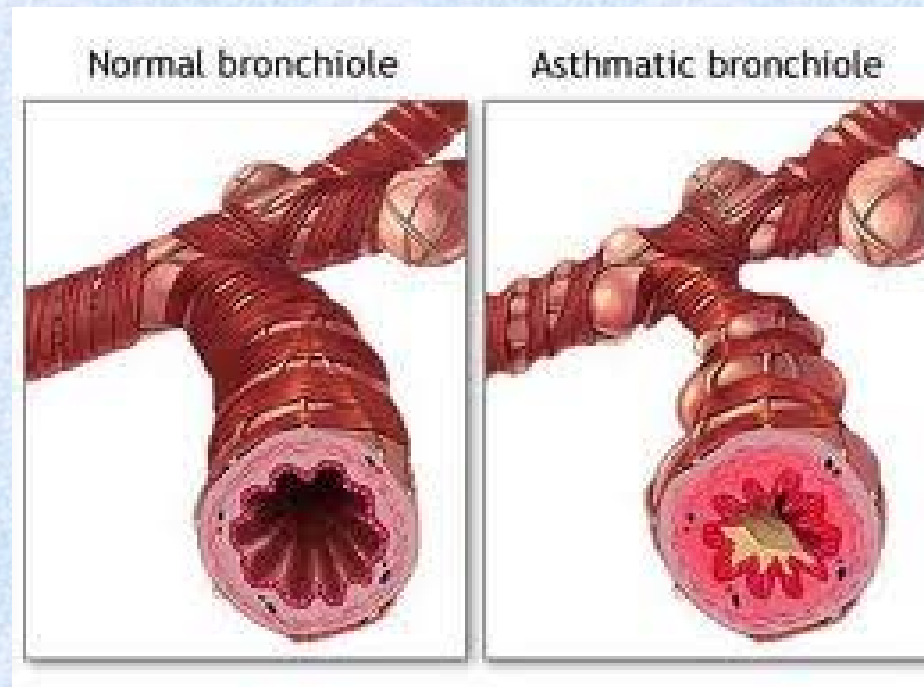


Bronchial Asthma

Pathophysiology and management



Dr Deepak Aggarwal
MD, FCCP
Asst. Professor
Pulmonary medicine

What is Asthma....Definition (GINA)

- Asthma is
 - 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

Causes/ Risk factors

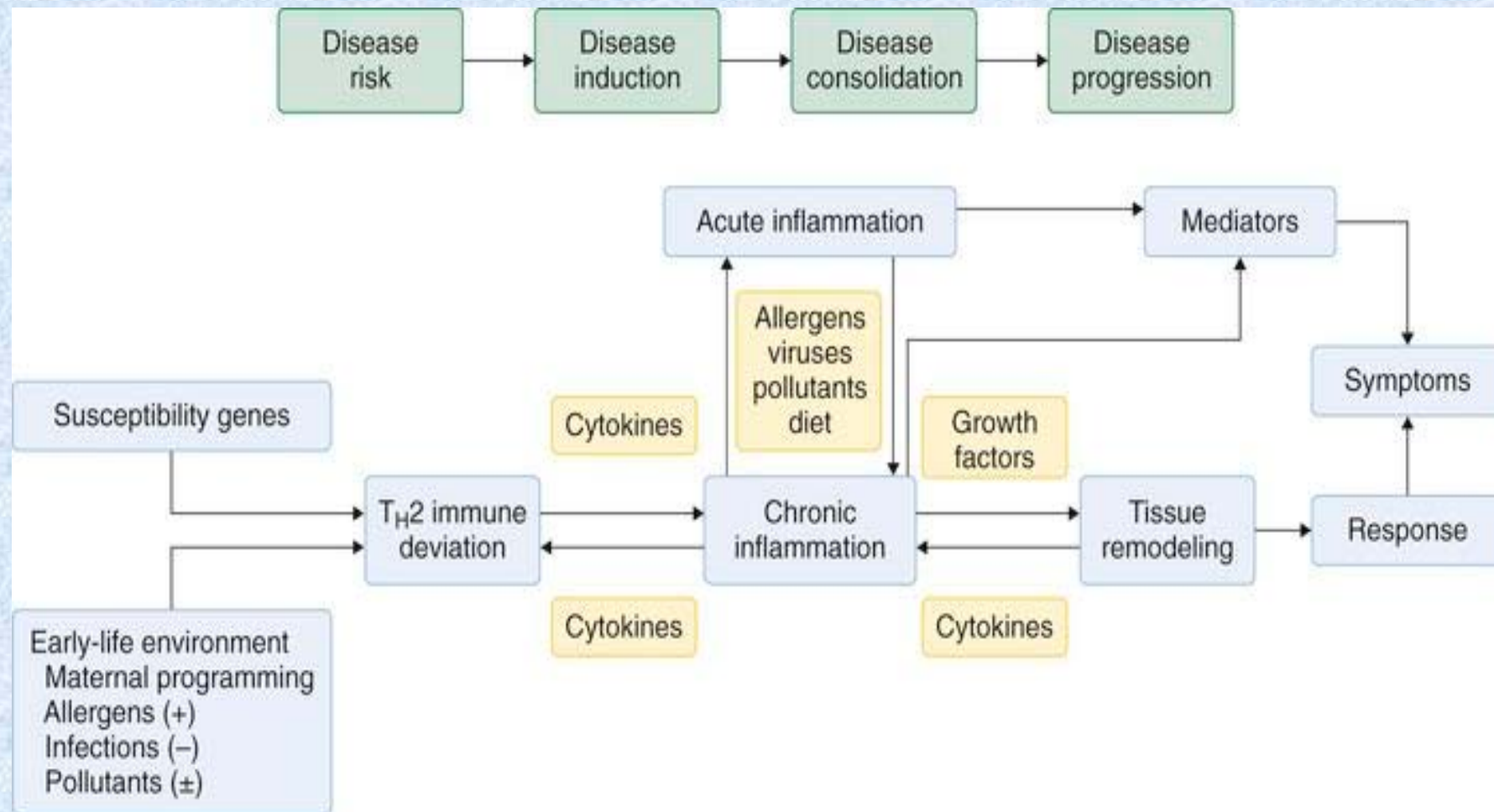
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graph TD; A[Causes/ Risk factors] --> B[GENETIC SUSCEPTIBILITY AND GENE-ENVIRONMENT INTERACTIONS]; A --> C[ENVIRONMENTAL RISK FACTORS]; C --> D[Perinatal Factors]; C --> E[Indoor and Outdoor Allergens]; C --> F[Smoking and Environmental Tobacco Smoke]; C --> G[Other Pollutants]; C --> H[Race/Ethnicity and Socioeconomic Status]; C --> I[Obesity]; C --> J[Respiratory Illnesses];
```

**GENETIC SUSCEPTIBILITY AND
GENE-ENVIRONMENT INTERACTIONS**

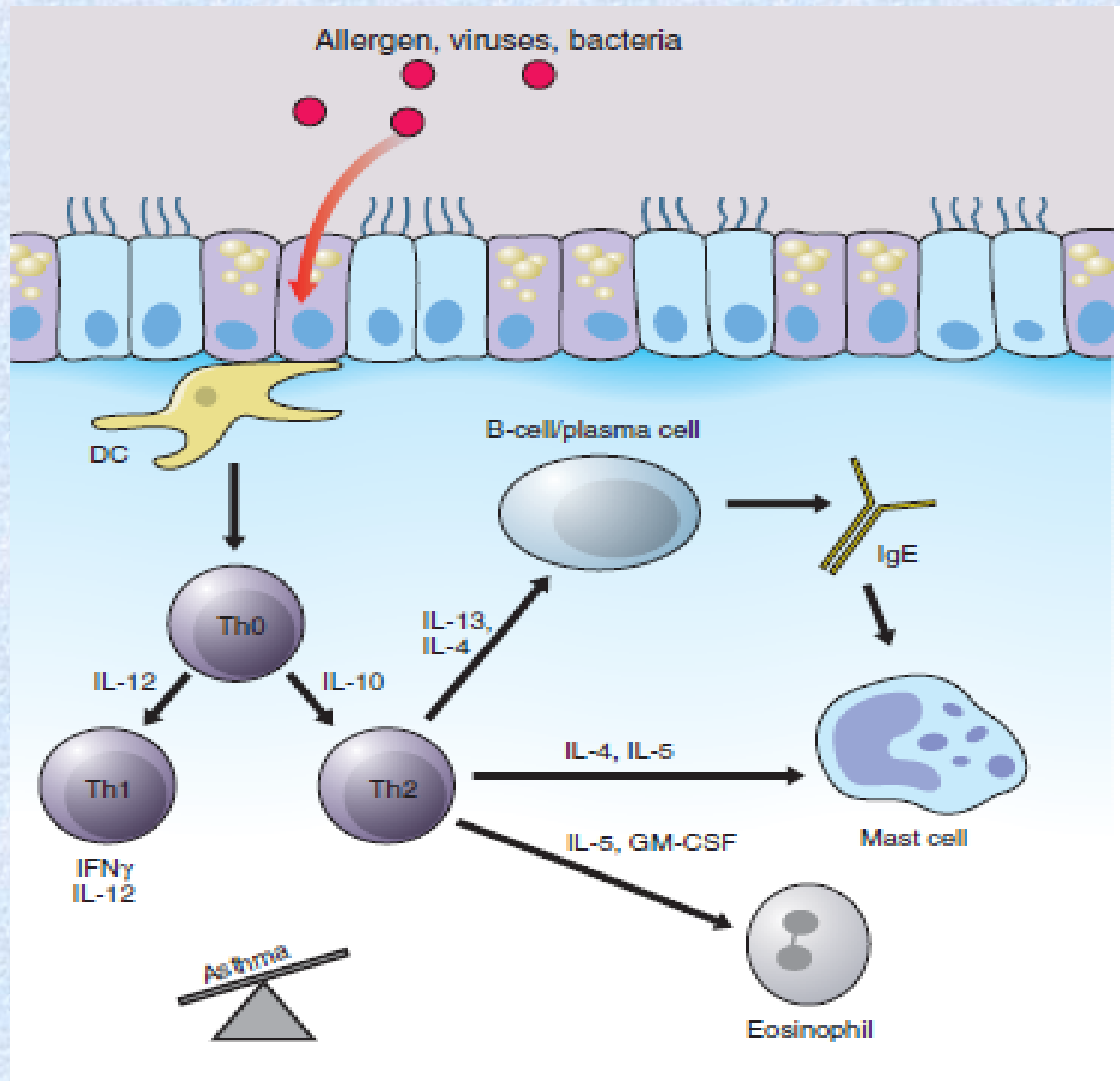
**ENVIRONMENTAL RISK
FACTORS**

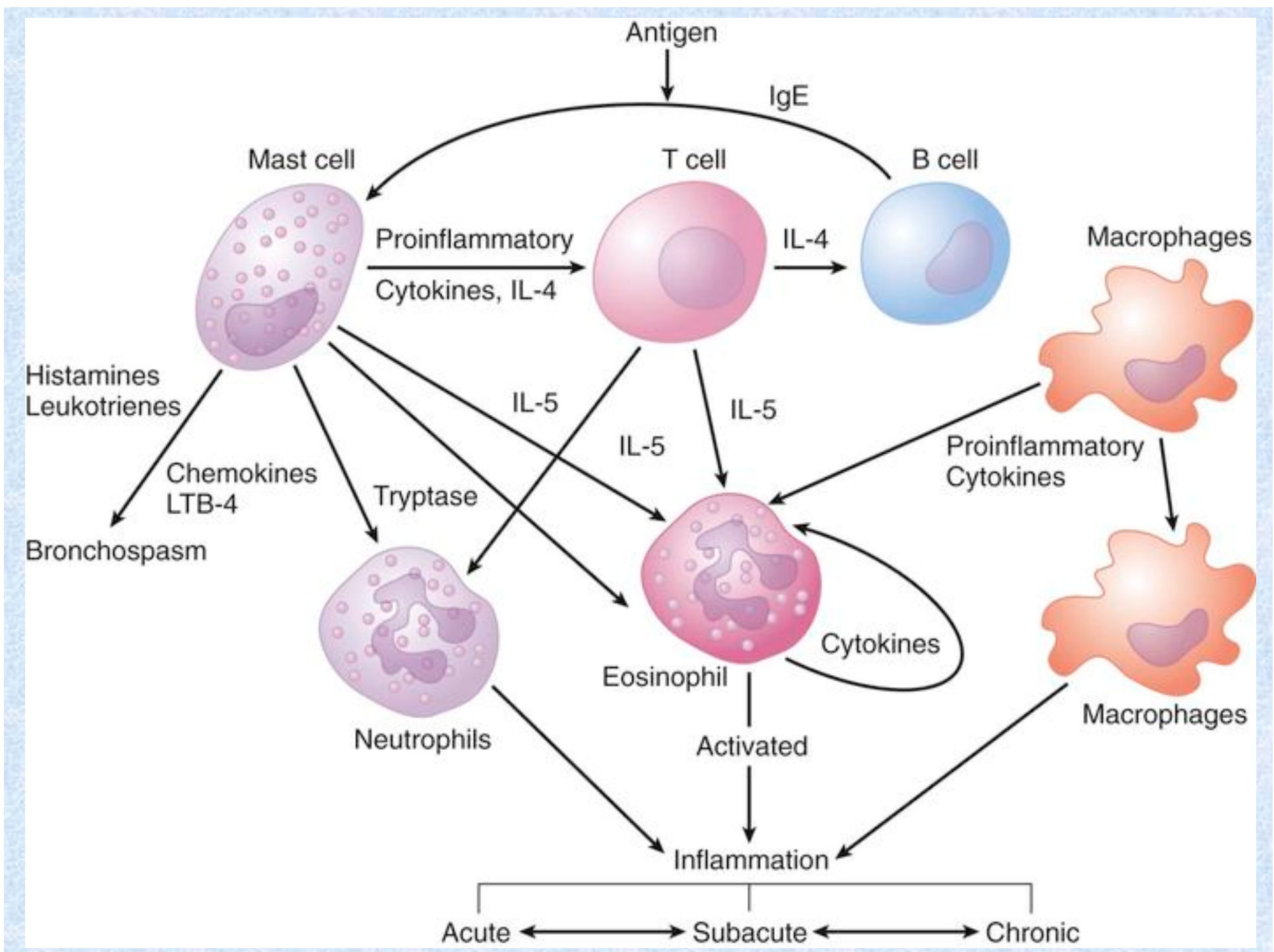
Perinatal Factors
Indoor and Outdoor Allergens
Smoking and Environmental Tobacco
Smoke
Other Pollutants
Race/Ethnicity and Socioeconomic
Status
Obesity
Respiratory Illnesses

How Asthma develops.....

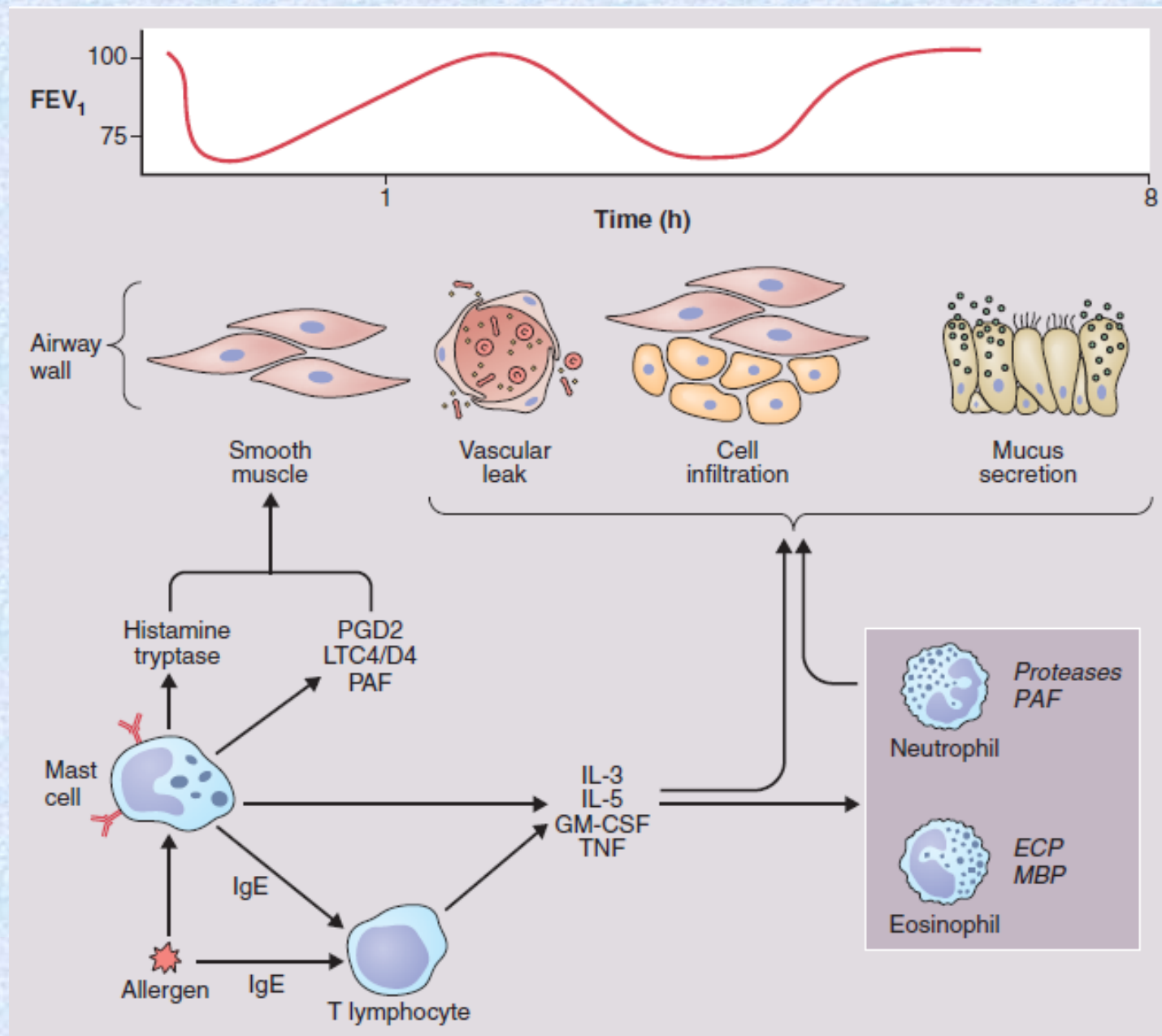


PATHOGENESIS

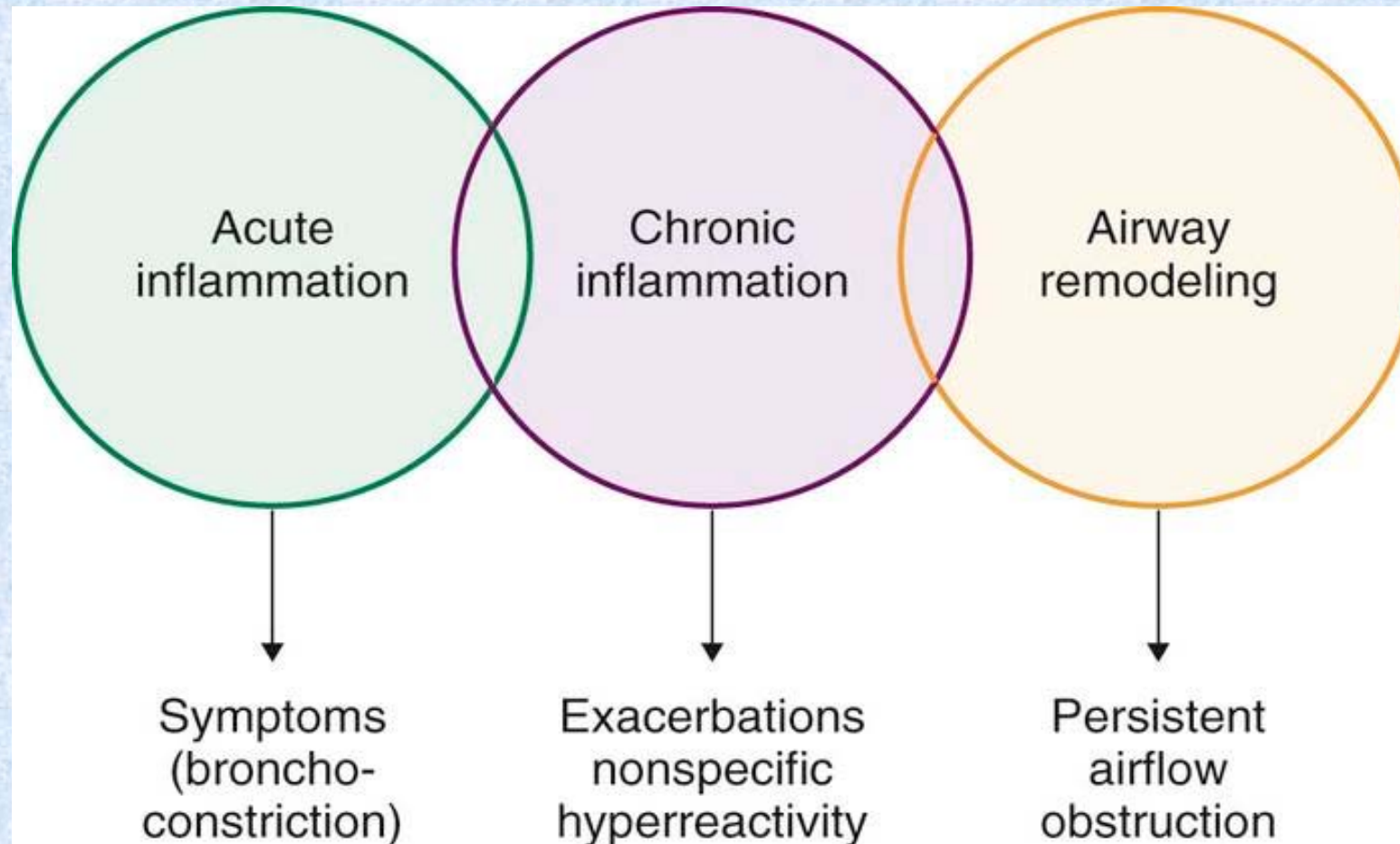




PATHOGENESIS



ASTHMA - PATHOPHYSIOLOGY

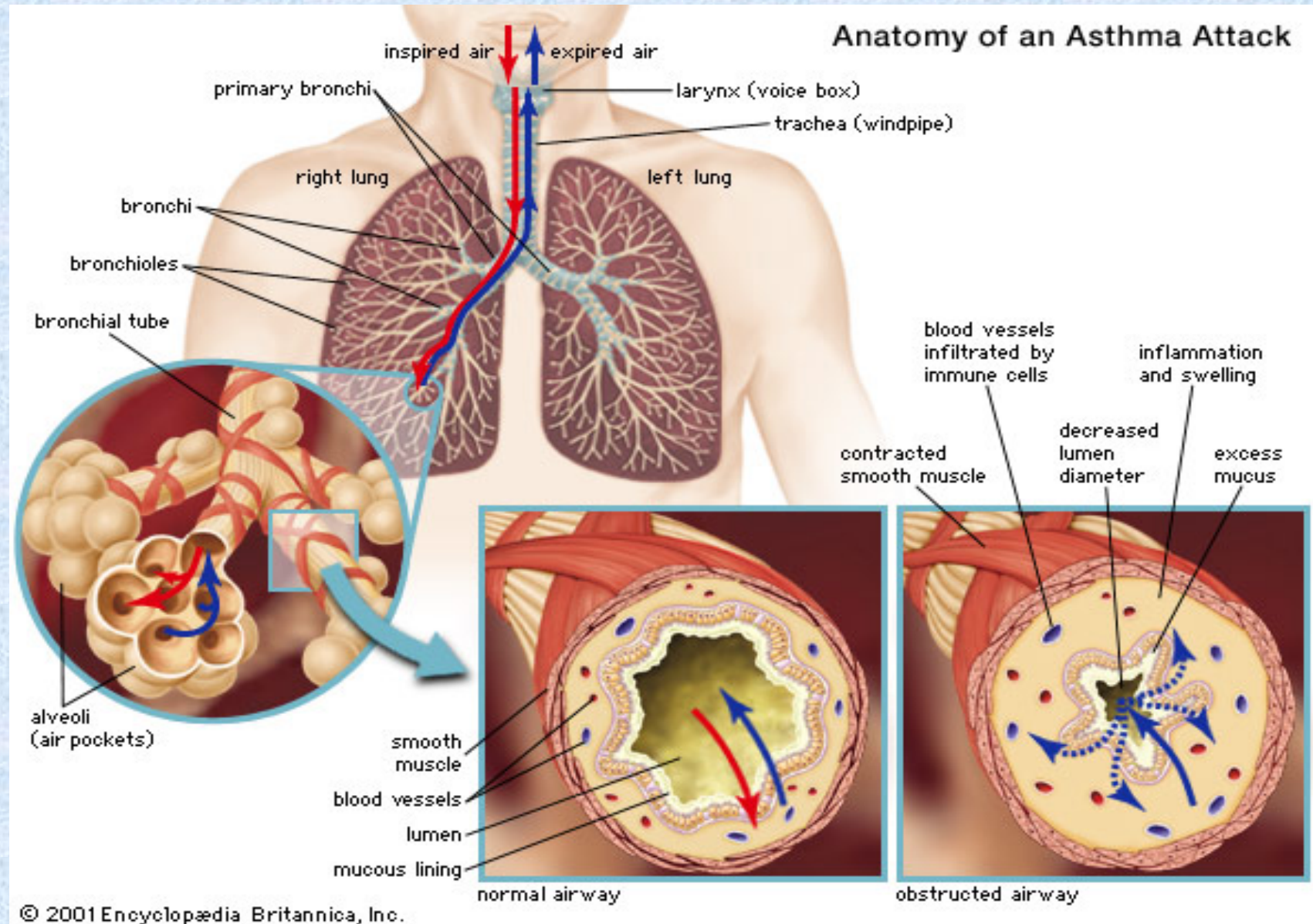


Genetic predisposition
Intrinsic vulnerability
Atopy/allergy

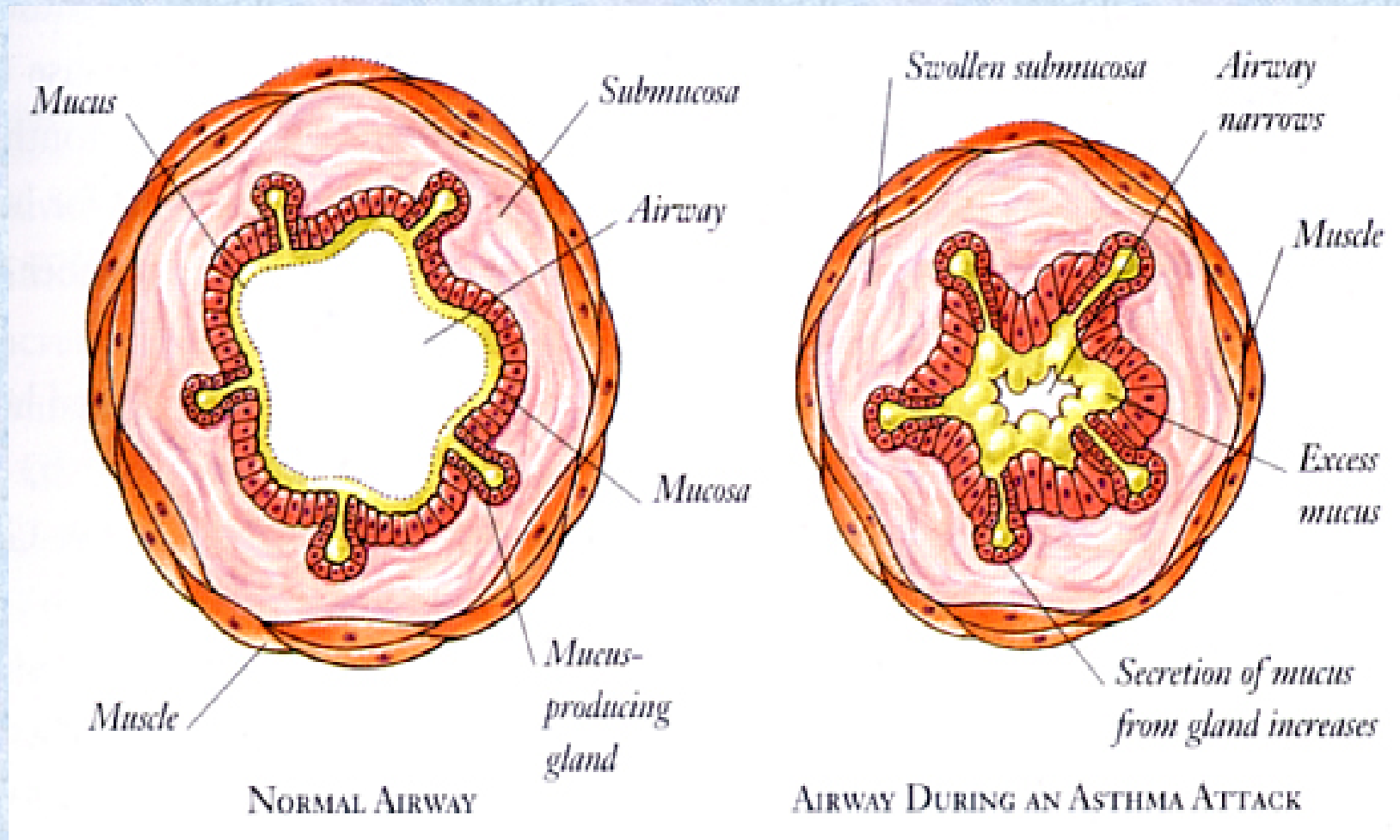
Inflammation underlies disease processes
Phenotype varies by individual and over time

Clinical symptoms also vary by individual and over time

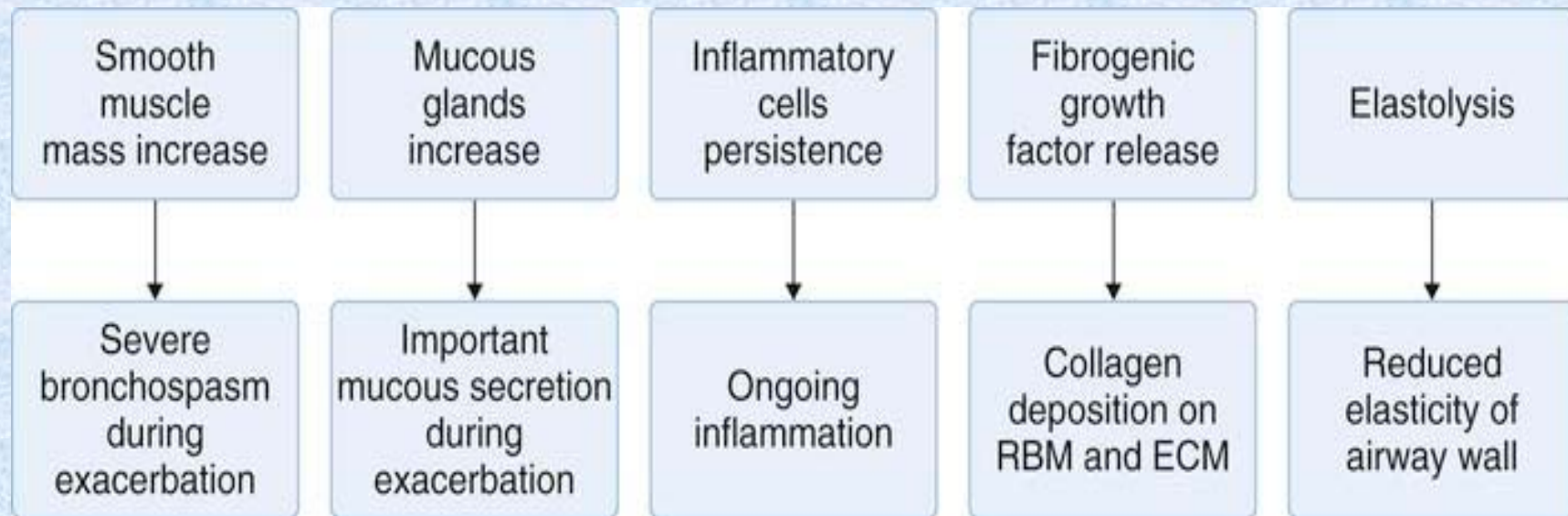
PATHOLOGY



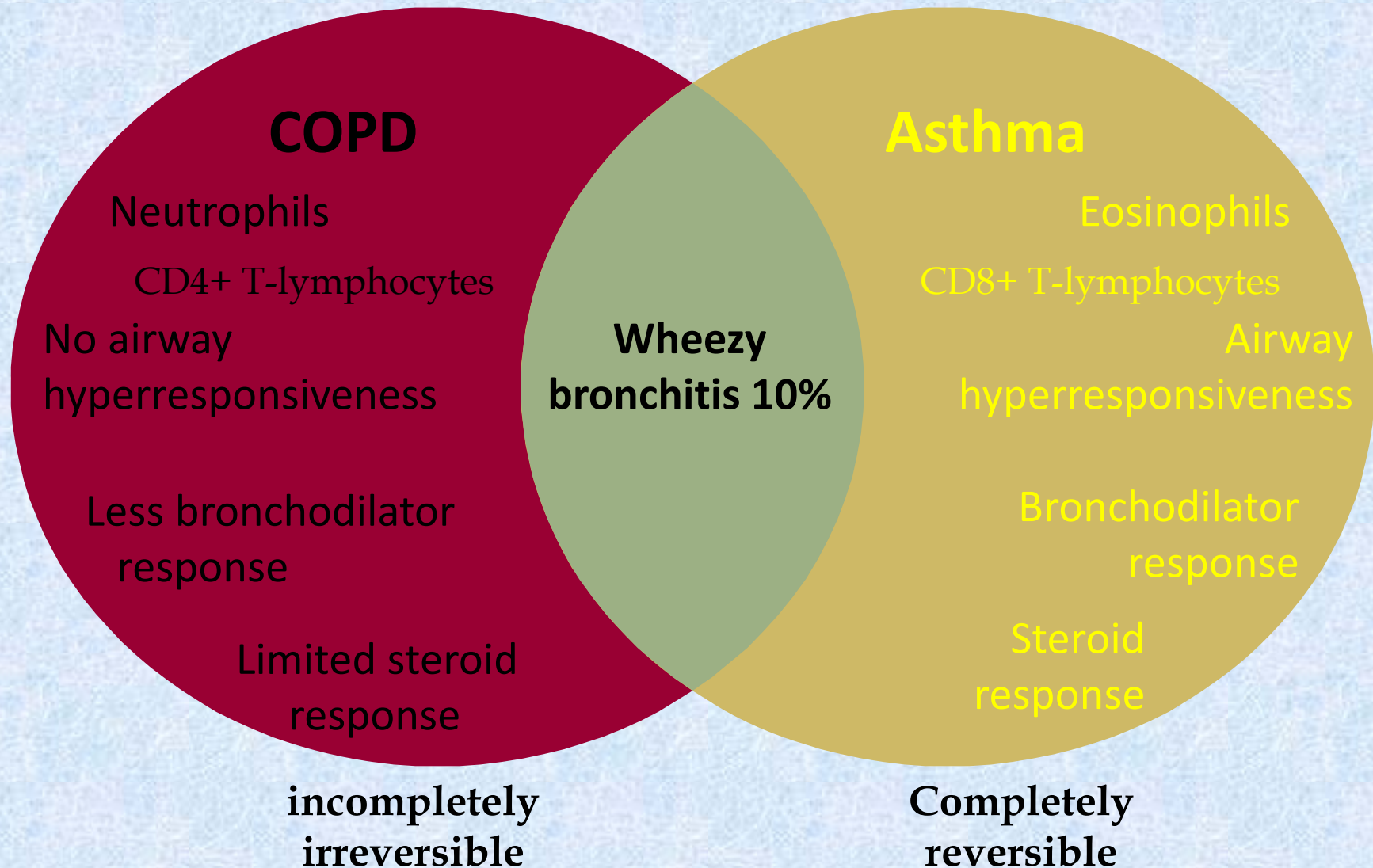
Asthma: Pathological changes



Pathology and consequences



Difference and overlap



Physiologic Differences

Asthma

- Normal DLCO
- Normal lung volume
- Normal elastic recoil

COPD

- Abnormal DLCO
- Hyperinflation
- Decreased elastic recoil

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

+++

—

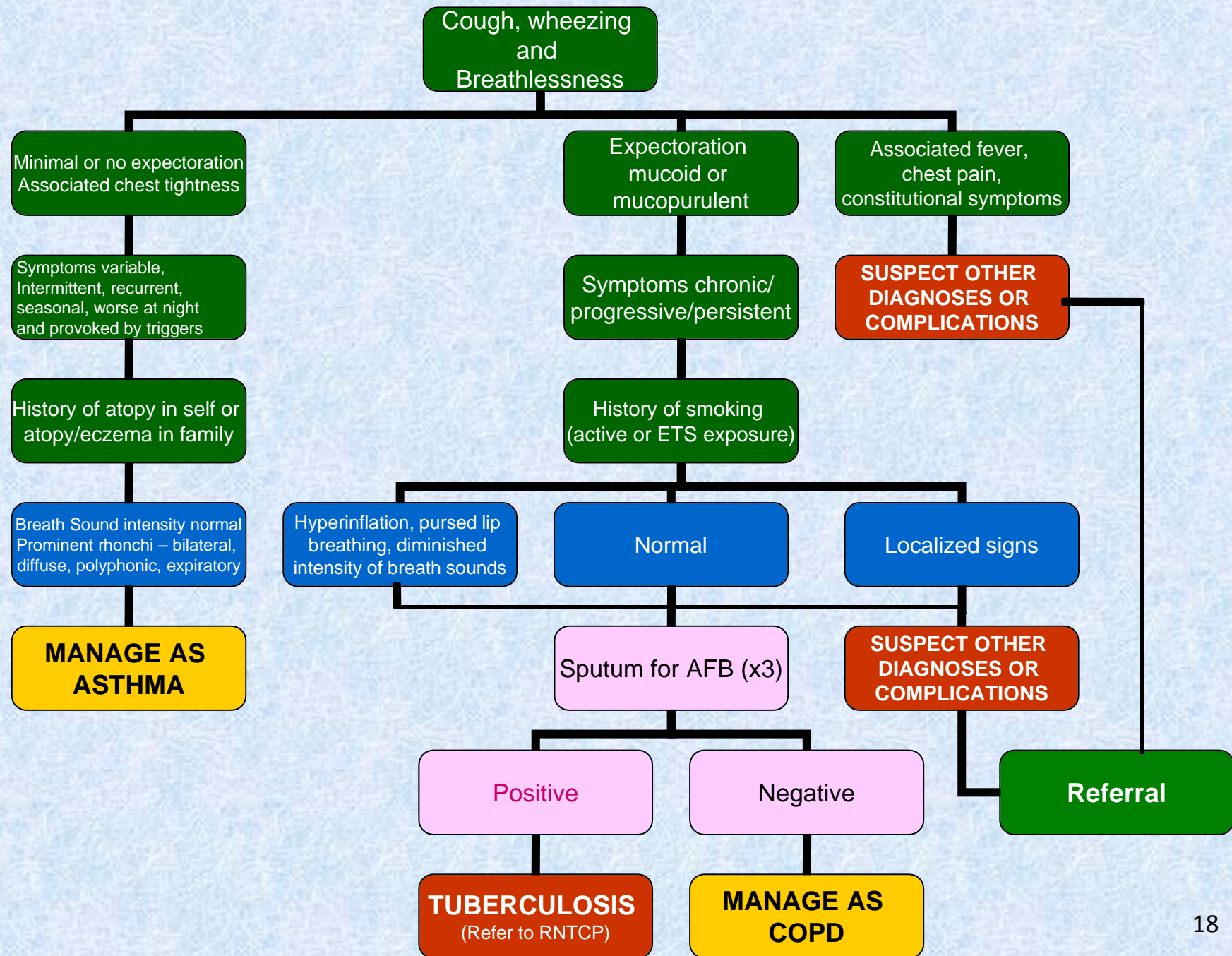
Asthma-Classic presentation

- Intermittent episodic, acute/subacute onset
- Breathlessness/chest tightness usually with wheeze
- Cough nocturnal or early morning.
- Diurnal and seasonal variation
- History of atopy, family history
- Polyphonic wheeze, prolonged expiration
- However, the examination can be normal.

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
- Serum electrolytes (Mg, Na, K)
- Spirometry
- Other test to rule out specific diseases

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 FEV_1 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



TREATMENT

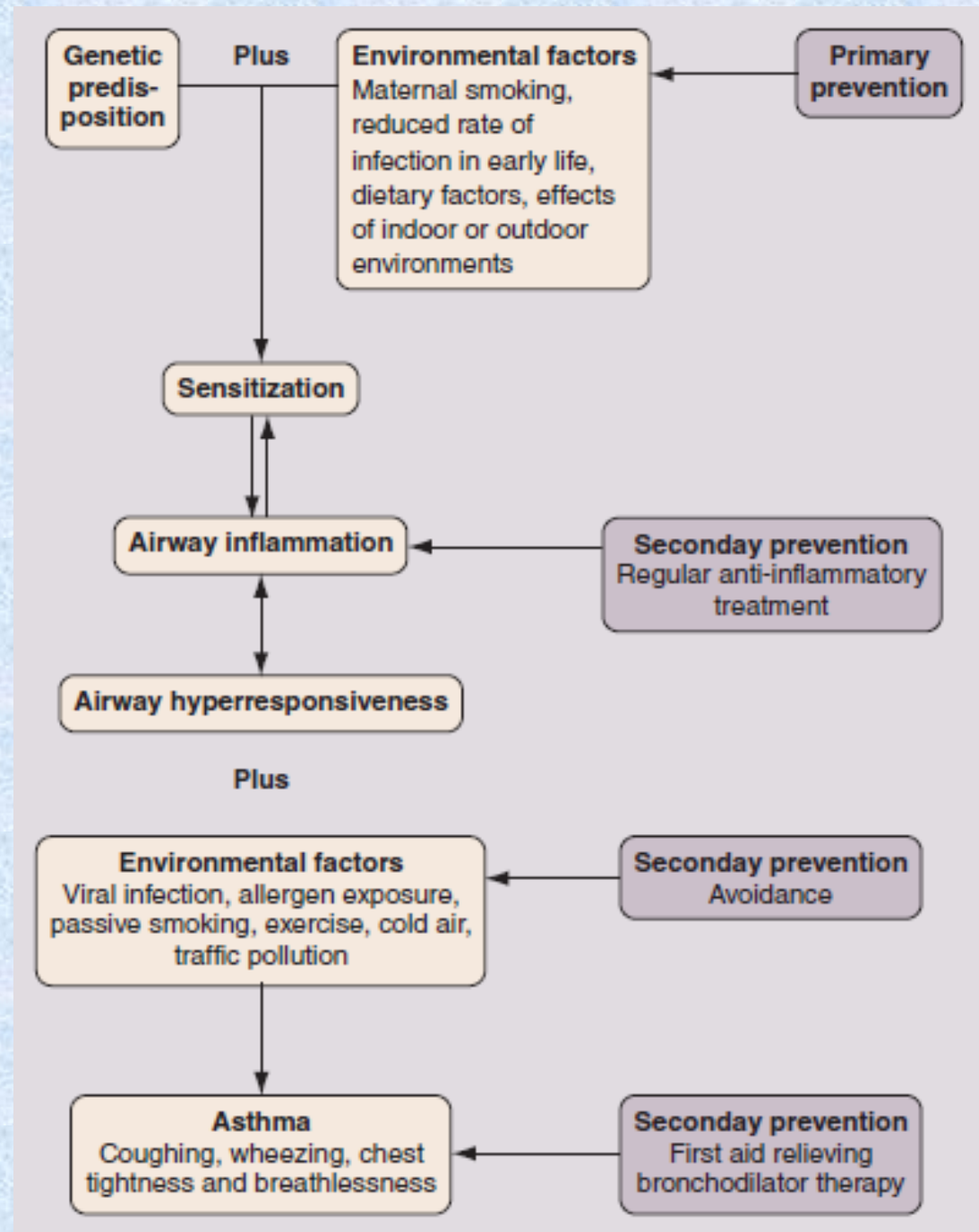
Goals of Asthma Therapy

- 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

GINA Levels of Asthma Control

Characteristic	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	1 in any week

Levels of prevention



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. Zafirlukast 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>

What are Controllers?

Control/treat chronic inflammation

Prevent future attacks

Long term control

Prevent airway remodeling

Anti-inflammatory action to prevent asthma attacks	Sustained bronchodilator action but weak or unproven anti-inflammatory effect
Inhaled corticosteroids 1. Beclomethasone 2. Budesonide 3. Fluticasone 4. Ciclesonide	Long-acting beta-agonists 1. Salmeterol 2. Formoterol
Leukotriene modifiers 1. Montelukast 2. Zafirlukast Oral corticosteroids 1. Prednisone 2. Prednisolone 3. Methylprednisone 4. Methylprednisolone	Sustained-release theophylline preparations

What Are Relievers?

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

**For quick relief of symptoms
and use in acute attacks as
PRN dosage only**

Short-acting beta-agonists

1. Salbutamol
2. Fenoterol
3. Terbutaline

Anti-cholinergics

Ipratropium bromide

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

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

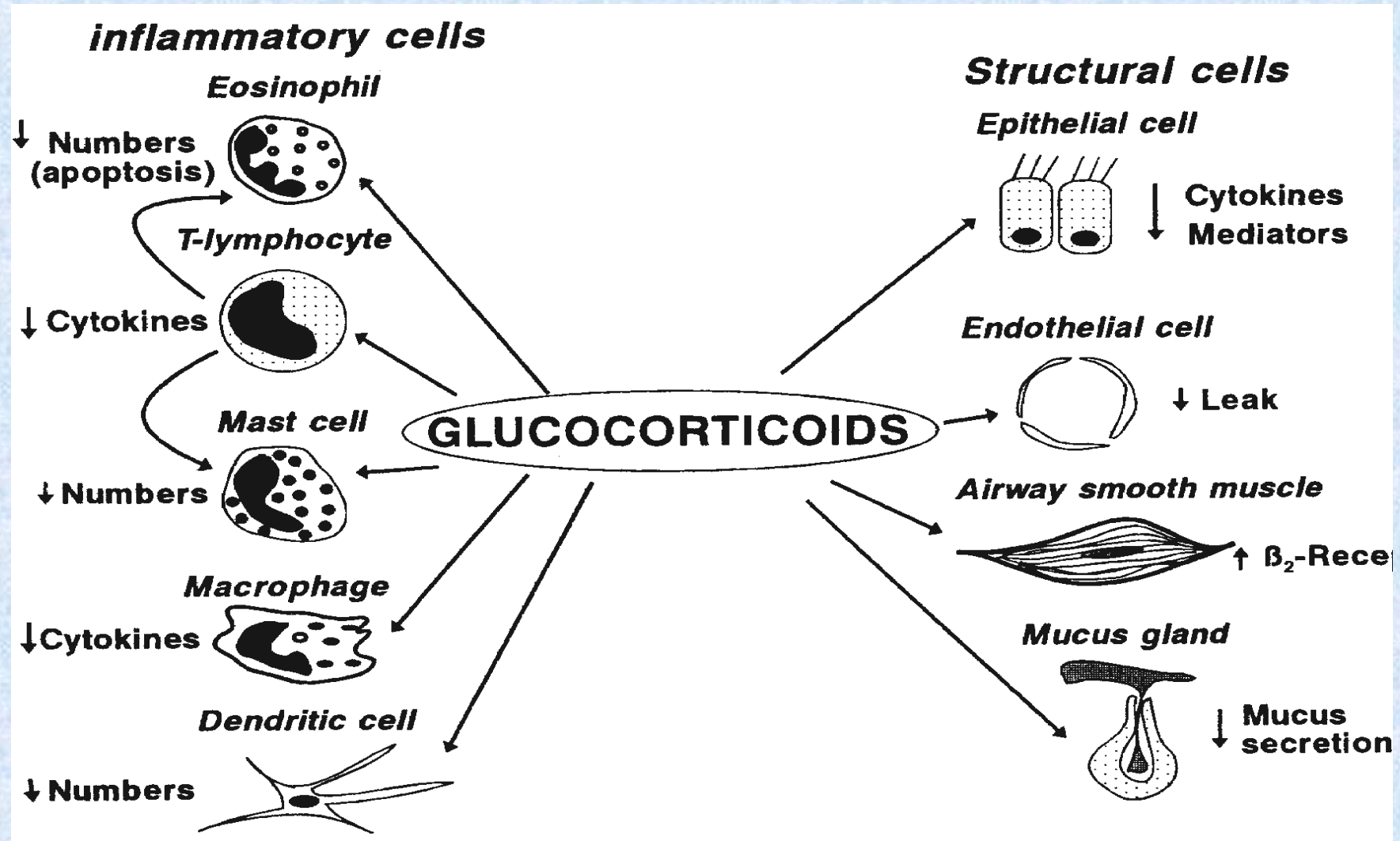
****NEVER FOR RESCUE PURPOSES****

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)

CONTROLLERS

Long-acting Beta₂-agonists

- Salmeterol, Formoterol
 - Indication: Daily long-term control
- Advantages
 - Blunt exercise induced symptoms for longer time
 - Decrease nocturnal symptoms
 - Improve quality of life
- Combination therapy beneficial when added to inhaled corticosteroids

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 dose
 - Zafirlukast – Twice daily – Empty Stomach

- 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
 - Not as effective as inhaled corticosteroids
 - No food restrictions

RELIEVERS

Short-Acting Beta₂-agonist

- Salbutamol
- Terbutaline
- levosalbutamol

RELIEVERS

Short-Acting Beta₂-Agonists

- Most effective medication for relief of acute bronchospasm
- Increased need for these medications indicates uncontrolled asthma (and inflammation)
- Use “as needed” as regular use
 - 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

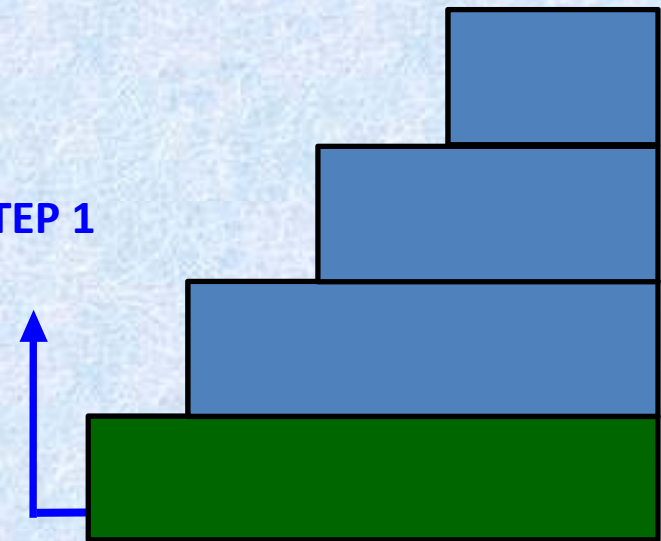
Controller – Daily

- Not needed

Reliever – Quick Relief

- Short-acting inhaled β_2 -agonist
- Increasing use, or use more than 2x/week, may indicate need for long-term-control therapy
-

STEP 1



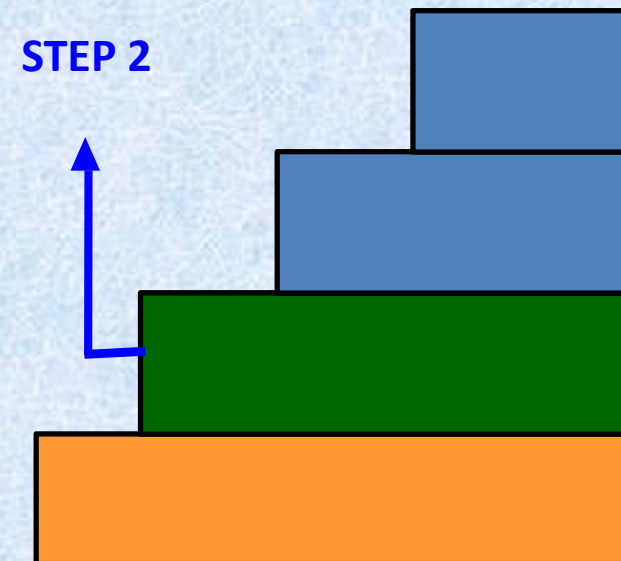
Step 2 Treatment for Adults and Children > 5: Mild Persistent

Controller – Preferred Daily

- Low dose inhaled corticosteroid

Alternatives

- leukotriene modifier,
OR
- Sustained-release theophylline



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

Controller – Preferred Daily

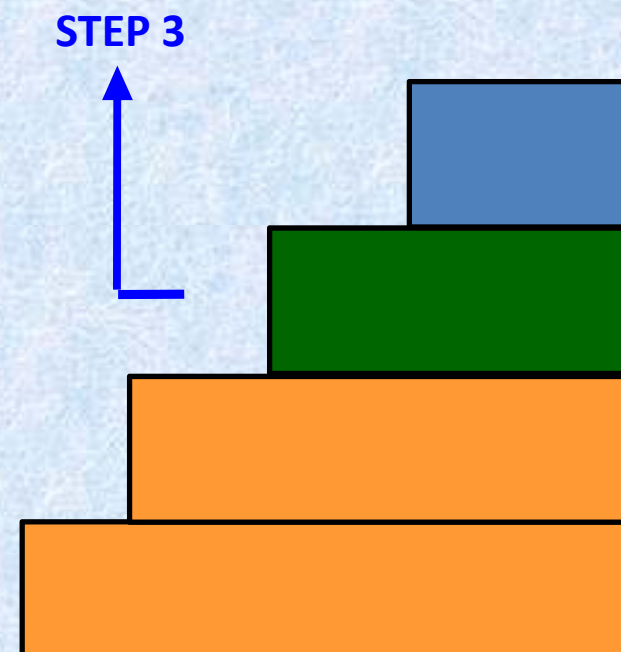
- *Low to medium dose inhaled corticosteroid (medium dose) and long-acting β_2 -agonist*

Alternatives

- 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)

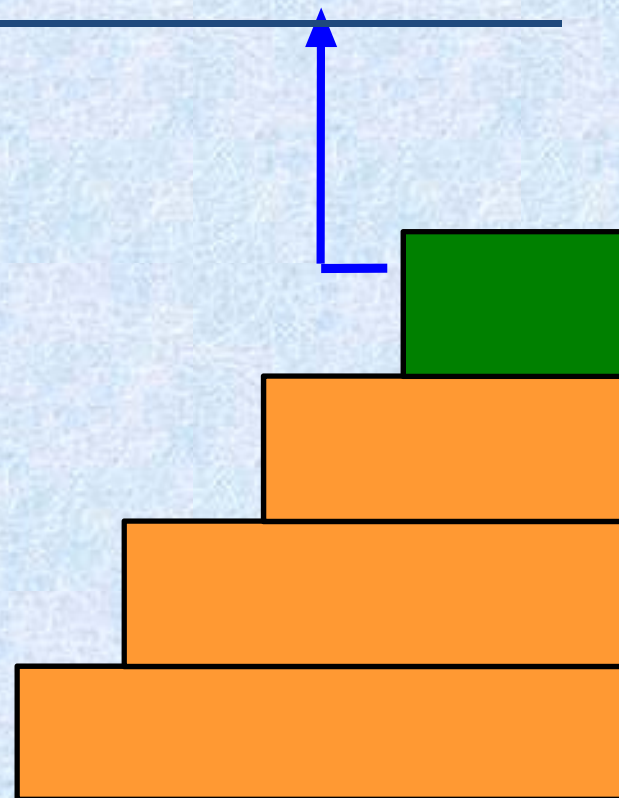
STEP 4

Controller

- Medium dose inhaled corticosteroid (medium dose) and long-acting β_2 -agonist

Alternatives

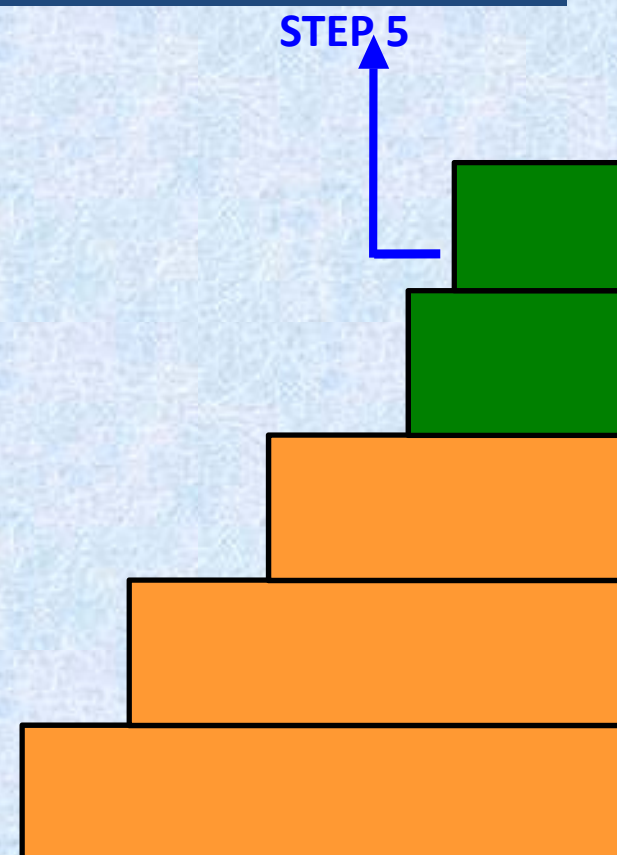
- Medium dose inhaled corticosteroid (medium dose) and either leukotriene modifier or theophylline
- High dose inhaled corticosteroid
- **Consider referral to a specialist**

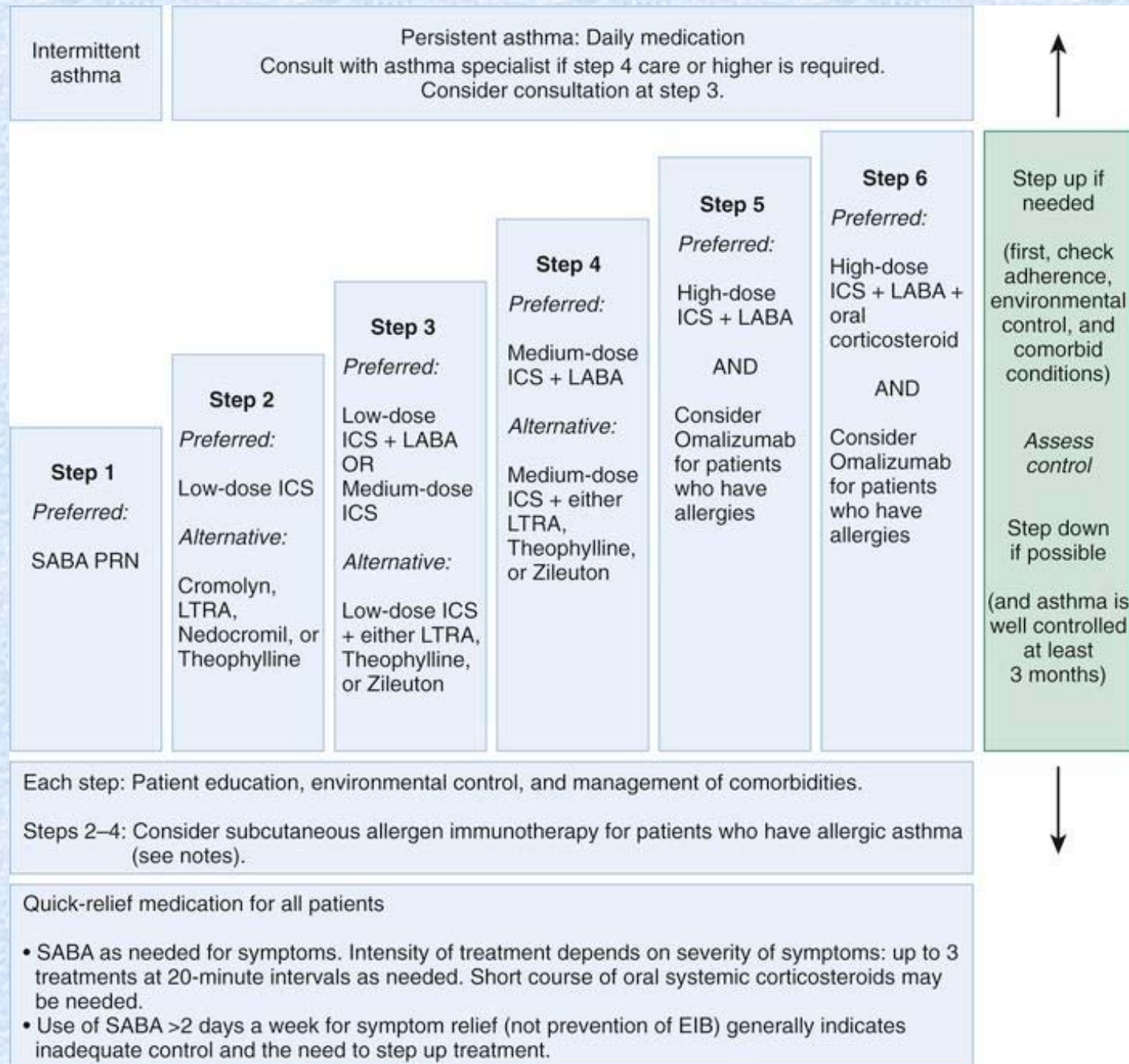


Step 4 Treatment for Adults and Children > 5: Severe Persistent

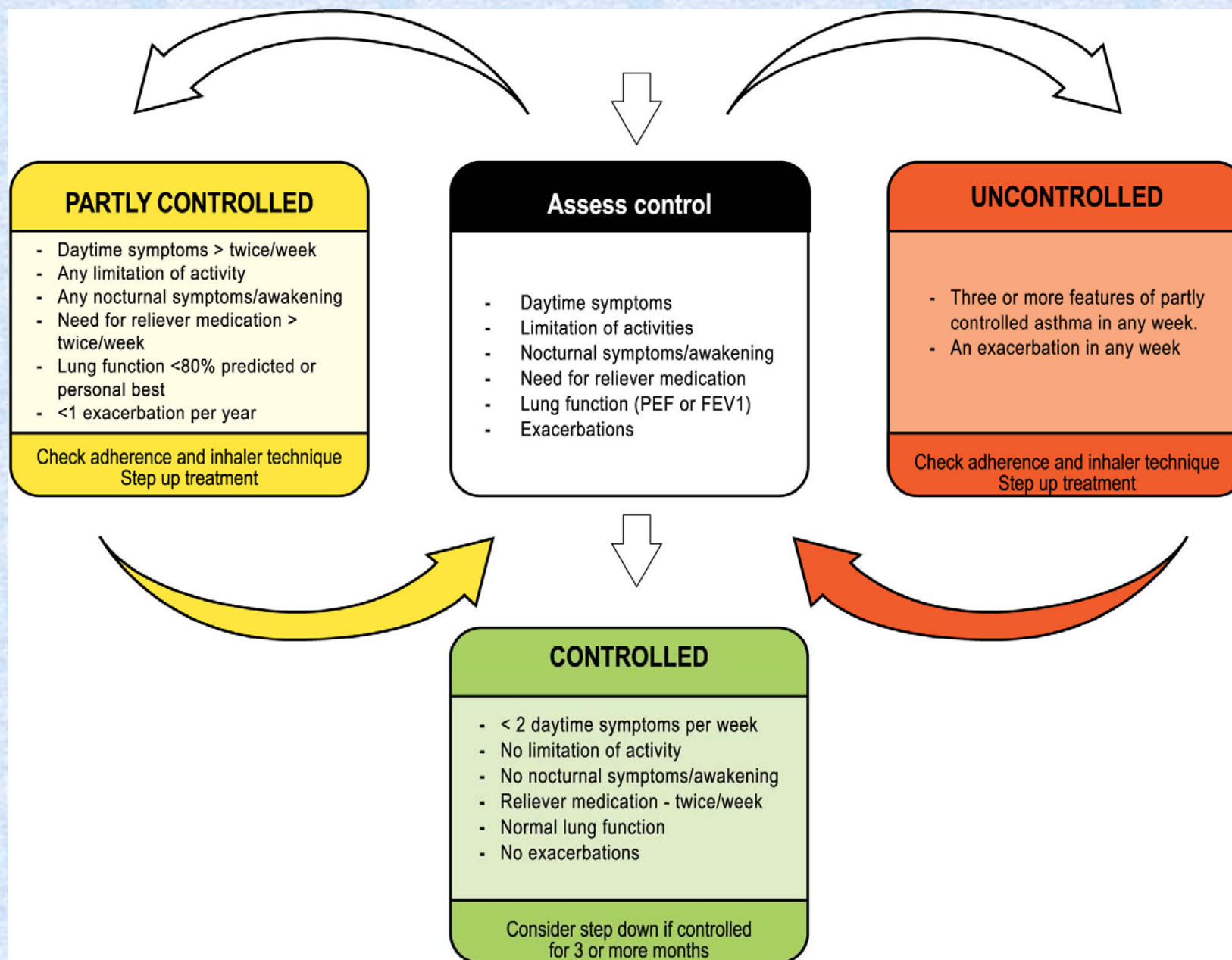
Controller – Daily

- *High-dose inhaled corticosteroid **AND***
- *Long-acting inhaled beta₂-agonist **AND**, if needed,*
- Add leukotriene antagonists & theophylline
- Corticosteroid tablets





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

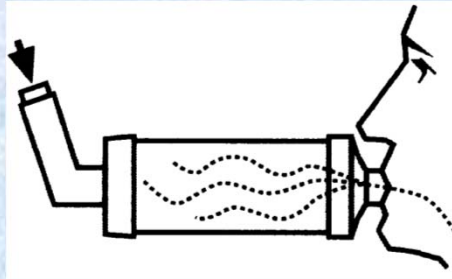
Unsuitable for children < 5-6

Unsuitable for the elderly,

Cold jet may irritate throat

**Limited amount of drug
delivered per puff**



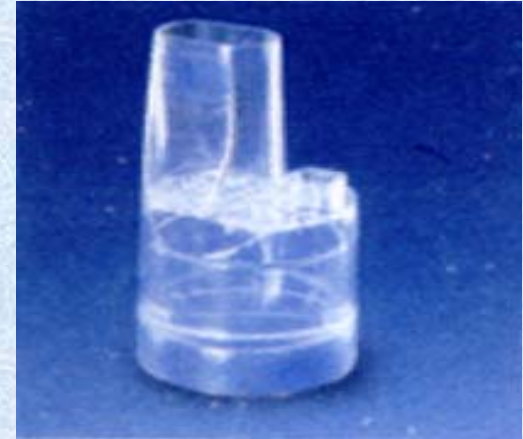


Spacers and Holding Chambers

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 to 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 and can start at any age
- Asthma can be effectively controlled
- 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.

Thank you