess, Treat and Monitor Asthma

- The goal of asthma treatment, to achieve and maintain clinical control
- can be achieved in a majority of patients with a pharmacologic intervention strategy.

GINA Levels of Asthma Control

<i>Characteristic</i>	Controlled	Partly controlled (Any present in any week)	Uncontrolled
Daytime symptoms	None (2 or less / week)	More than twice / week	3 or more features of partly controlled asthma present in any week
Limitations of activities	None	Any	
Nocturnal symptoms / awakening	None	Any	
Need for rescue / “reliever” treatment	None (2 or less / week)	More than twice / week	
Lung function (PEF or FEV₁)	Normal	< 80% predicted or personal best (if known) on any day	
Exacerbation	None	One or more / year	

Asthma drug classification

CONTROLLERS		RELIEVERS
Anti-inflammatory action to prevent asthma attacks	Sustained bronchodilator action but weak or unproven anti-inflammatory effect	For quick relief of symptoms and use in acute attacks as PRN dosage only
Inhaled corticosteroids <ol style="list-style-type: none"> 1. Beclomethasone 2. Budesonide 3. Fluticasone 4. Ciclesonide 	Long-acting beta-agonists <ol style="list-style-type: none"> 1. Salmeterol 2. Formoterol 	Short-acting beta-agonists <ol style="list-style-type: none"> 1. Salbutamol 2. Fenoterol 3. Terbutaline
Leukotriene modifiers <ol style="list-style-type: none"> 1. Montelukast 2. Zafirlkast Oral corticosteroids <ol style="list-style-type: none"> 1. Prednisone 2. Prednisolone 3. Methylprednisone 4. Methylprednisolone 	Sustained-release theophylline preparations	Anti-cholinergics <p>Ipratropium bromide</p>

Methods of Medication Delivery

- Metered-dose inhaler (MDI)
 - Spacer/holding chamber/face mask
- Dry-powder inhaler (DPI)
- Nebulizer
- Oral Medication
 - Tablets, Liquids
- Intravenous Medication
 - IV Corticosteroids, IV Aminophylline

What are Controllers?

- Prevent future attacks
- Long term control of asthma
- Prevent airway remodeling

What Are Relievers?

- Rescue medications
- Quick relief of symptoms
- Used during acute attacks
- Action lasts 4-6 hrs

CONTROLLERS

Inhaled Corticosteroids

- [Treatment of choice for](#) long-term control of persistent asthma
- Benefits
 - Reduced airway inflammation through topical activity
 - Decreases airway hyper-responsiveness.
 - Improve lung function and quality of life
 - Reduce the frequency of exacerbations
 - Reduced use of quick-relief medicine

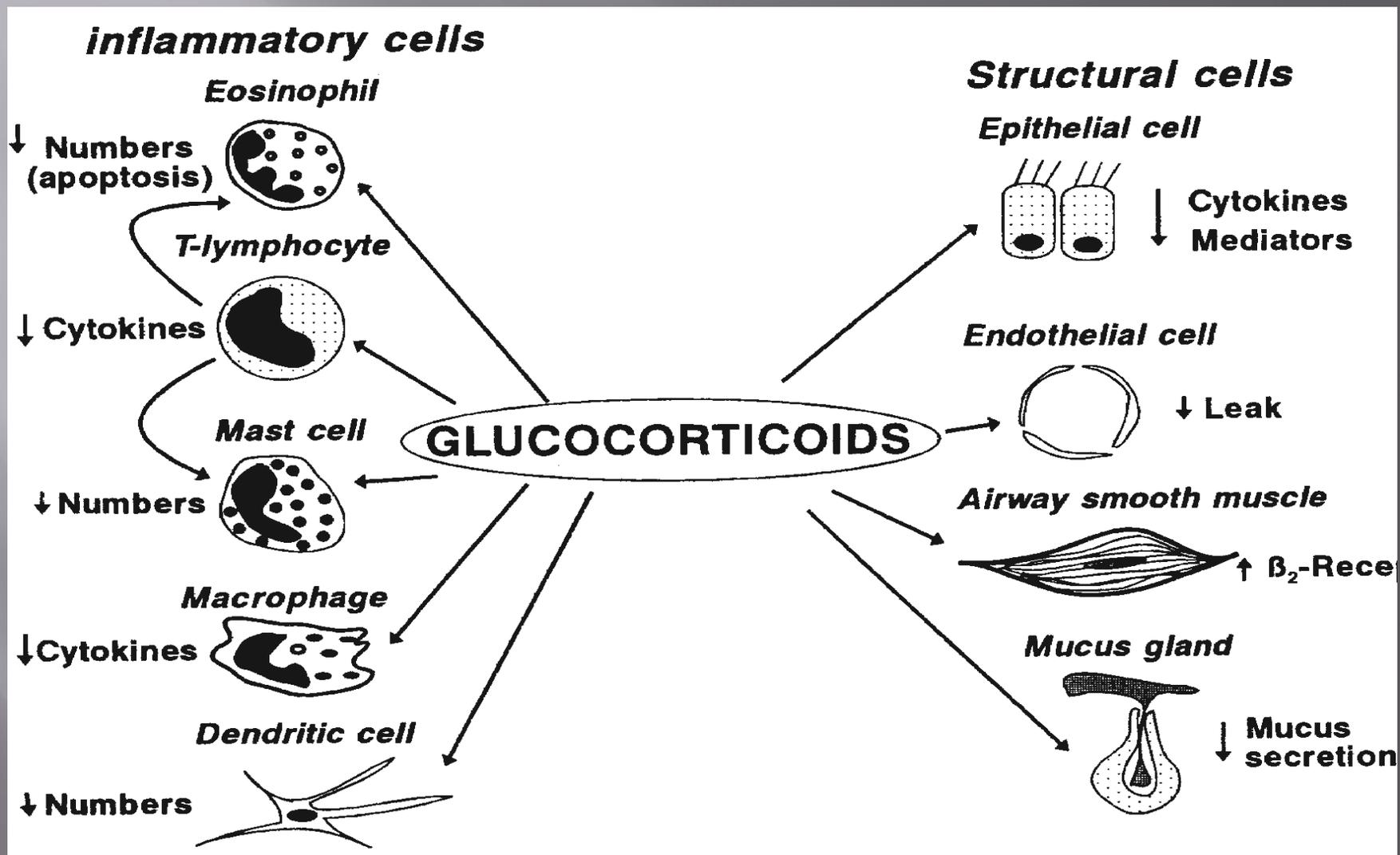
**** NEVER FOR RESCUE PURPOSES ****

CONTROLLERS

Corticosteroids

- Inhaled
 - Beclomethasone
 - Fluticasone
 - Triamcinolone
 - Budesonide
 - Flunisolide

Anti-inflammatory Effect of Glucocorticoid



Estimated Comparative Daily Dosages for Adults of Inhaled Corticosteroids

Drug	Low Dose Step 2	Medium Dose Step 3	High Dose Step 4
Beclomethasone	1-3 puffs 80 - 240 mcg	3-6 puffs 240 - 480 mcg	>6 puffs > 480 mcg
Budesonide DPI	1-3 puffs 200 – 600 mcg	3-6 puffs 600 – 1,200 mcg	> 6 puffs > 600 mcg
Flunisolide	2-4 puffs 500–1,000 mcg	4-8 puffs 1,000–2,000 mcg	> 8 puffs > 2,000 mcg
Fluticasone	2-6 puffs (44) 88-264 mcg	2-6 puffs (110) 264-660 mcg	> 6 puffs (110) > 660 mcg
Triamcinolone	4-10 puffs 400-1,000 mcg	10-20 puffs 1,000–2,000 mcg	> 20 puff > 2,000 mcg

Corticosteroid Side Effects

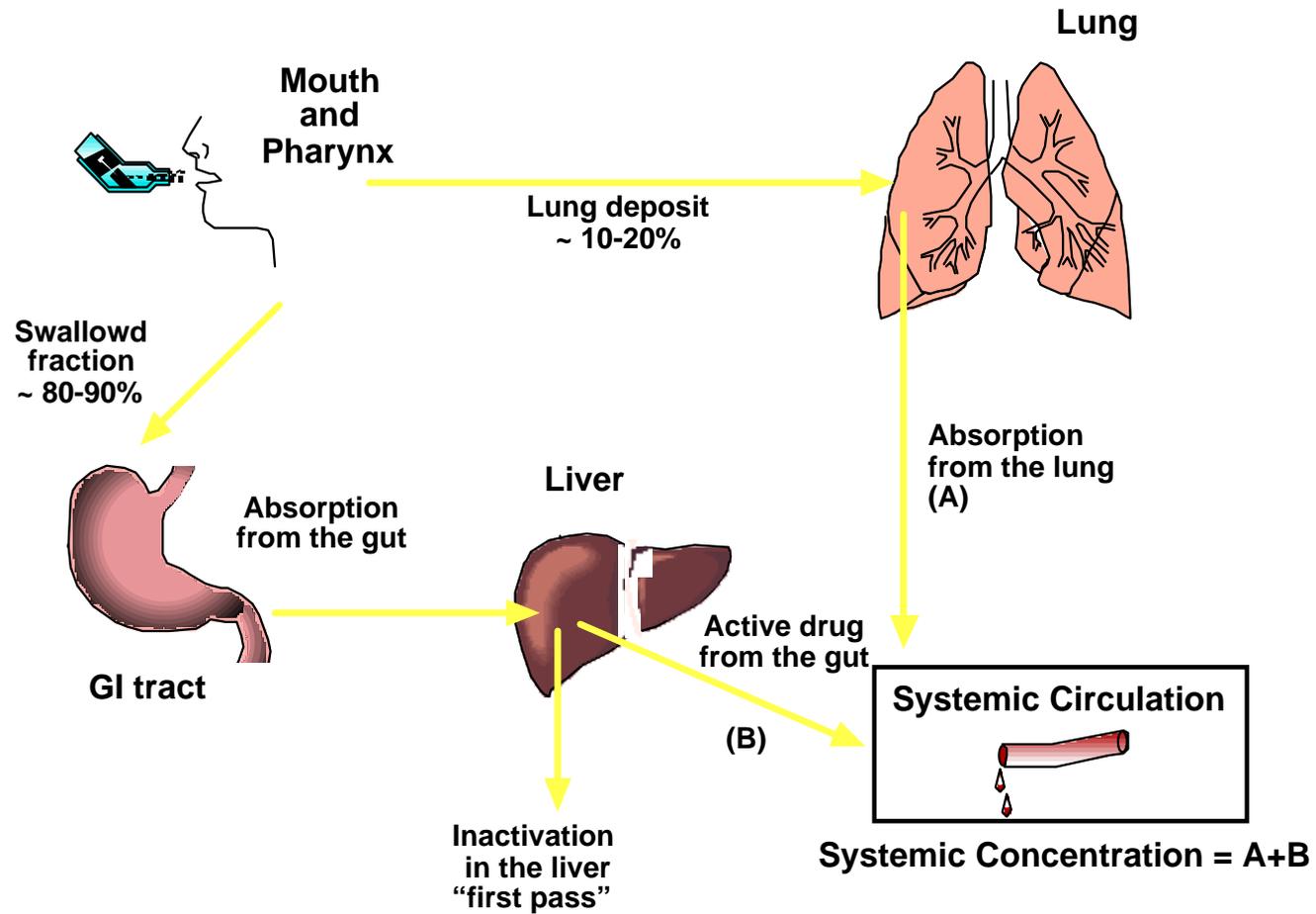
Inhaled Local

- Dysphonia
- Cough/throat irritation
- Thrush
- Impaired growth (high dose)?

Systemic (oral, IV)

- Fluid retention
- Muscle weakness
- Ulcers
- Malaise
- Impaired wound healing
- Nausea/Vomiting, HA
- Osteoporosis (adults)
- Cataracts (adults)
- Glaucoma (adults)

The Fate of Inhaled Steroids



CONTROLLERS

Long-acting Beta₂-agonists

- Salmeterol, Formoterol

- Indication: Daily long-term control

Bronchodilate by long-term stimulation of beta₂ receptors

- Advantages

- Blunt exercise induced symptoms for longer time
 - Decrease nocturnal symptoms
 - Improve quality of life

- Combination therapy beneficial when added to inhaled corticosteroids

Decrease the need to increase inhaled corticosteroid dose by dose

CONTROLLERS

Long-acting Beta₂-agonists

- **NOT** for acute symptoms or exacerbations
 - Onset of effect → 30 minutes
 - Peak effect → 1-2 hours
 - Duration of effect → up to 12 hours
- **NOT** a substitute for anti-inflammatory therapy
- **NOT** appropriate for monotherapy

Useful Beta Adrenergic Effects

- **Relax bronchial smooth muscle**
- Inhibit mediator release from mast cells, eosinophils, macrophages
- Decrease mucous secretion (submucosal gl)
- Increase mucociliary transport
- Inhibit bronchial oedema
- Inhibit cholinergic transmission
- Decrease airway hyperresponsiveness

CONTROLLERS

Leukotriene Modifiers

- Cysteinyl Leukotriene Receptor Antagonists
 - [Montelukast](#) – Once a day in PM – indicated at age 1
 - Zafirlukast – Twice daily – Empty Stomach
 - Many drug interactions
- 5-Lipoxygenase inhibitors
 - Zileuton – Four times daily
 - Many drug interactions

Add-on Controllers

Leukotriene Modifiers

- Montelukast

- Improves lung function and asthma control
- May protect against exercise induced bronchoconstriction
- Improves lung function when added to inhaled corticosteroids
- Not as effective as inhaled corticosteroids
- 4 mg, 5 mg chewable and 10 mg tablet
 - Once daily dosing (evening)
- Pediatric indication > 1 year
- No food restrictions

RELIEVERS

Short-Acting Beta₂-agonist

- Salbutamol
- Pirbuterol
- Terbutaline
- levosalbutamol

RELIEVERS

Short-Acting Beta₂-Agonists

- Most effective medication for relief of acute bronchospasm
- Preferably use inhaled rather than oral preparations
- Increased need for these medications indicates uncontrolled asthma (and inflammation)
- Regularly scheduled use not generally recommended – use “as needed”
 - May lower effectiveness
 - May increase airway hyperresponsiveness

RELIEVERS

Short-Acting Beta₂-Agonists

- Side Effects:
 - Increased Heart Rate
 - Palpitations
 - Nervousness
 - Sleeplessness
 - Headache
 - Tremor

Unwanted Beta Adrenergic Effects

- Hypokalemia (K shift into muscle tissue)
- Hyperglycemia (glycogenolysis)
- Hypoxia (pulmonary vasodilation causing increased ventilation/perfusion mismatch)

Oral Steroid Short Course

- **Prednisone 30-40mg x 10-14 days for acute exacerbation of Asthma**
- no weaning of dose unless long term use

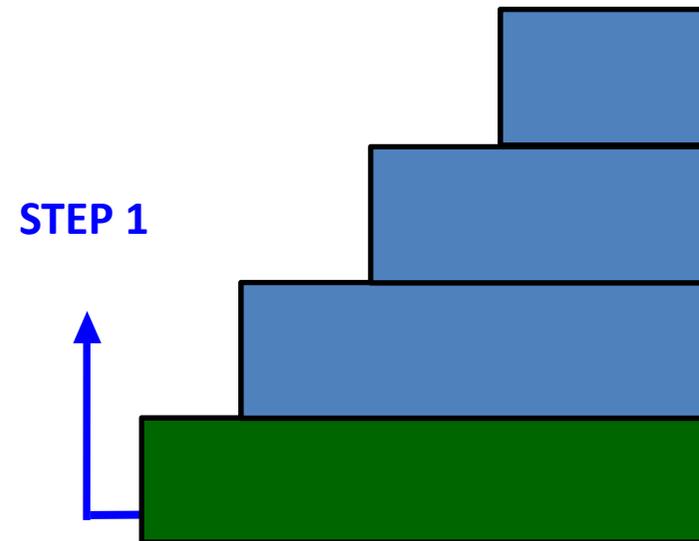
Step 1 Treatment for Adults and Children > 5: Mild Intermittent

Controller – Daily

- Not needed

Reliever – Quick Relief

- Short-acting inhaled beta₂-agonist
- Increasing use, or use more than 2x/week, may indicate need for long-term-control therapy
- Intensity of treatment depends on severity of exacerbation



Step 2 Treatment for Adults and Children > 5: Mild Persistent

Controller – Preferred Daily

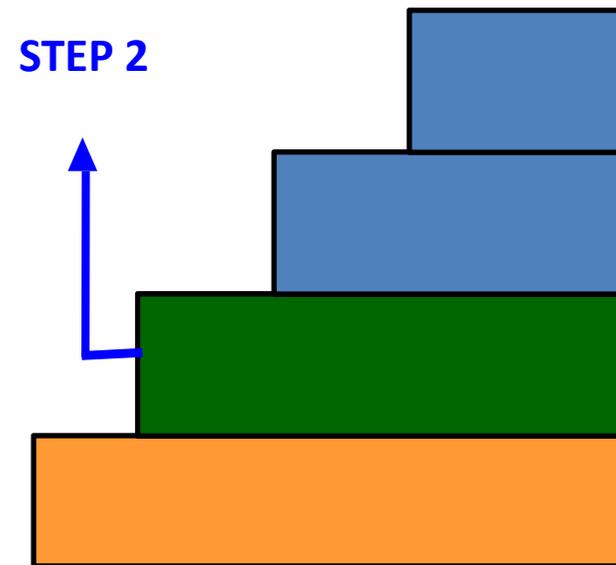
- Low dose inhaled corticosteroid

Alternatives (alphabetically)

- Cromolyn, leukotriene modifier, nedocromil

OR

- Sustained-release theophylline to serum concentration of 5-15mcg/ml



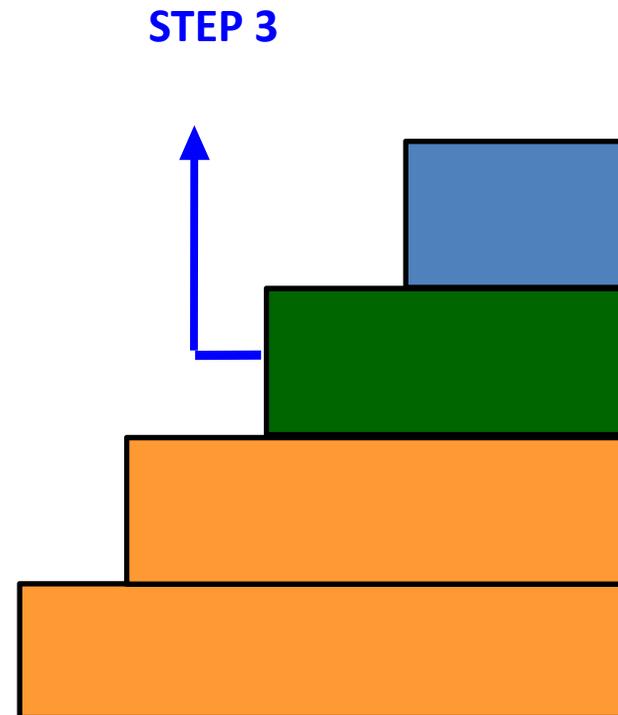
Step 3 Treatment for Adults and Children > 5: Moderate Persistent

Controller – Preferred Daily

- Low to medium dose inhaled corticosteroid (medium dose) and long-acting beta₂-agonist

Alternatives (alphabetically)

- Increase inhaled corticosteroids to medium-dose range
- OR**
- Low to medium dose inhaled corticosteroid (medium dose) and either leukotriene modifier or theophylline



Step 3 Treatment for Adults and Children > 5: Moderate Persistent

(patients with recurring severe exacerbations)

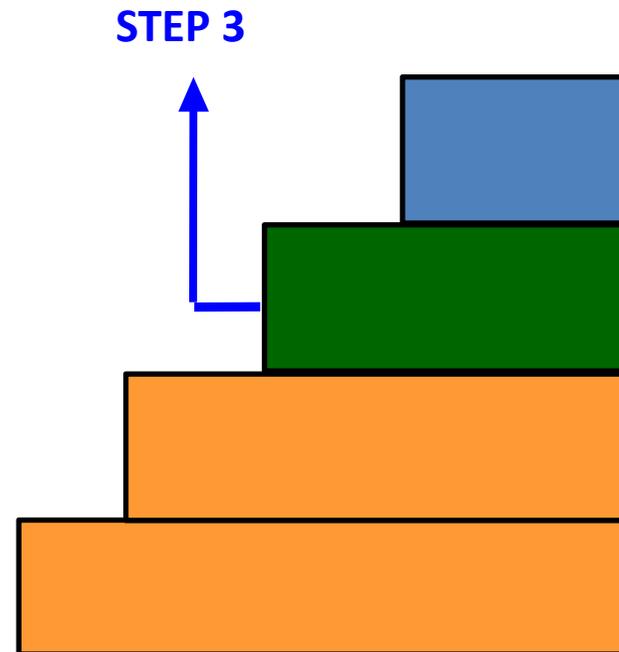
Controller – Preferred Daily

- Medium dose inhaled corticosteroid (medium dose) and long-acting beta₂-agonist

Alternatives (alphabetically)

- Medium dose inhaled corticosteroid (medium dose) and either leukotriene modifier or theophylline

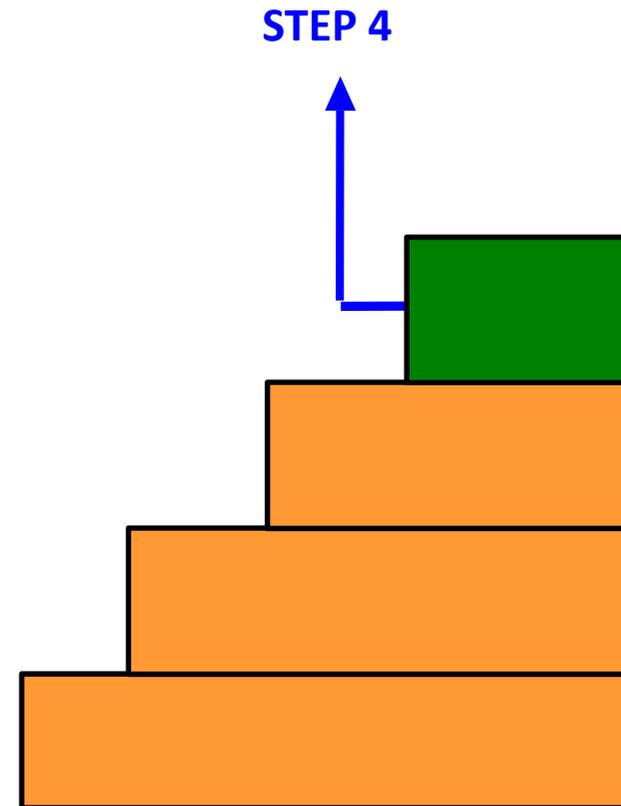
- **Consider referral to a specialist**

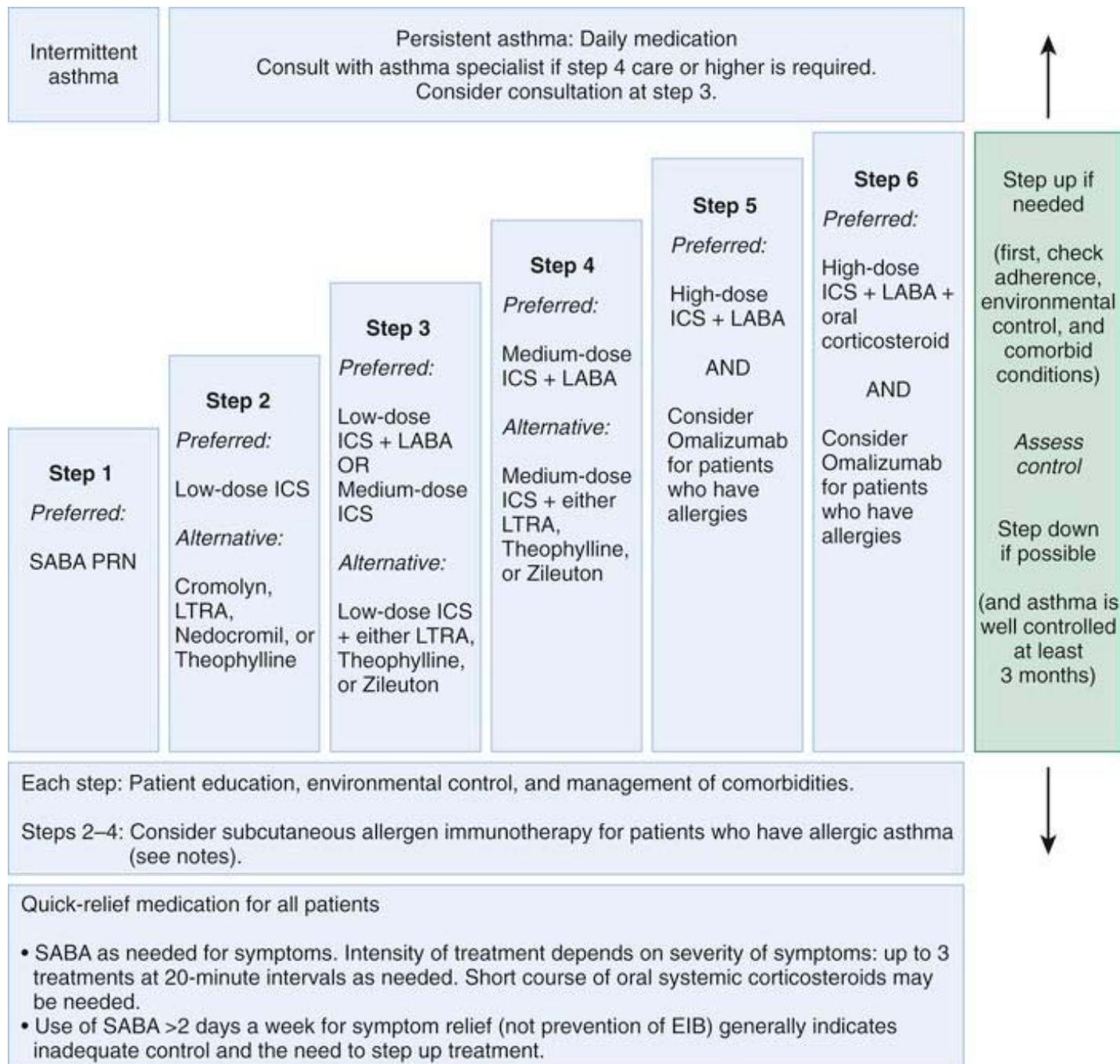


Step 4 Treatment for Adults and Children > 5: Severe Persistent

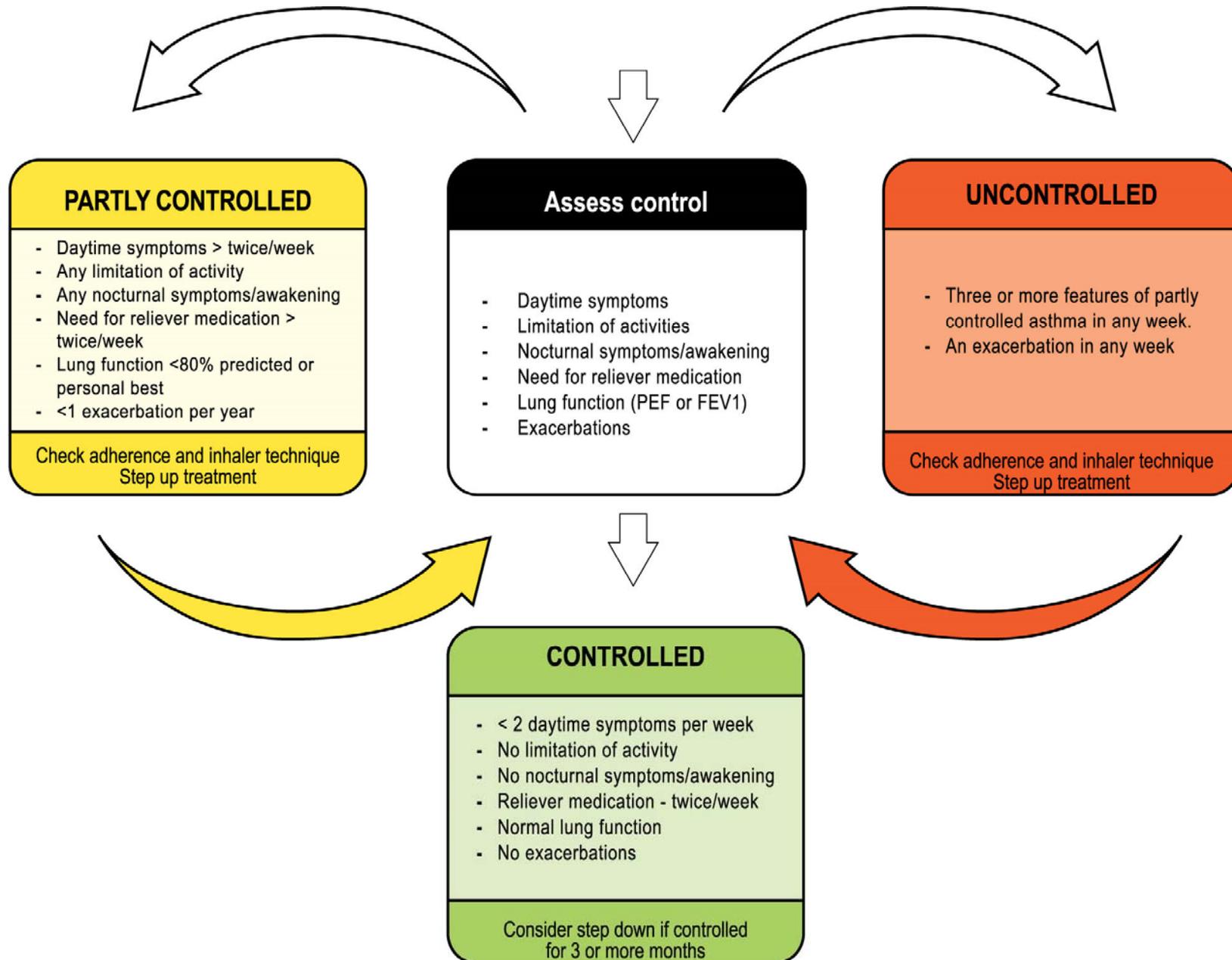
Controller - Daily

- High-dose inhaled corticosteroid **AND**
- Long-acting inhaled beta₂-agonist **AND**, if needed,
- Corticosteroid tablets or syrup long term (2 mg/kg/day, generally \leq 60 mg/day). (Make repeat attempts to reduce dose and maintain control with high-dose inhaled corticosteroid).
- **Recommend referral to a specialist**





Monitor Asthma Control



Treating to Maintain Asthma Control

Stepping down treatment when asthma is controlled

- When controlled on medium- to high-dose inhaled glucocorticosteroids: 50% dose reduction at 3 month intervals (Evidence B)
- When controlled on low-dose inhaled glucocorticosteroids: switch to once-daily dosing (Evidence A)

Treating to Maintain Asthma Control

Stepping up treatment in response to loss of control

- Rapid-onset, short-acting or long-acting inhaled β 2-agonist bronchodilators provide temporary relief
- Need for repeated dosing over more than one/two days signals need for possible increase in controller therapy

Managing the well controlled patient

As soon as good control:

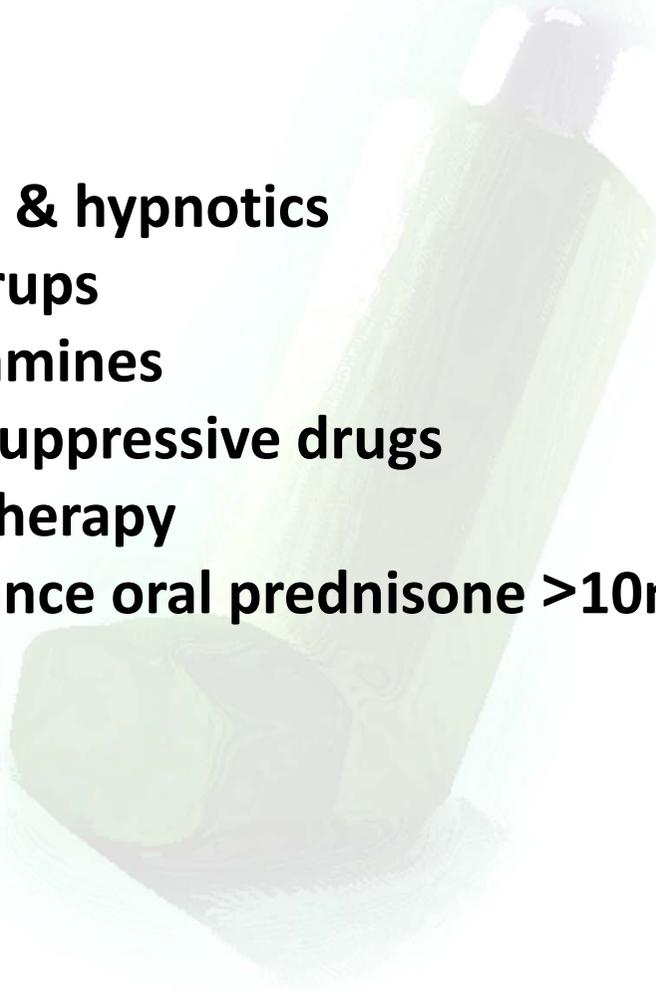
- Reduce oral steroids first, then stop
- Reduce relievers before controllers

When good control for 3+ months:

- Reduce inhaled steroids

Therapy to avoid!

- **Sedatives & hypnotics**
- **Cough syrups**
- **Anti-histamines**
- **Immunosuppressive drugs**
- **Immunotherapy**
- **Maintenance oral prednisone >10mg/day**



Managing partly/uncontrolled asthma

- Check the inhaler technique
- Check adherence and understanding of medication
- Consider aggravation by:
 - Exposure to triggers/allergens at home or work
 - Co-morbid conditions: GI reflux, rhinitis/sinusitis, cardiac problem
 - Medications: Beta-blockers, NSAIDs, Aspirin

The Asthma Action Plan

- Helps patients/caregivers manage asthma
 - Uses Peak Flows
 - Spells out medication instructions
- Green Zone 80-100% Peak Flow
- Yellow Zone 50-80% Peak Flow
- Red Zone Below 50% Peak Flow

Medication Delivery Demonstrations

- Breath Actuated Inhalers
- Metered Dose Inhalers with Spacer/Holding Chamber
- Dry Powder Inhalers
- Nebulizers

pMDIs



Advantages

Small and portable

Quick to use

Disadvantages

difficult to learn technique

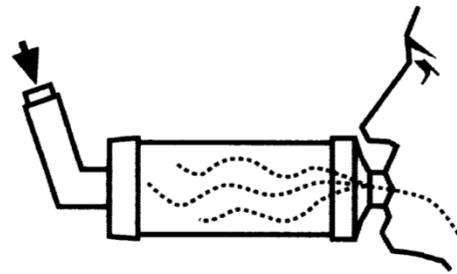
Unsuitable for children < 5-6

Unsuitable for the elderly,

Cold jet may irritate throat

Limited amount of drug

delivered per puff



Spacers and Holding Chambers

A spacer device enhances delivery by decreasing the velocity of the particles and reducing the number of large particles, allowing smaller particles of drug to be inhaled.

- A spacer device with a one-way valve, i.e., holding chamber, eliminates the need for the patient to coordinate actuation with inhalation and optimizes drug delivery.
- A simple spacer device without a valve requires coordination between inhalation and actuation.

DPIs



- Generally easier to use
- A minimal inspiratory flow rate is necessary to inhale from a DPI; difficult for some pts to use during an exacerbation
- More ecological than MDIs
- Storage may be difficult in humid climates

Nebulizer

Advantages

No Coordination required

Can be used for all ages

Effective in severe asthma

Disadvantages

Cumbersome

Expensive

Noisy

Treatment takes time

Which inhalation device for which patient?

- Infants and children up 5 y/o pMDI+spacer, nebulizer
- Children 5-9 y/o pMDI+spacer, nebulizer, DPI
- Competent older children and adults pMDI, DPI
- Incompetent older children/adults pMDI+spacer, nebulizer

Key Messages

- Asthma is common-can happen to anybody
- Asthma can be effectively controlled, although it cannot be cured.
- Effective asthma management programs include education, objective measures of lung function, environmental control, and pharmacologic therapy.
- A stepwise approach to pharmacologic therapy is recommended.
- The aim is to accomplish the goals of therapy with the least possible medication.