Bronchial asthma
Case- discussion

By

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CASE HISTORY

- A 13-year-old male presents to the emergency department with acute onset of breathlessness.

- He has had recurrent, episodic attacks of wheezing, cough, dyspnea, itchy red eyes, nasal discharge, and occasional chest tightness for past 2 years.

- Initially, his symptoms were relieved by short-acting β-Agonist, albuterol.
- However, the frequency and the severity of the symptoms have increased for the past 1 month with the patient waking up with these symptoms.
- He has a history of eczema. His family history is significant for asthma in his mother

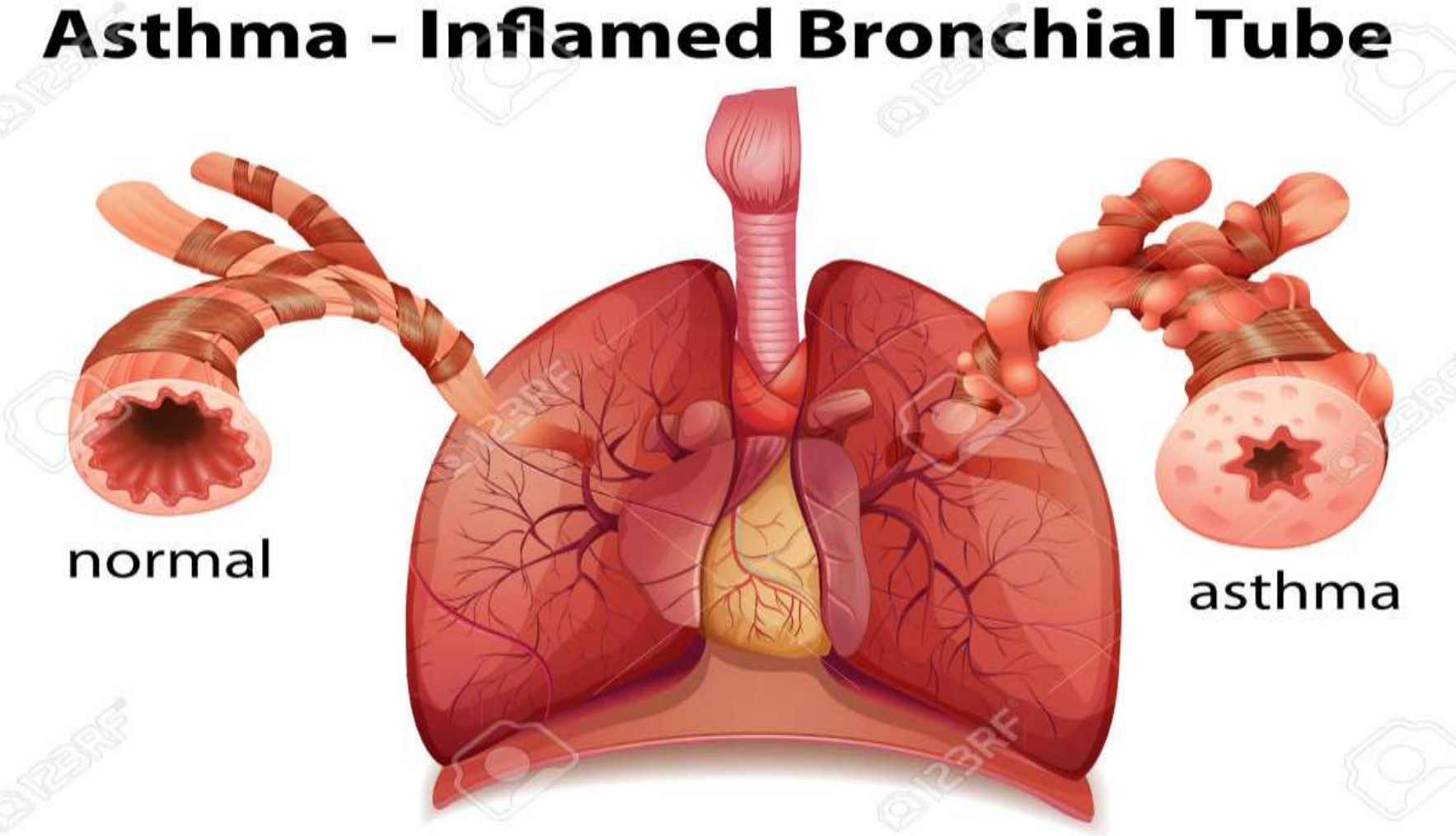
- Physical examination reveals respiratory rate of 22c/min and diffuse wheezing all over the lung fields.

What is the most probable diagnosis ?

a. Bronchial asthma
b. COPD
c. Bronchiectasis
d. Extrinsic allergic alveolitis

- **Definition of bronchial asthma**
- **Etiologic factors**
- **Immunology**
- **Pathophysiology**
- **Diagnosis**
- **Differential diagnosis**
- **Treatment guidelines**

What is asthma?



Definition of asthma

- A chronic inflammatory disorder of the airways, in which many cells and cellular elements play a role.
- This Chronic inflammation is associated with airway hyperresponsiveness that leads to airflow obstruction resulting in recurrent episodes of chest symptoms in the form of; wheezing, breathlessness, chest tightness, and coughing.
- This airflow obstruction is Reversible either spontaneously or with treatment and Variable allover the day with its peak at late night or in early morning

- **Many cellular elements play a role, in particular,**

- **Mast cells,**
- **Eosinophils,**
- **T lymphocytes,**
- **Macrophages,**
- **Neutrophils, and epithelial cells**

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Factors Influencing the Development and Expression of Asthma

- Asthma is a complex trait
- Heritable and environmental factors contribute to its pathogenesis

Factors Influencing the Development and Expression of Asthma

Host factors

- Genetic, e.g.
  - Genes pre-disposing to Atopy
  - Genes pre-disposing to airway hyperresponsiveness
- Obesity
- Sex

Factors Influencing the Development and Expression of Asthma

Environmental factors

- **Allergens**
  - Indoor: Domestic mites, furred animals (dogs, cats, mice), cockroach allergen, fungi, molds, yeasts
  - Outdoor: Pollens, fungi, molds, yeasts
- **Infections** (predominantly viral)
- **Occupational sensitizers**
- **Outdoor/Indoor Air Pollution**

Factors Influencing the Development and Expression of Asthma

Contributing Factors

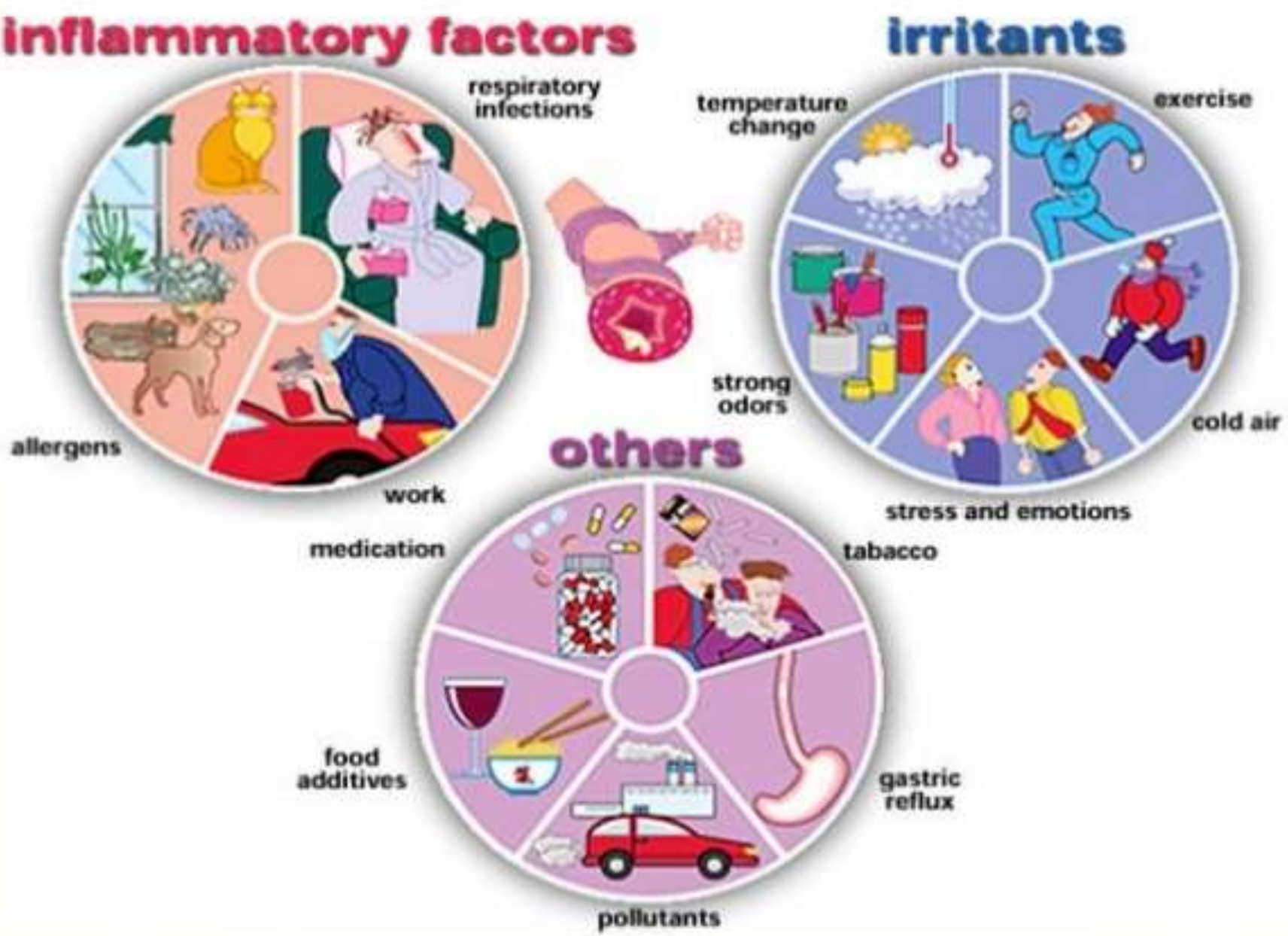
- Respiratory infections; the most common cause of acute exacerbation of asthma. Respiratory viruses are the major factors.

- Physical activity
- Psychological factors

- Gastroesophageal reflux disease
- Upper airway disease
- Medication
- Diet

- Smoking
  - Passive Smoking
  - Active Smoking

TRIGGERS


inflammatory factors
respiratory infections
allergens
work
irritants
temperature change
exercise
strong odors
cold air
stress and emotions
others
medication
tabacco
food additives
gastric reflux
pollutants

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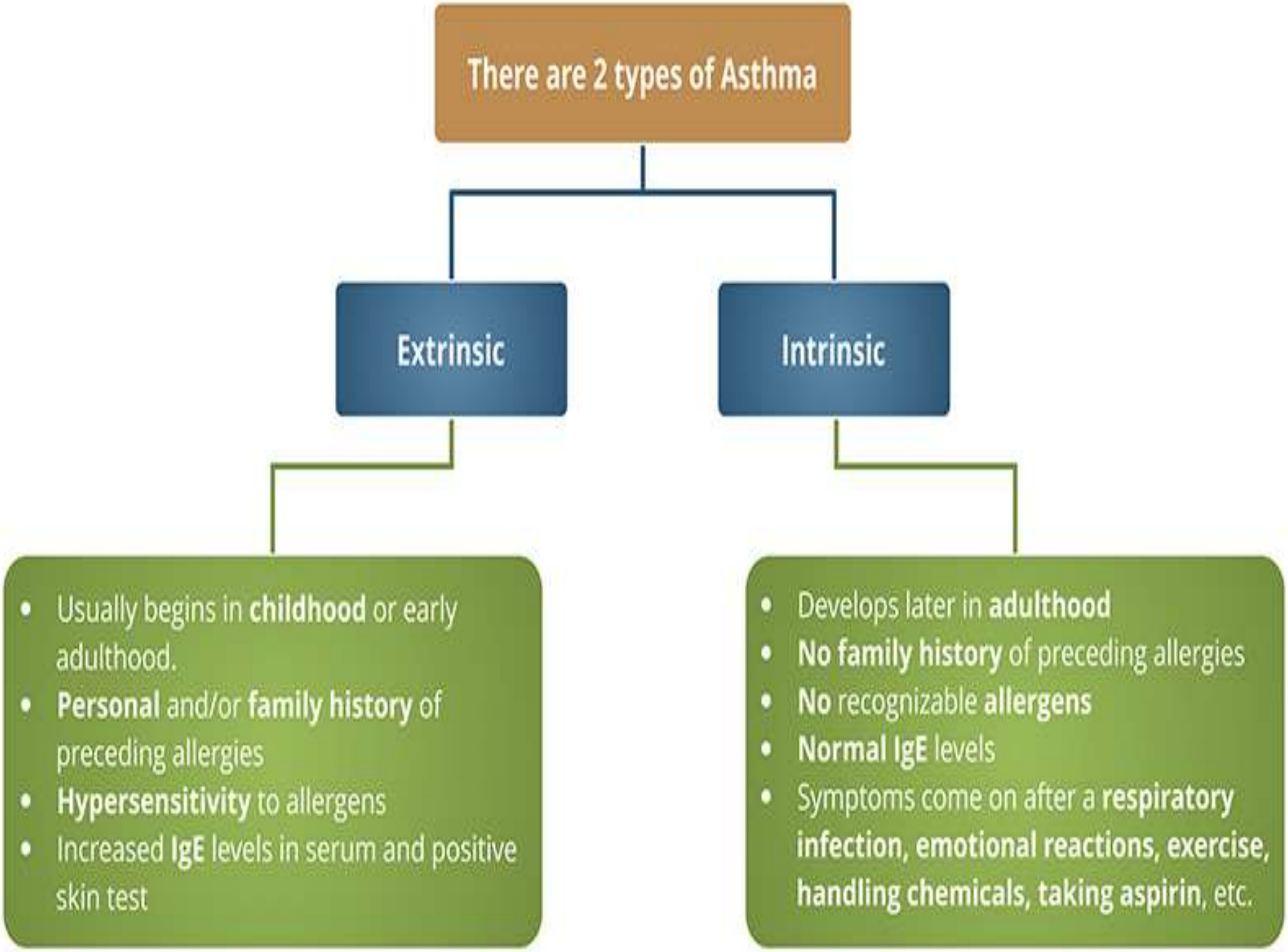
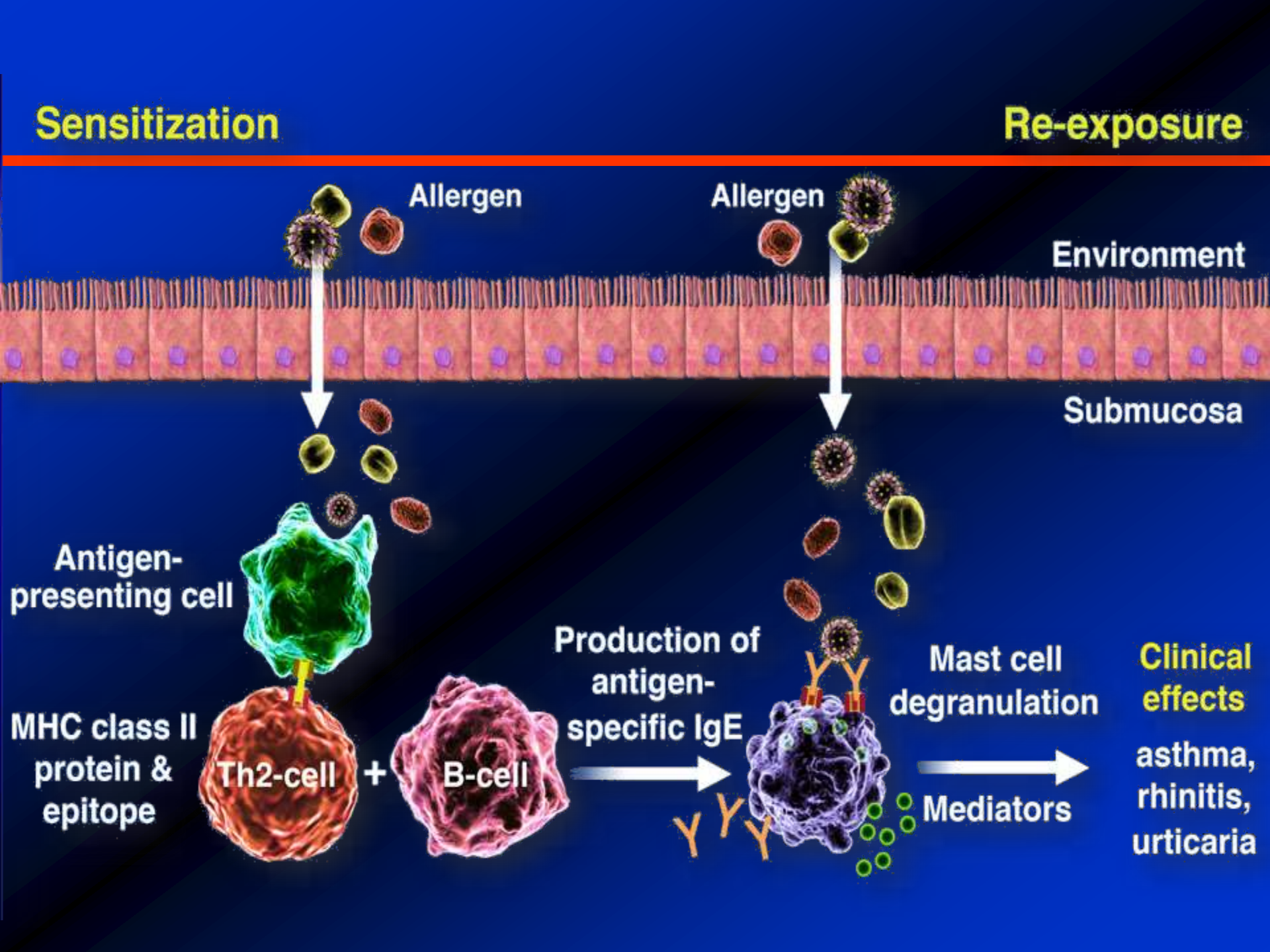

There are 2 types of Asthma
Extrinsic
Intrinsic
• Usually begins in **childhood** or early adulthood.
• **Personal** and/or **family history** of preceding allergies
• **Hypersensitivity** to allergens
• Increased **IgE** levels in serum and positive skin test
• Develops later in **adulthood**
• **No family history** of preceding allergies
• **No** recognizable **allergens**
• **Normal IgE** levels
• Symptoms come on after a **respiratory infection, emotional reactions, exercise, handling chemicals, taking aspirin**, etc.


Sensitization
Re-exposure
Allergen
Allergen
Environment
Submucosa
Antigen-presenting cell
MHC class II protein & epitope
Th2-cell
+
B-cell
Production of antigen-specific IgE
Mast cell degranulation
Mediators
Clinical effects
asthma, rhinitis, urticaria

All of the following are the main cause of airway obstruction in asthma except:

a. Bronchospasm
B. Mucus Hypersecretion
C. Inflammation Of Bronchial Wall
D. Extra bronchial compression

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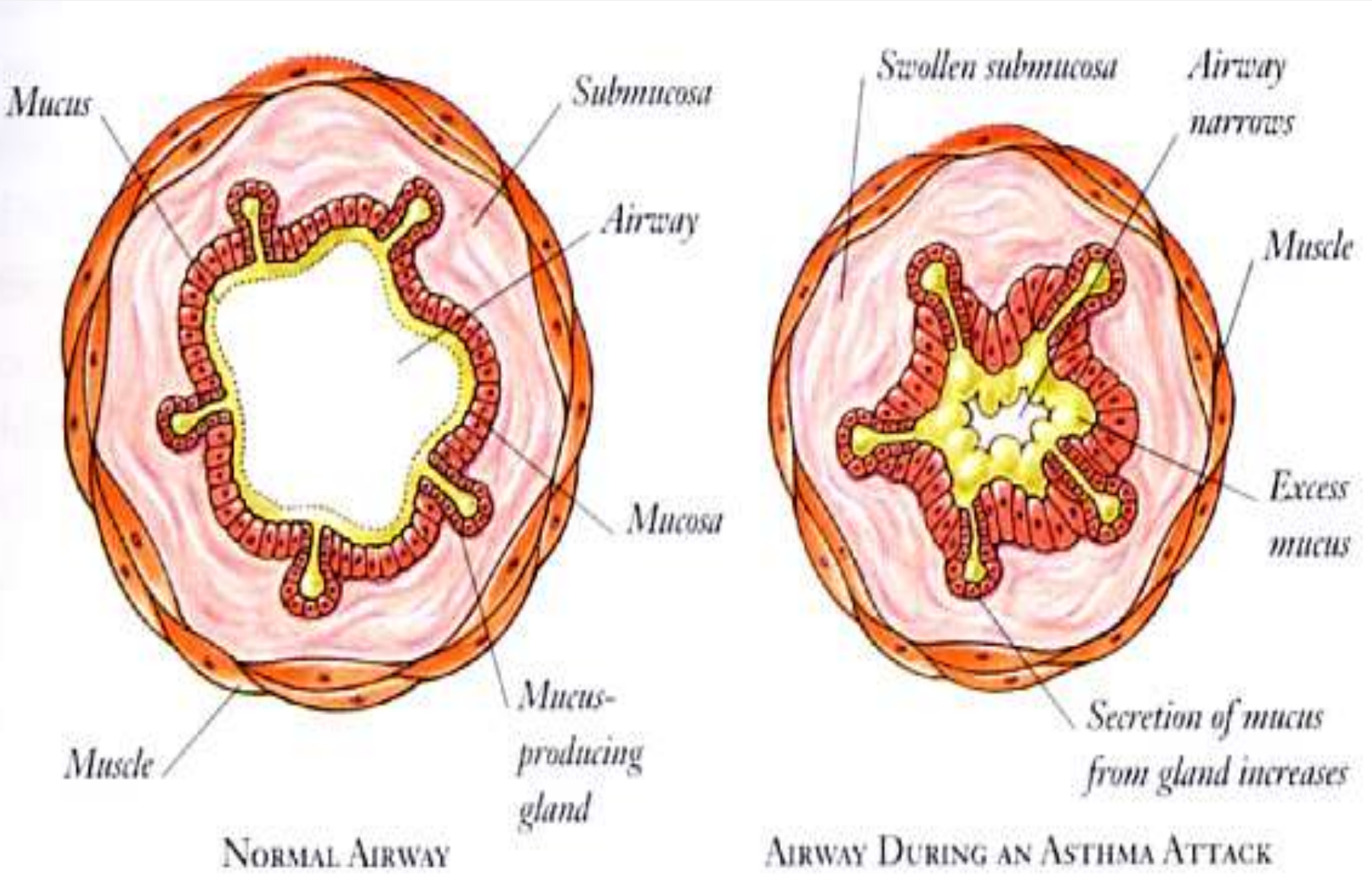
Pathophysiology

A. Airway Narrowing in Asthma:

- Airway narrowing is the final common pathway leading to symptoms and physiological changes in asthma.

- Several factors contribute to the development of airway narrowing in asthma.
  1. Excessive mucus obstruction
  2. Mucosal and submucosal edema
  3. Smooth muscle contraction

Asthma: Pathological changes

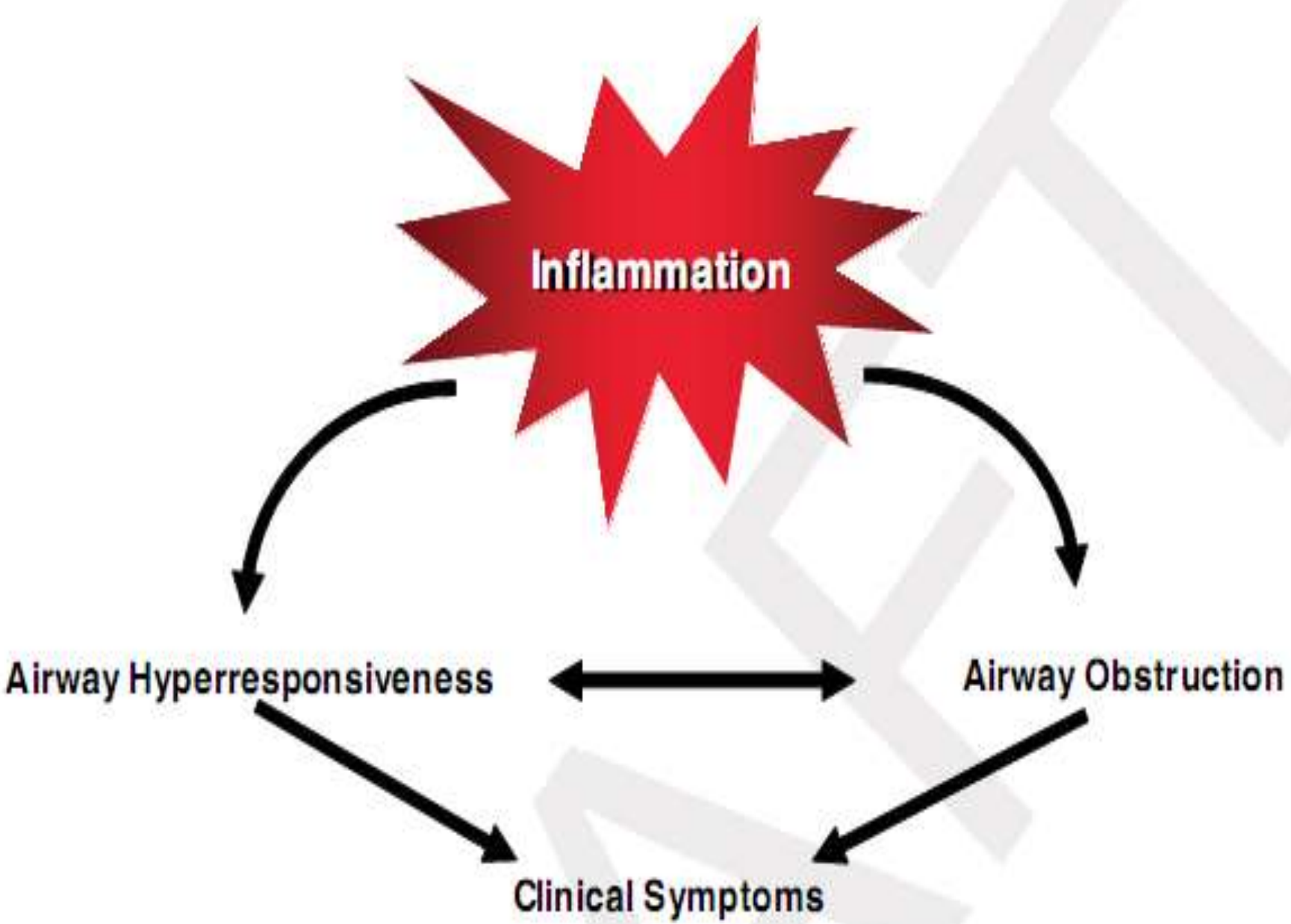


B. Bronchial hyperreactivity

Exaggerated response of bronchial smooth muscle to **Trigger Stimuli.**

- Physical,
- Chemical,
- Immunological and,
- Pharmacologic stimuli

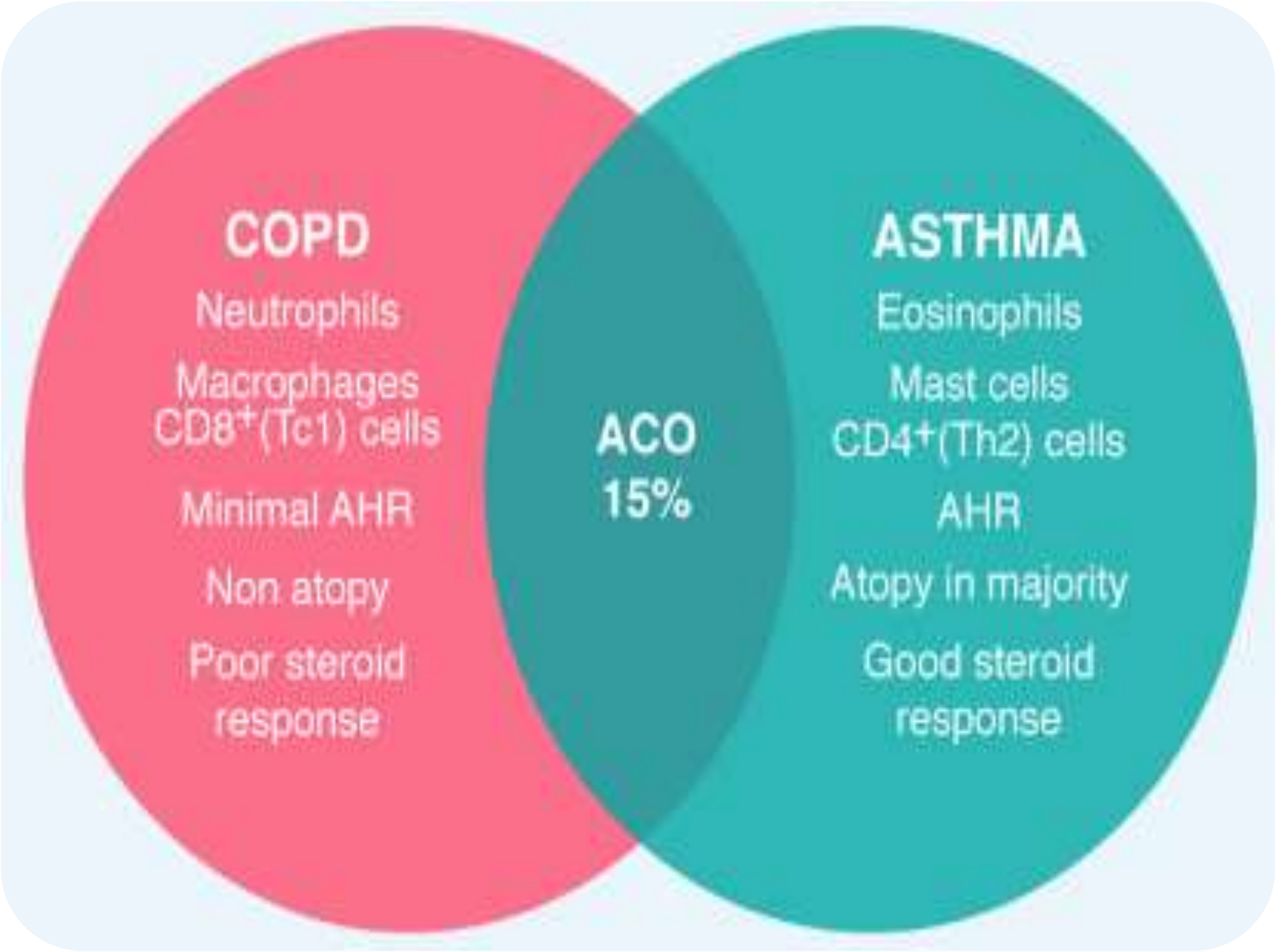
It is the characteristic **functional abnormality** of asthma, results in airway narrowing in response to a stimulus **that would be ineffective** in a normal person.


Inflammation
Airway Hyperresponsiveness
Airway Obstruction
Clinical Symptoms

C. Airway remodeling

- Structural changes in airways of asthmatic patient→ Fibrosis and fixed airway narrowing

  - Deposition of collagen under basement membrane leading to subepithelial fibrosis,
  - Inflammatory cells infiltrate,
  - Hypertrophy of smooth muscle


COPD
Neutrophils
Macrophages
CD8+(Tc1) cells
Minimal AHR
Non atopy
Poor steroid response
ACO
15%
ASTHMA
Eosinophils
Mast cells
CD4+(Th2) cells
AHR
Atopy in majority
Good steroid response

- **Definition of bronchial asthma**
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Diagnosis of Asthma

- History and patterns of symptoms
- Physical examination
- Investigations

Patient History

- 1- Has the patient had an attack or Recurrent episodes of Cough, Wheezing, Chest tightness or SOB?
- 2- Does the patient have a troublesome cough, worse particularly at Night, or early morning? Or Particular season , spring and winter (or change of season)?
- 3- Does the patient cough may be triggered or worsened by factors such as;
  - Viral infections,
  - Allergens; eg cats, dust, or perfume
  - Tobacco smoke,
  - Exercise and Stress

Patient History

- 4- Do the patient's colds '**go to the chest**' or take more than 10 days to resolve?

- 5- Does the patient use any **medication** (e.g. bronchodilator) when symptoms occur? Is there a response?

If the patient answers "YES" to any of the above questions, suspect asthma.

Physical Examination

- Physical examination in people with asthma
  - Often normal
  - The most frequent finding is wheezing usually heard without a stethoscope or Rhonchi heard with a stethoscope on auscultation, especially on forced expiration

- Wheezing is also found in other conditions, for example:
  - Respiratory infections
  - COPD
  - Endobronchial obstruction
  - Inhaled foreign body

- **Remember** -

Absence of symptoms at the time of examination does not exclude the diagnosis of asthma

All of the following are possible complications of bronchial asthma except:

A. Pneumothorax.
B. Cor-pulmonale.
C. Pleural Effusion
D. Respiratory failure

Complications of Bronchial asthma

1. Pneumothorax:

- It may present as sudden worsening of dyspnea and sharp chest pain and on examination, hyperresonant lung with a shift of mediastinum. Chest x-ray confirms the diagnosis.

2. Atelectasis due to obstruction

3. Cor-pulmonale (Right ventricular hypertrophy with or without heart failure) :

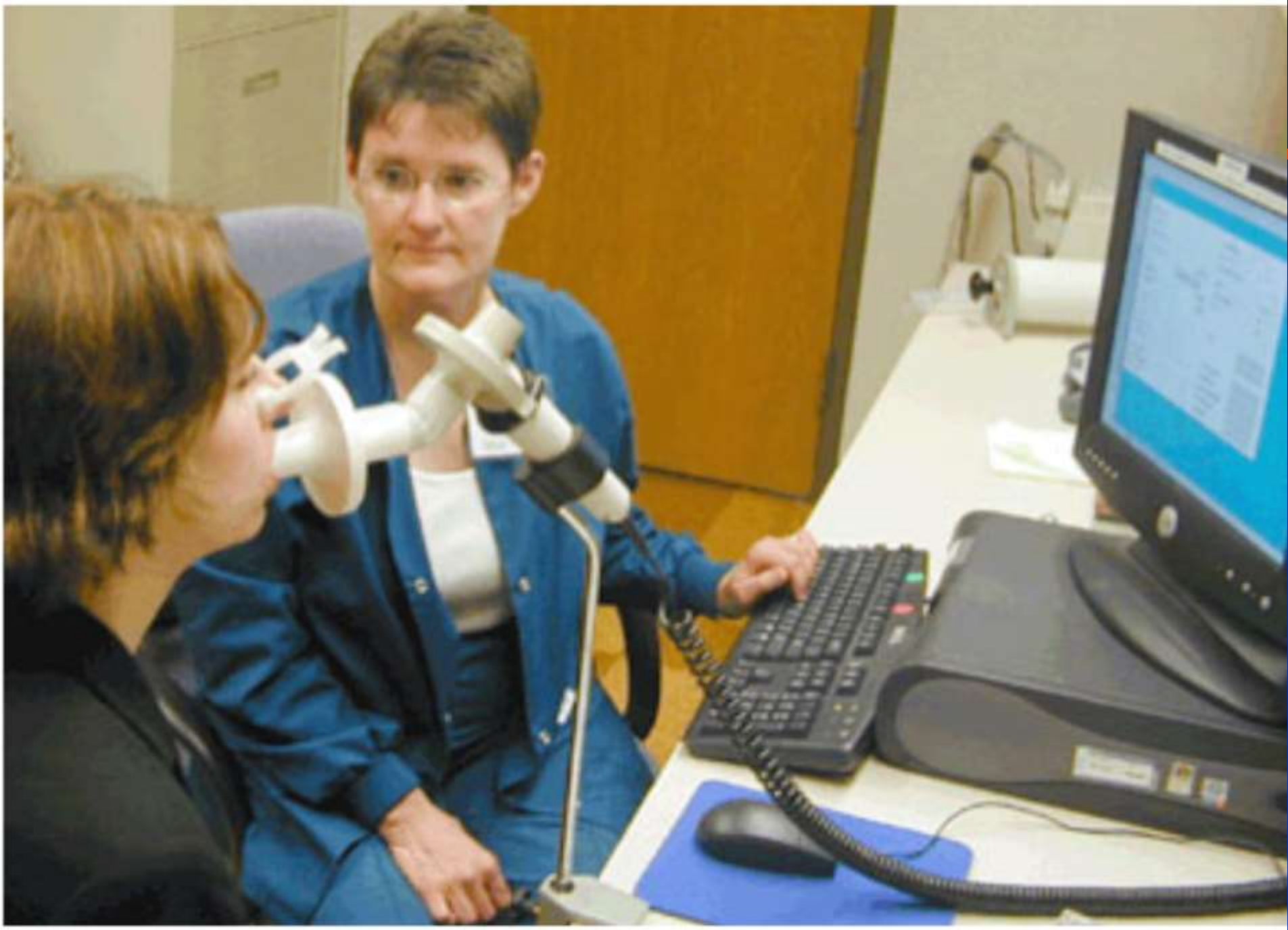
4. Respiratory failure

Which is the diagnostic test you will order to confirm diagnosis of asthmatic patient?

1. ABGs
2. Pulmonary Function Test
3. Pulse oximetry
4. CXR

Diagnostic testing

Diagnosis of asthma can be confirmed by using PFT ; *Spirometry* or *Peak flow meter*.



Obstructive airway defect is characterized on PFT by which one of the following

a. Reduced FEV1/FVC ratio
b. Decreased total lung capacity
c. Reduced residual volume
d. Decrease in diffusing capacity

Pulmonary Function Tests-Spirometry

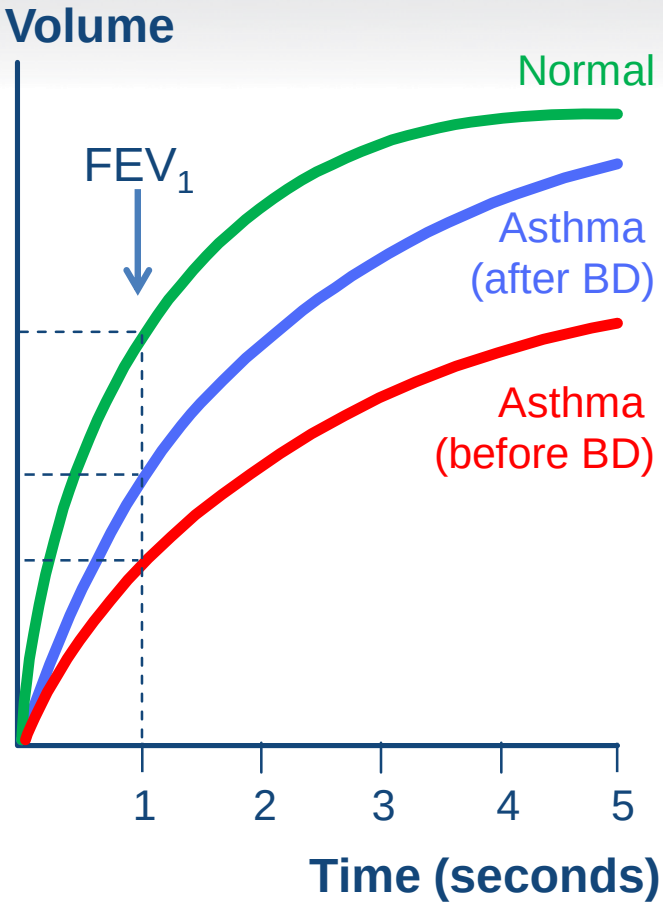
- FEV1
  - Is that volume of air exhaled in 1 second
- FVC
  - Forced vital capacity - volume of air exhaled with maximal rapid and forced effort

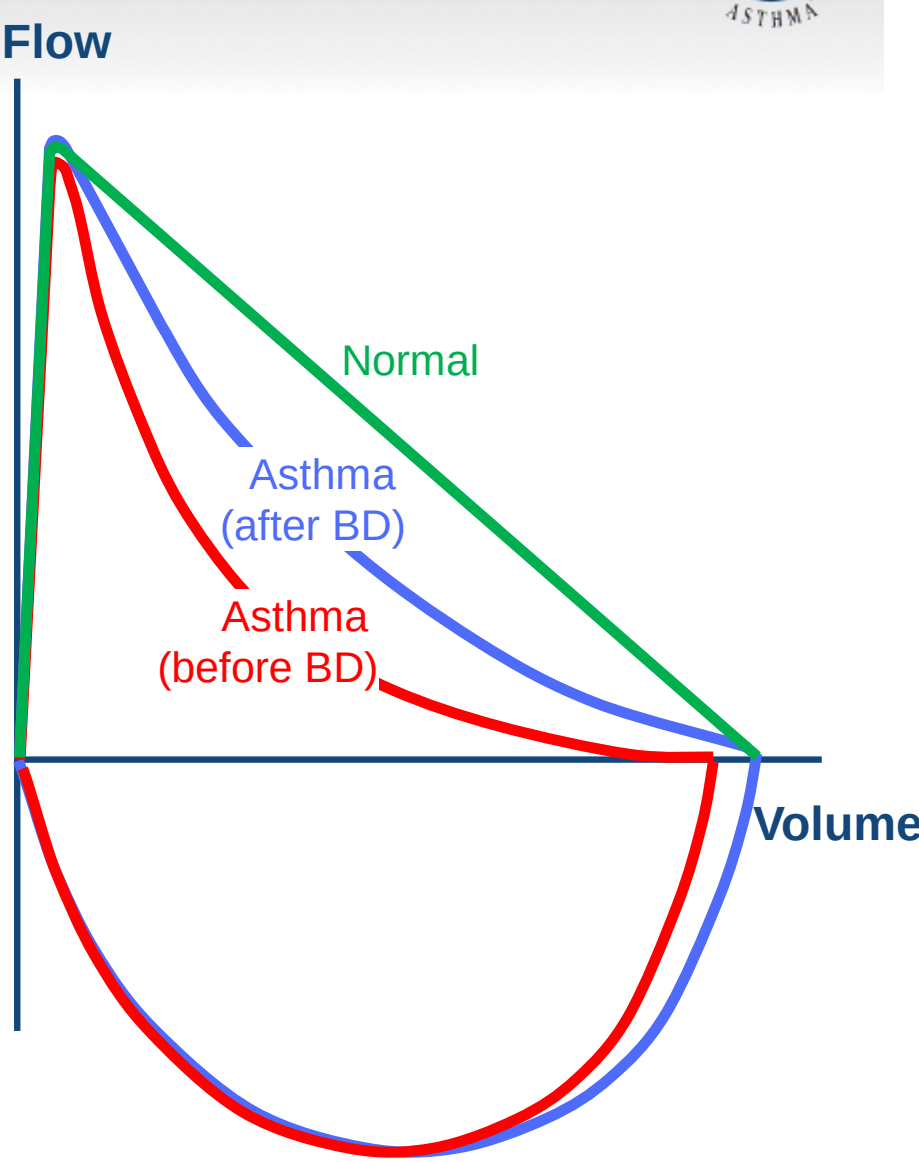
- FEV1/FVC ratio
  - Most reproducible of the PFT
  - Normal ratio is 70%
  - Decreased in obstructive pattern
  - Normal in restrictive pattern

Reversibility of Airflow Obstruction

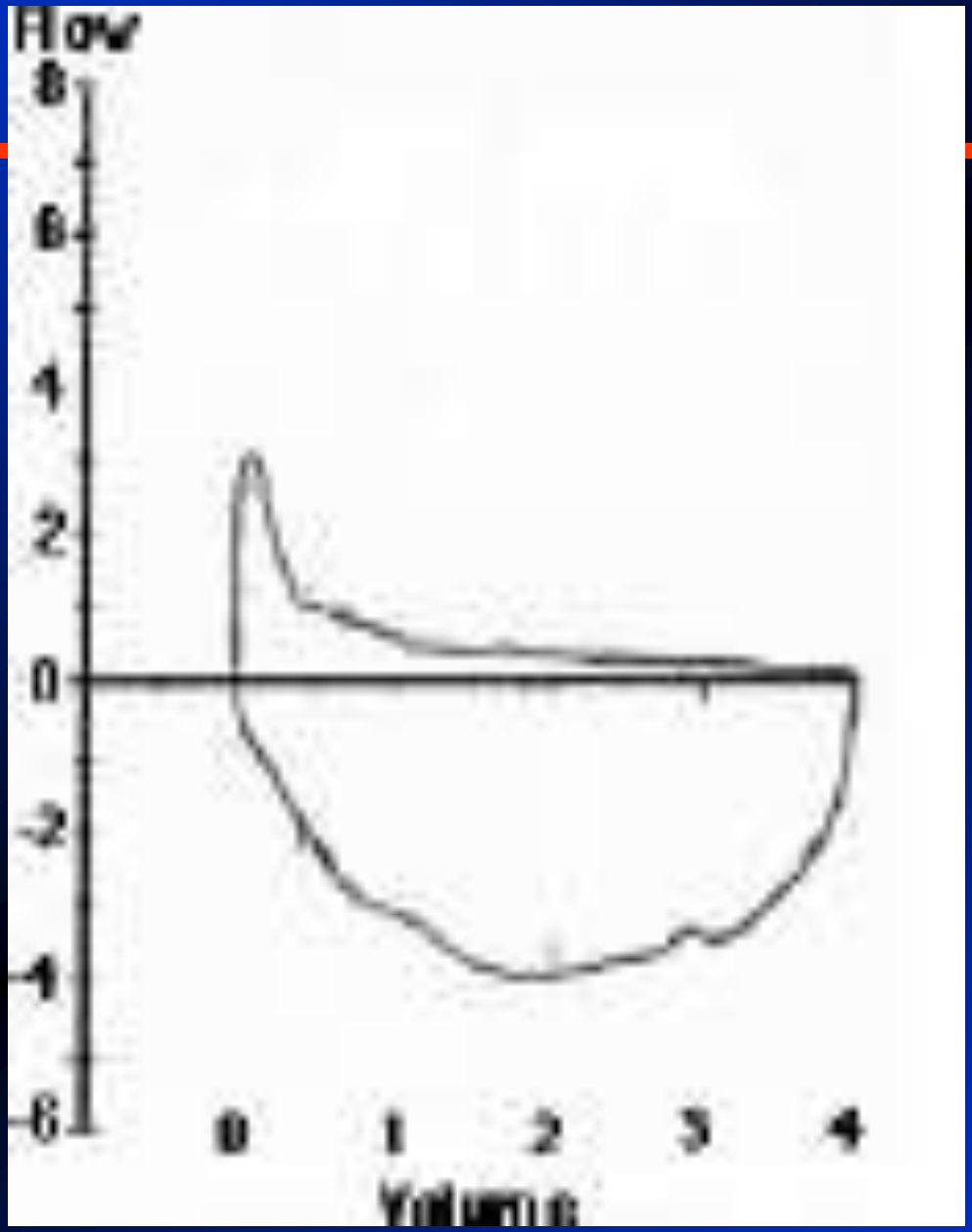
- Confirm presence of airflow obstruction
  - FEV_1/FVC is reduced + Reduced FEV_1
  - FEV_1/ FVC ratio is normally > 0.7
- Confirm presence of Bronchodilator reversibility
  - Increase in FEV_1 > 12% of predicted or >200mL after bronchodilator
- If initial testing is negative: Repeat when patient is symptomatic, or after withholding bronchodilators

Typical spirometric tracings





Note: Each FEV_1 represents the highest of three reproducible measurements


Flow
8
6
4
2
0
-2
-4
-6
0
1
2
3
4

Pulmonary function test (PFT) shows

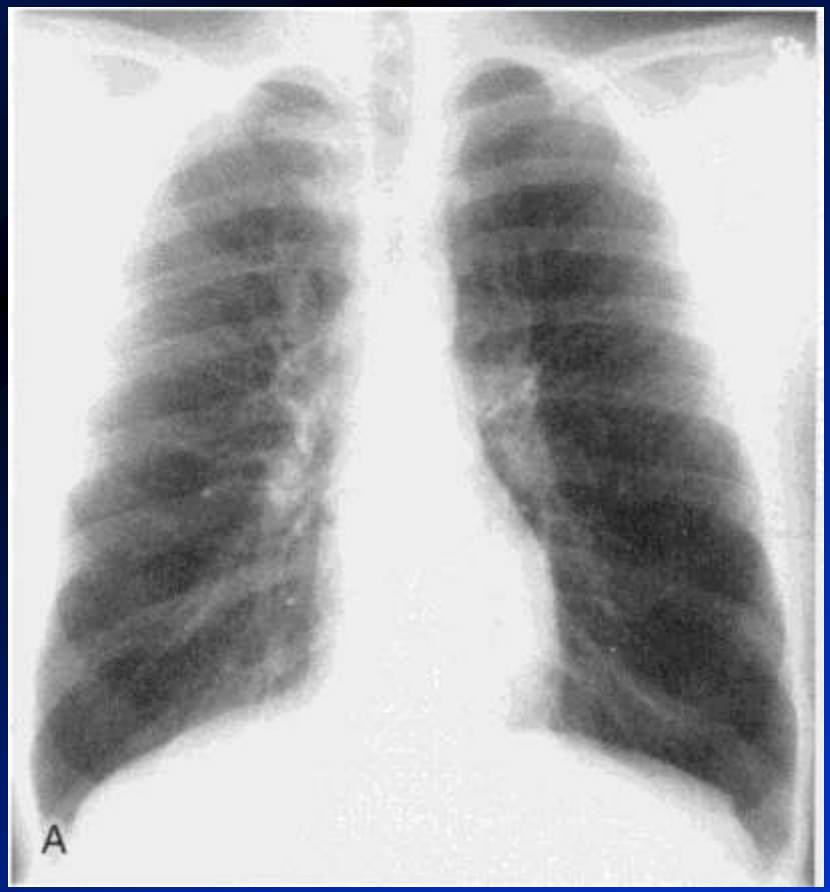
FEV1/FVC ⟹0.65.

FEV1 ⟹ 60% of predictive and

Post-bronchodilator FEV1⟹ 74% of predictive.

CXR

- Most patients with asthma have **normal x-rays.**
- Signs of **Hyperinflation** (Diaphragm is down - ribbon-shaped heart…) as in ASA
- **Diagnosis of Complications:**
  - Pneumonia
  - Pneumothorax



Blood Gas Measurements

- Best indicators of overall lung function are arterial blood gases
  - pH, PaO_2, $PaCO_2$, and HCO_3
- Oxygen saturation (O_2 sat)
  - Detect the percent of oxyhaemoglobin
  - Normal O_2 sat 95 – 99 %

What is the Differential Diagnosis

Our Goals

- Definition of bronchial asthma
- Etiologic factors
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- Pathophysiology
- Diagnosis
- **Differential diagnosis**
- Treatment guidelines

Conditions Mimicking Asthma

- COPD
- GERD
- Pulmonary embolism
- Bronchiectasis
- Cardiac disease
- Bronchiolitis
- ILD
- Cystic Fibrosis
- Psychogenic

- Foreign body
- Endobronchial tumors
- Extra bronchial com

Clinical Differences Between Asthma and COPD

Clinical features	Asthma	COPD
Age of onset	Usually early childhood, but may have onset at any age	Usually > 40 years old
Smoking history	May be non-, ex- or current smoker	Usually > 10 pack-years
Atopy	Often	Infrequent
Family history	Asthma or other atopic disorders commonly present	Not a usual feature
Clinical symptoms	Intermittent and variable	Persistent and gradually progressive worsening
Cough	Nocturnal cough or on exertion	Morning cough with sputum
Sputum production	Infrequent	Often
Reversibility of airflow obstruction	Characteristic of asthma	Airflow limitation may improve but never normalises
Exacerbations	Common at all levels of severity except in mild disease	Increase in frequency with increasing severity of disease

Our Goals

- Definition of bronchial asthma
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Which one of the following is the first-line therapy in the management of an acute asthma attack?

a. Steroids
b. β2-agonists
c. Theophylline
d. Antibiotics
e. Magnesium sulfate

Management of Acute exacerbation of Bronchial Asthma

Oxygen Therapy:

- By nasal Cannula or mask to achieve SpO2 > 90%
- Controlled O2 therapy in patients with elevated CO2

Bronchodilators:

- Nebulized B2 agonists Combined with nebulised Ipratropium bromide
- Given continuously for one hour, then every 60 min, after that regularly every 4-6 hours,
- Reduced according to response.

Corticosteroids:

- Hydrocortisone 100 mg every 6-8 hours for 5 days
- Dexamethasone or methyl prednisolone
- Later ,then inhaled preparations started.

Antibiotics: when signs of bacterial infection

Aminophylline:

Intravenous infusion every 8 hours to be transformed into oral long acting preparation after improvement of acute attack.

Intravenous magnesium sulphate.

Acute severe asthma

1. Anxiety, SOB (cannot complete one sentence), use of accessory muscles.
2. Tachycardia ≥ 110
3. Tachypnea ≥ 25
4. Pulsus paradoxus
5. Generalized rhonchi
6. PEF ≤ 50%
7. Pao2 <60, Paco2 < 35

Life-threatening BA

1. Confusion and Cyanosis
2. Bradycardia
3. Bradypnea
4. Hypotension
5. Silent chest
6. PEF < 33%
7. Pao2<60 ,paco2 ≥ 50

All of the following are accurate indicators of a life threating asthma except:

a. The presence of wheezing
b. The use of accessory muscles
c. The presence of diaphoresis and cyanosis
d. The presence of a pulsus paradoxus > 12mmHg

Key Components of Asthma Therapy

- Patient education
- Trigger control
- Pharmacologic therapy
- Assessment and monitoring

I- Patient Education

- Explain nature of the disease (i.e. inflammation)
- Explain action of prescribed drugs
- Stress need for regular, long-term therapy
- Peak flow reading
- Treatment booklet

II- Trigger control

- **Trigger control** is an important step in overall management programs especially for difficult asthma.
- Environmental exposures to **allergens**, **dusts** and **smoke** require avoidance.
- Both the active tobacco **smoking** and **passive** environmental tobacco smoke (ETS) exposure are important and avoidable asthma triggers.

II- Trigger control

- **The concurrent drug intake, occupational exposures, GERD and psychogenic factors.**

- **Although foods are commonly blamed for asthma attacks, only the clearly identified items need avoidance.**

  - Food avoidance should not be recommended until an allergy has been clearly demonstrated.
  - Sulfites (common food preservatives found in such foods as processed potatoes, dried fruits, and wine) have often been implicated in causing severe asthma exacerbations.

II- Trigger control

Obesity

- Weight reduction in obese patients with asthma has been demonstrated to improve lung function, symptoms, and morbidity.

Emotional Stress

- Emotional stress (laughing, crying, anger, fear or Panic attacks) may lead to asthma exacerbations through hyperventilation and hypocapnia, which can cause airway narrowing.

Rhinitis, and sinusitis, are frequently associated with asthma and need to be treated. Apart from sinusitis, there is little evidence that bacterial infections exacerbate asthma.

Pharmacological Treatments

- The goal of asthma treatment is to achieve and maintain clinical control.
- Medications to treat asthma can be classified as controllers or relievers.

Which drug is the cornerstone in treatment and control of asthmatic patients.

a. Inhaled Long acting β2-agonists 'LABA'
b. Inhaled Corticosteroids, 'ICS'
c. Leukotriene antagonist
d. Theophylline

I-Controllers:

- **These are medications taken daily on a long-term basis to keep asthma under clinical control chiefly through their anti-inflammatory effects.**

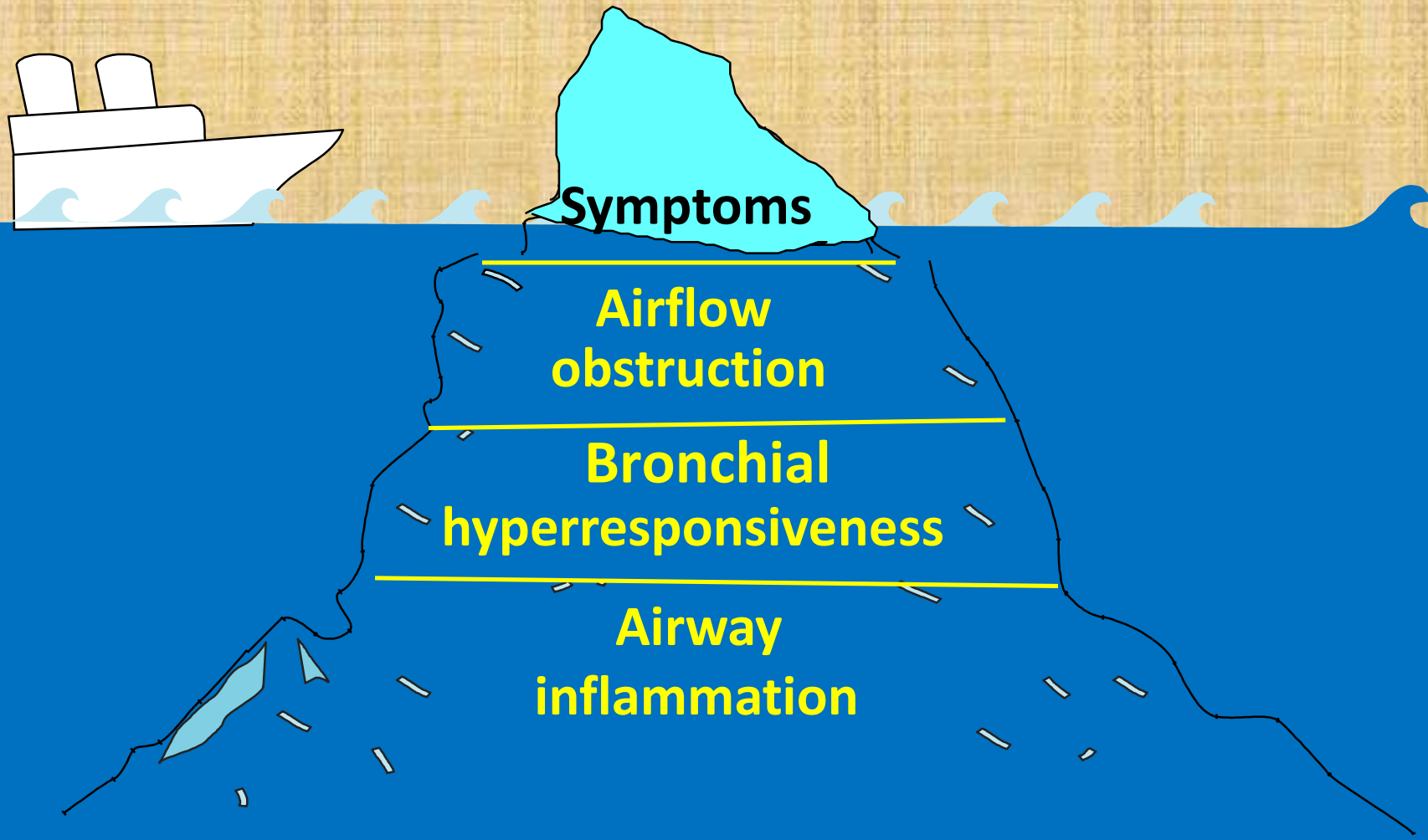
- **Controller medications include:**
  - Systemic and inhaled glucocorticoids, ICS
  - Leukotriens modifiers,
  - Long-acting inhaled B2-agonists, LABA
  - Long-acting inhaled muscarinic receptor antagonists, LAMA
  - Sustained-release theophylline,
  - Immunomodulators: 1.Omalizumab
    2.Allergen-specific immunotherapy

2-Relievers:

- **These are medications used as-needed that act quickly to reverse bronchoconstriction and relieve its symptoms.**

- **Relievers medications include:**
  - Inhaled short-acting B2- agonists, SABA
  - Inhaled short-acting anticholinergic
  - Short-acting theophylline,
  - Short-acting oral B2-agonists.

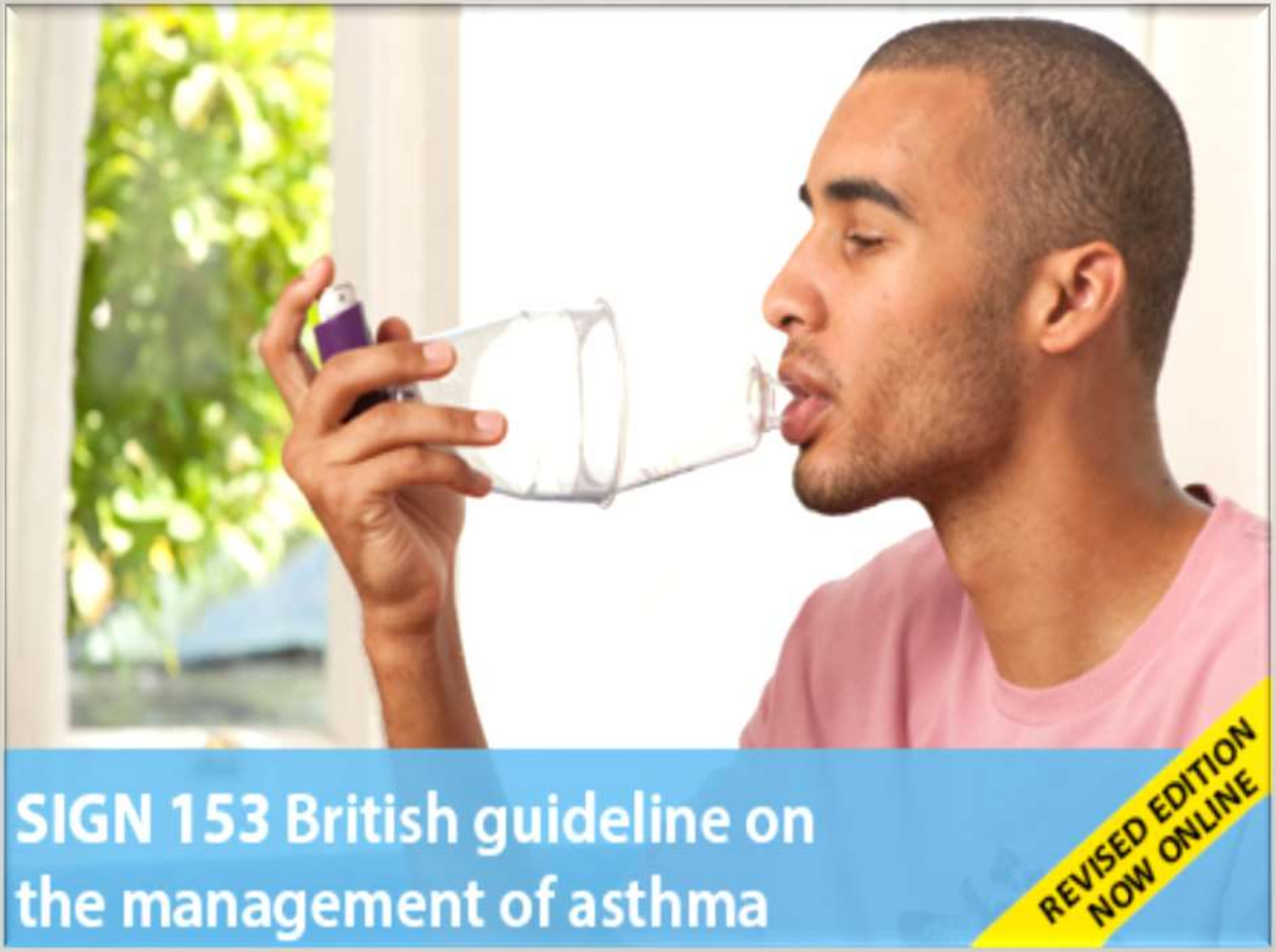
A Lot Going On Beneath The Surface

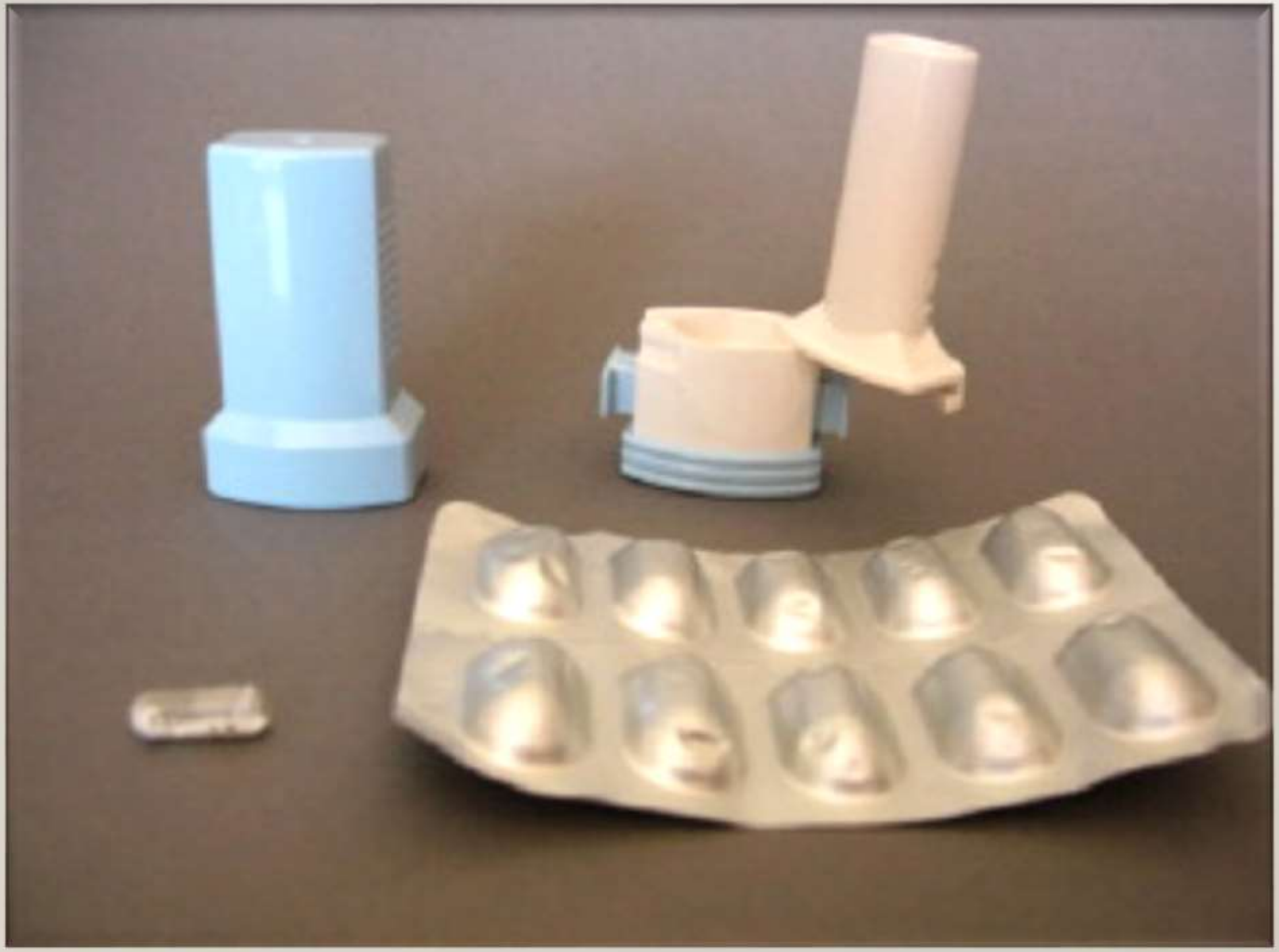


Route of Administration

- The major advantage of inhaled therapy is:
  - Drugs are delivered directly into the airways,
  - Producing higher local concentration
  - Significantly less risk of systemic side effects.

- Inhaled medications for asthma are available as:
  - Pressurized metered-dose inhalers (MDIs),
  - Turbohailers
  - Dry powder inhalers (DPIs),
  - Discus,
  - Nebulizer .


SIGN 153 British guideline on
the management of asthma
REVISED EDITION
NOW ONLINE



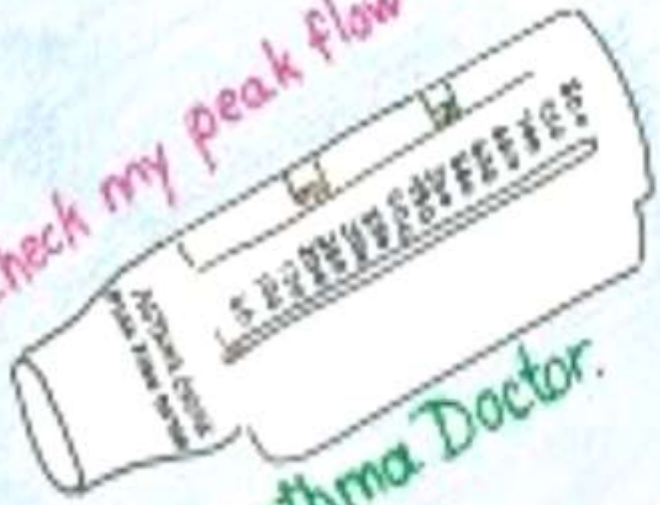

ADVAIR
100/50


Seretide 500
500


Symbicort
budesonide/
formoterol
120
doses
Turbuhaler
160/4.5µg/dose
Inhalation powder
160
4.5
AstraZeneca
Symbicort
160

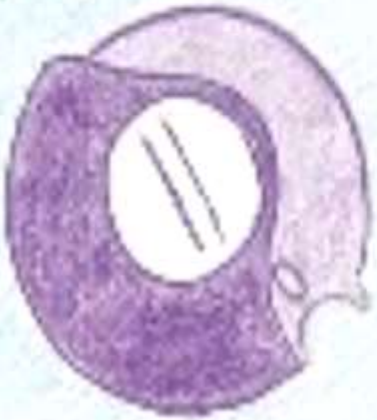
I CAN CONTROL MY ASTHMA

Check my peak flow meter.



Visit my asthma Doctor.

Take my inhalers



Take my meds

Avoid triggers

Mechanism of action & side effects of medications used in treatment of asthma

Inhaled Corticosteroid

- ICS are the most effective anti-inflammatory medications for the treatment of persistent asthma (Corner Stone) .

- Studies have demonstrated their efficacy in:
  - Controlling airway inflammation,
  - Decreasing airway Hyperresponsiveness,
  - Reducing asthma symptoms,
  - Reducing frequency and severity of exacerbations,
  - Improving lung function

Inhaled Corticosteroid

- **Local administration** of surface-active corticosteroids are relatively safe
  - Beclomethasone
  - Budesonide
  - Fluticasone
  - Ciclosonide
- Systemic (oral corticosteroids)
  - **Used chronically** only if other therapies fail

Beta-2 agonists

- Most important sympathomimetic used to reverse bronchoconstriction
- Almost given exclusively by inhalation
  - Decreases the systemic dose and adverse effects
  - Occasionally by nebulizer

Beta-2 agonists

- **Short-acting B2 agonist**
  - Salbutamol,
  - Terbutaline,
  - Drug of choice for acute attacks

- **Salmeterol and formoterol**
  - Long-acting
  - 12 h or more
  - Used as controller

Beta-2 agonists

LABAs

- Salmeterol, Formoterol
- Formeterol: faster onset of action
- Duration of action: 12 hrs; given BD
- Do not control underlying inflammation and increase mortality in asthmatics

- NOT TO BE USED AS MONOTHERAPY
- Used as an adjunct to ICS therapy in persistent asthma
- May be used before exercise to prevent EIA
- Dose: Salmeterol- 50µg BD; Formeterol- 12µg BD

Beta-2 agonists

- **Toxicity**
  - Skeletal muscle **tremor**
  - Significant β_1 effects (**tachycardia**) at high clinical dosage
  - **Arrhythmias** may occur when used excessively
  - Hypokalemia.

Leukotrienes antagonists, montelukast

- Effective in preventing exercise-induced asthma, and aspirin-induced asthma.
- Interfere with the synthesis or action of Leukotrienes
- Not effective as corticosteroids in severe asthma
- Low toxicity

Methylxanthines

- **Bronchodilatation** is the most important therapeutic effect

- CNS stimulation, cardiac stimulation, and slight increase in BP (due to release of NE from adrenergic nerves, and **vasodilatation** (if given rapidly intravenous).

- Sustained-release theophylline
  - For **control of nocturnal asthma**

- **Toxicity**
  - Common adverse effects
    - GI distress
    - Tremors
    - Insomnia
    - Hiccough
  - Overdosage
    - Severe nausea and vomiting
    - Hypotension
    - Cardiac arrhythmias
    - Convulsion

Muscarinic Antagonists

- Competitively **blocks muscarinic receptors** in the airways
- **Prevents bronchoconstriction** mediated by vagal discharge
- **Ipratropium** Short –acting; Delivered to the airways by pressurized aerosol
- **Tiotropium** Newer longer-acting analog

Toxicity

- Delivered directly to the airway, minimally absorbed
- Systemic effects are small
- In excessive dosage, minor atropine- like toxic effects may occur
- **Does not cause tremor or arrhythmias**

Cromolyn and nedocromil

- **No bronchodilator action** but can prevent bronchoconstriction by its **mast cell** stabilization effect

- **Important role in**
  - Asthma in children--- **Most important use**
  - Food allergy
  - Hay fever -- Nasal and eye drop formulations

Anti-IgE antibody

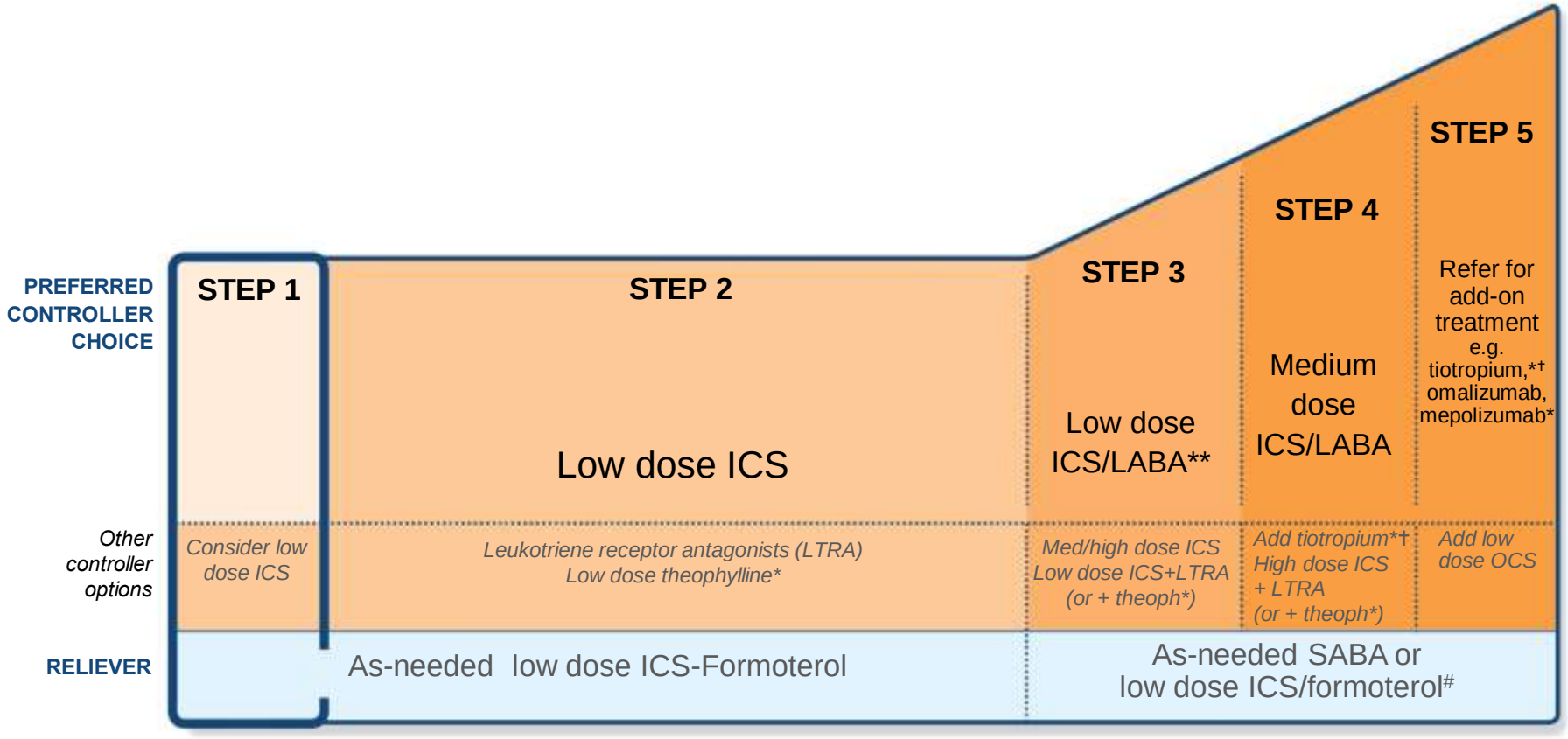
- **Omalizumab**
  - Monoclonal antibody to human IgE
  - management of severe persistent asthma not controlled with maximum therapy.
  - Given parenterally

Global Initiative for Asthma (GINA)

What's new in GINA 2018?

GINA Global Strategy for Asthma Management and Prevention

Step 1 – As-needed low dose ICS-Formoterol



*Not for children <12 years
**For children 6-11 years, the preferred Step 3 treatment is medium dose ICS
#For patients prescribed BDP/formoterol or BUD/ formoterol maintenance and reliever therapy
† Tiotropium by mist inhaler is an add-on treatment for patients ≥12 years with a history of exacerbations

Angiotensin-converting Enzyme Inhibitor–induced Cough

- Cough due to ACE inhibitors is a drug class effect, not dose related, and may occur a few hours to weeks or months after a patient takes the first dose of the ACE inhibitor.

- The diagnosis of ACE inhibitor–induced cough can only be established when cough disappears with elimination of the drug. The median time to resolution is 4 weeks.

- Substituting an angiotensin II receptor antagonist for the ACE inhibitor can also eliminate an ACE inhibitor–induced cough.