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-blocker, 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 i your diagnosis

What is the most probable diagnosis ?

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

Conditions Mimicking Asthma

- **Obstruction of small airways**
  - COPD
  - Aspiration
  - Bronchiolitis
  - Cystic Fibrosis
- **Obstruction of large airways**
  - Foreign body
  - Cardiac disease
  - Endobronchial tumors
  - Extra bronchial obstruction
  - Psychogenic

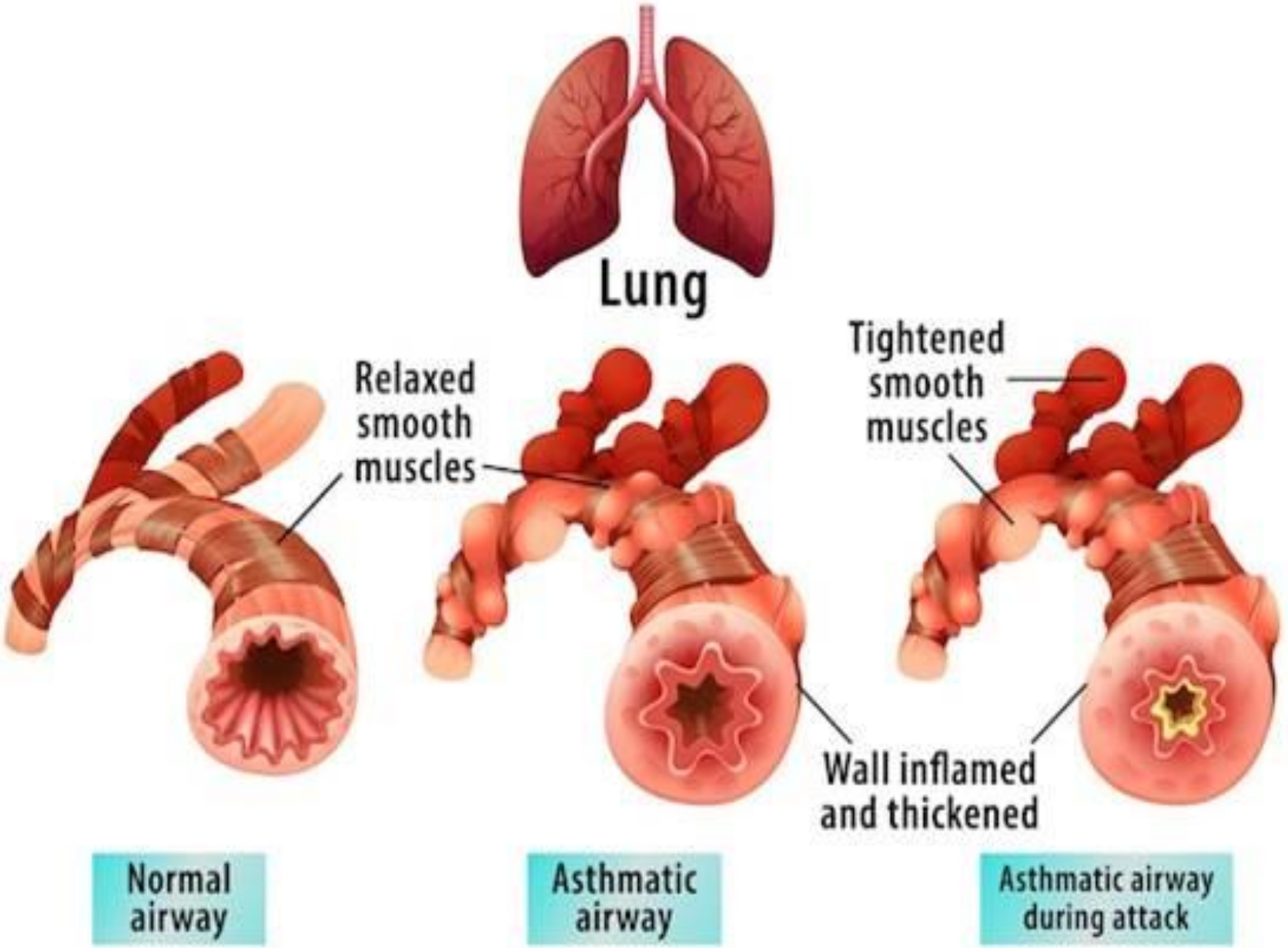
Clinical Differences Between Asthma and COPD

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

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

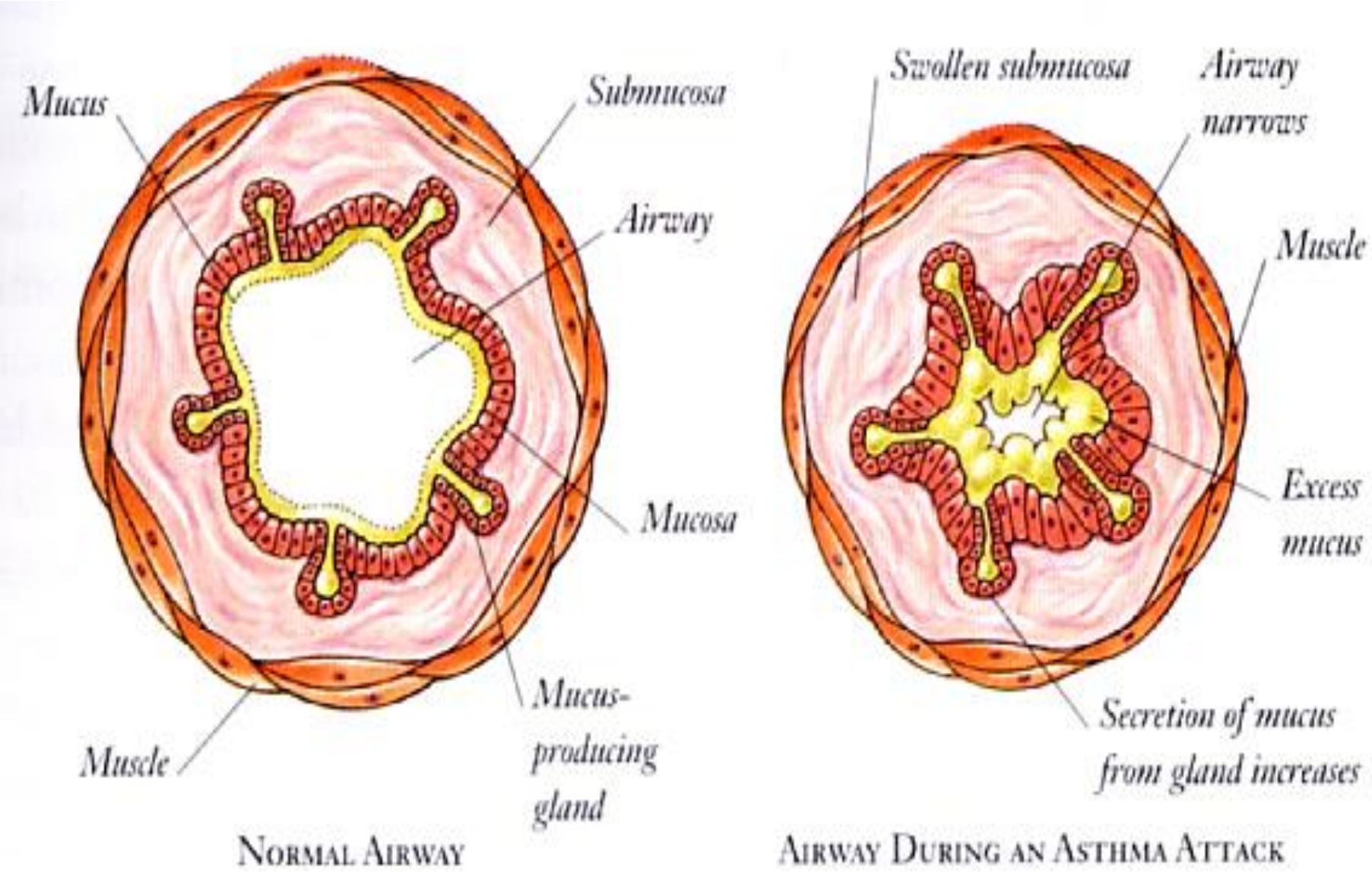
ASTHMA


Lung
Relaxed smooth muscles
Tightened smooth muscles
Wall inflamed and thickened
Normal airway
Asthmatic airway
Asthmatic airway during attack

What is an asthma attack?

- When you breathe normally, muscles around your airways are relaxed, letting air move easily and quietly. During an asthma attack, three things can happen:
- **Bronchospasm:** The muscles around the airways constrict (tighten). When they tighten, it makes your airways narrow. Air cannot flow freely through constricted airways.
- **Inflammation:** The lining of your airways becomes swollen. Swollen airways don't let as much air in or out of your lungs.
- **Mucus production:** During the attack, your body creates more mucus. This thick mucus clogs airways

Asthma: Pathological changes



What are Factors Influencing the Development and Expression of Asthma

Factors Influencing the Development and Expression of Asthma

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

Host factors

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

- Obesity
- Sex

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**
- **Diet**

Contributing Factors

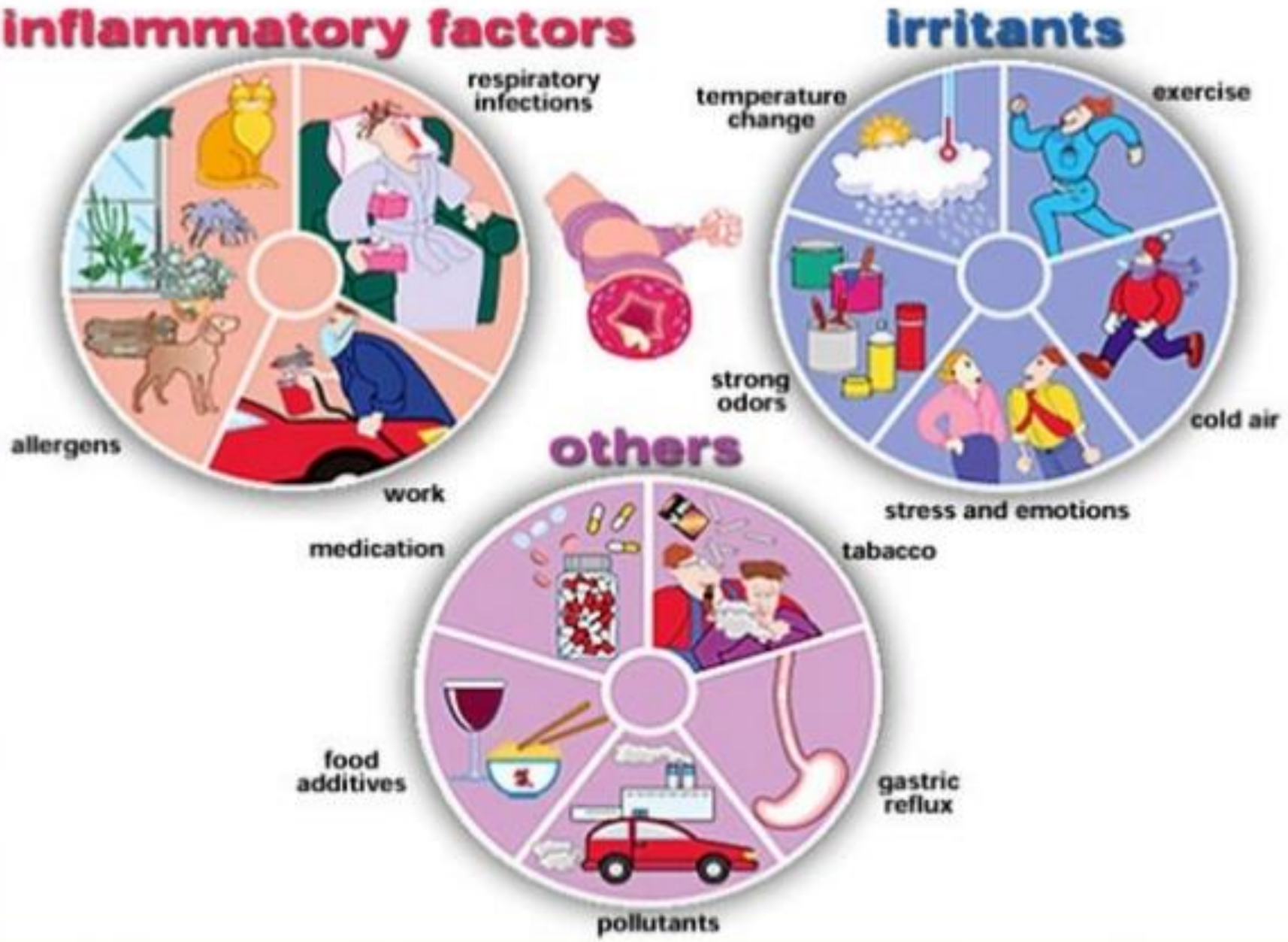
- **Respiratory infections;** The most common cause of acute exacerbation of asthma. Respiratory viruses are the major factors.
- **Physical activity**

- **Psychological factors**
- **Medication**

- **Gastroesophageal reflux disease**
- **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

History and patterns of symptoms

Physical examination

Patient History

- Has the patient had an attack or Recurrent episodes of Cough, Wheezing, Chest tightness or SOB?
- Does the patient have a troublesome cough, worse particularly at Night, or early morning?
- 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
  - Particular season , spring and winter (or change of season)?

Patient History

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

- **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 may be absent during severe asthma exacerbations ('silent chest')

- **Remember -**

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

Complications

Pneumothorax:

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

- **Mediastinal and subcutaneous emphysema** due to alveolar rupture.

- **Atelectasis due to obstruction**

- **Dilated right heart chambers (Cor-pulmonale)** :
  - from chronic hypoxemia and pulmonary hypertension
- **Respiratory failure**

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

(a) ABGs
(b) PFTs (PEFR or FEV1)
(c) Pulse oximetry
(d) CXR

Diagnostic testing

Diagnosis of asthma can be confirmed by demonstrating the presence of reversible airway obstruction using PFT ; *Spirometry* or *Peak flow meter*.

Pulmonary Function Tests-Spirometry

- Healthy individuals can exhale 75-80% of VC in 1 second and almost all in 3 seconds
- FEV1
  - Is that volume of air exhaled in 1 second
- FVC
  - Forced vital capacity - volume of air exhaled with maximal forced effort

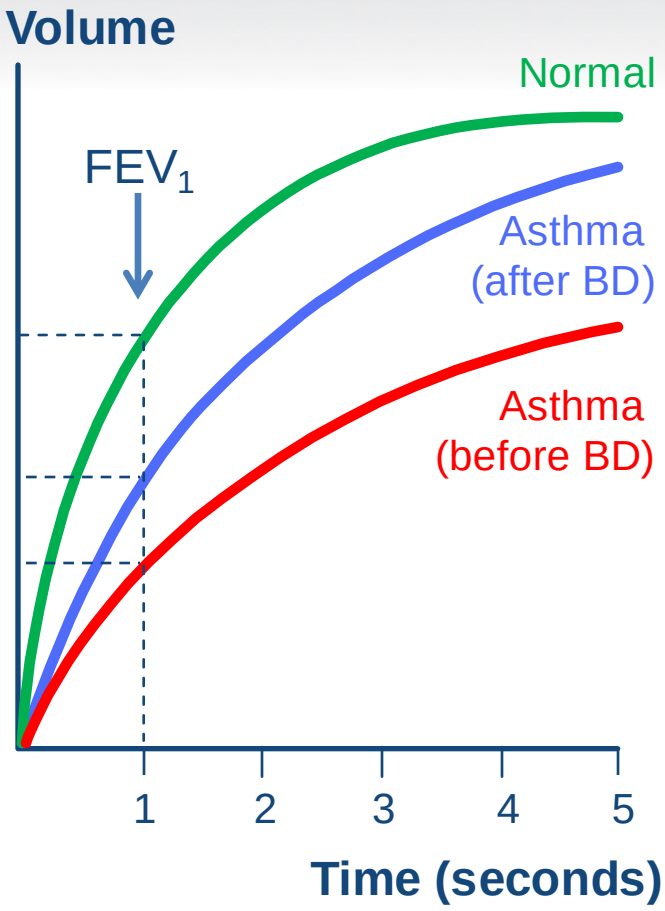
FEV1:FVC ratio

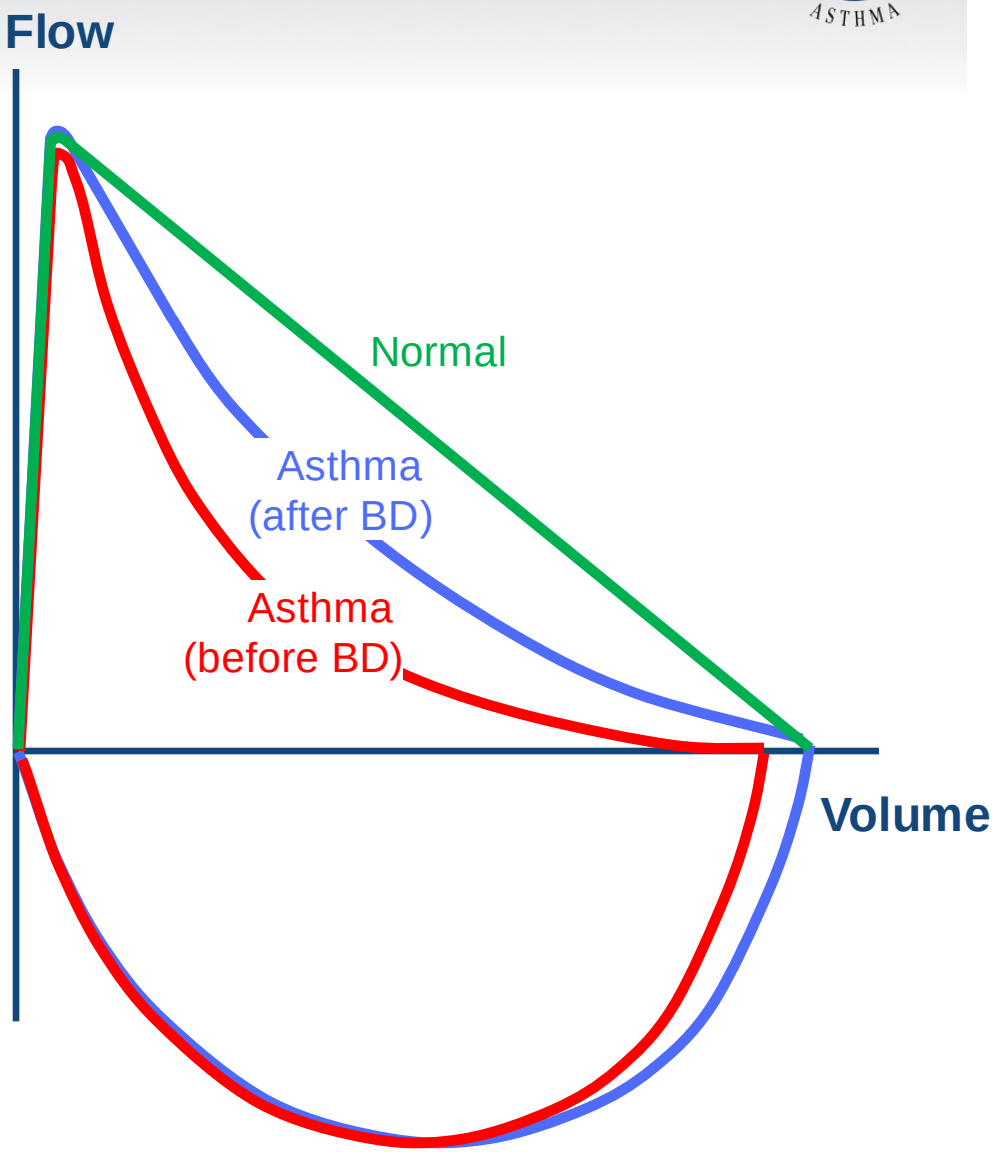
- Most reproducible of the PFTs
- Normal ratio is 70%
- Decreased in obstructive pattern
- Increased or even normal in restrictive pattern

Reversibility and variability of Airflow Obstruction

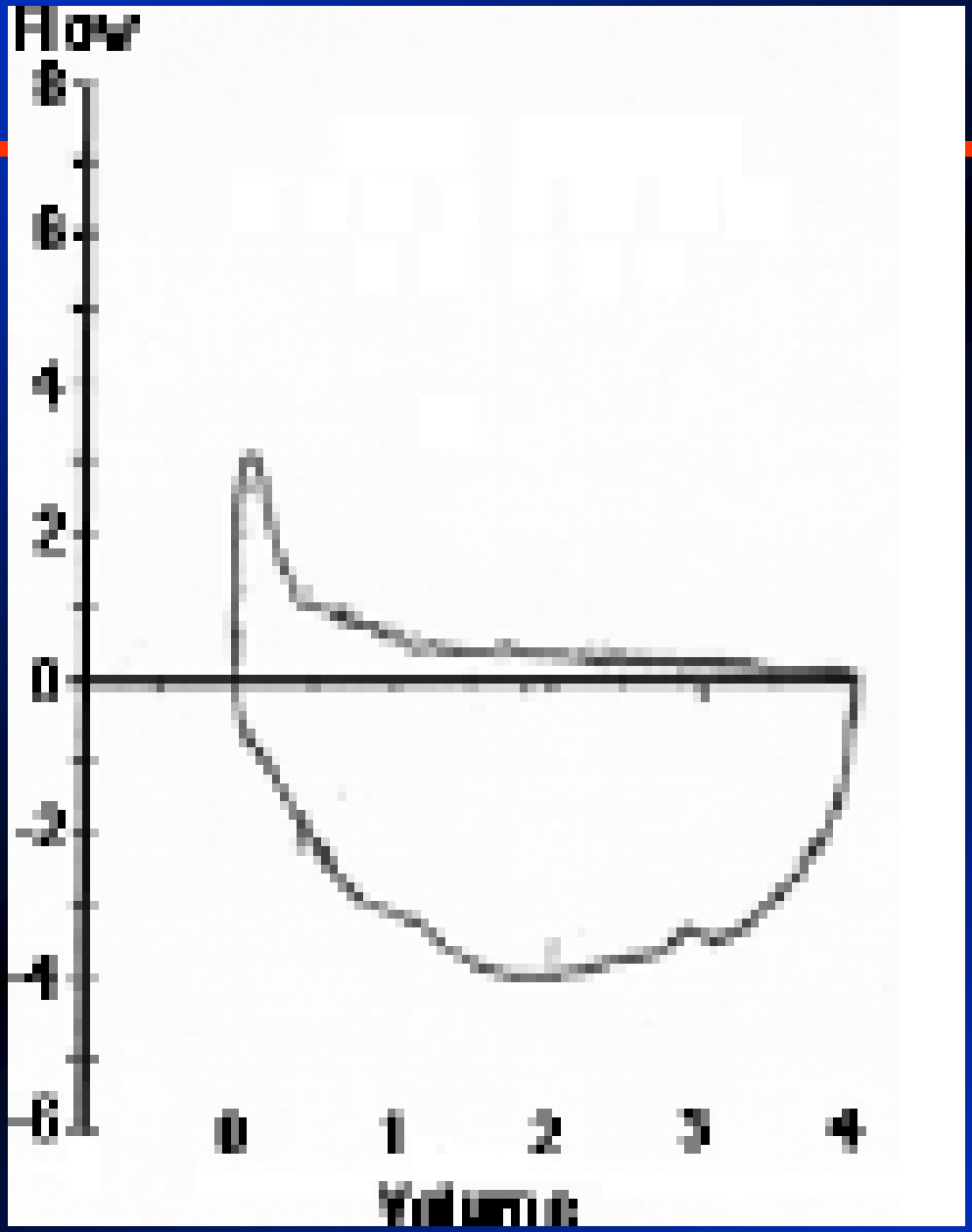
- **Confirm presence of airflow limitation**
  - **FEV_1/FVC is reduced + Reduced FEV_1**
  - **FEV_1/ FVC ratio is normally > 0.75 in healthy adults, and > 0.90 in children**
- **Confirm presence of Bronchodilator reversibility**
  - **Increase in FEV_1 > 12%of predicted or >200mL after bronchodilator**
- **Confirm presence of variation in lung function;**
  - **The greater the variation measured PEF monitoring , or the more times variation is seen, the greater probability that the diagnosis is asthma**
- **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

Preferred Measurement	Alternative Measurements
- Spirometry Showing Reversible Airway Obstruction: (1) ↓FEV_1/FVC below lower limit of normal Adults: <0.75 to 0.8 in adults Children age 6+: <0.8-0.9 AND (2) ↑FEV_1≥12% and, 200 mL in adults after bronchodilator or controller therapy	**- Peak Expiratory Flow Variability:** ↓in PEF after a bronchodilator or course of controller therapy Adults: PEF ↓60 L/min (min. 20%) OR Diurnal variation >8% for twice daily readings (20% for multiple daily readings) Children age 6+: PEF ↓20% **- Positive Challenge Test:** (1) Methacholine challenge: positive if FEV_1 ↓>20% when 4 mg/mL of inhaled methacholine is given; borderline if 4-16 mg/mL is required OR (2) Post-exercise: ↓FEV_1 ≥10-15%

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 test (PFT) shows

FEV1/FVC ⇛0.65.

FEV ⇛ 60% of predictive and

Post-bronchodilator FEV1⇛ 74% of predictive.

Sex: Male Age: 72
Factor: 100(Caucasian)
Height: 163cm Weight: 55kg BMI: 20.7

	FEV1	FVC	PEF	Var	Quality	Time:	Date:
Base	1.21	2.90	161	0%	Good blow	10:03	31-07-09
Base	1.20	2.88	178	0%	Good blow	10:03	31-07-09
Base	1.06	2.72	195	-12%	Good blow	10:03	31-07-09
Post 1	1.63	3.96	236	0%	Good blow	10:28	31-07-09
Post 1	1.63	3.79	236	0%	Good blow	10:28	31-07-09
Post 1	1.59	3.73	245	-2%	Good blow	10:28	31-07-09

Variation is based on FEV1

Best Spirometry Result:

			Normal			Post1			
	Base	%Pr	Min	Pred	Max	Post	%Pr	%Chg	
EVC	2.95	89	2.36	3.28	4.20	3.94	120	34	l
FEV1	1.21	49	1.59	2.43	3.27	1.63	67	35	l
FVC	2.90	91	2.18	3.18	4.18	3.96	124	37	l
PEF	161	37	304	424	543	236	55	47	l/m
FEV1/VC	41.0					41.4		1	%
FEV1/FVC	41.7	56	62.5	74.3	86.1	41.2	55	-1	%
MEF75	1.11	17	3.53	6.34	9.15	1.41	22	27	l/s
MEF50	0.42	11	1.43	3.60	5.77	0.60	16	43	l/s
MEF25	0.14	13		1.04	2.32	0.21	20	50	l/s
[illegible]T	10.9					11.6		6	s

[illegible]dns Age: 106

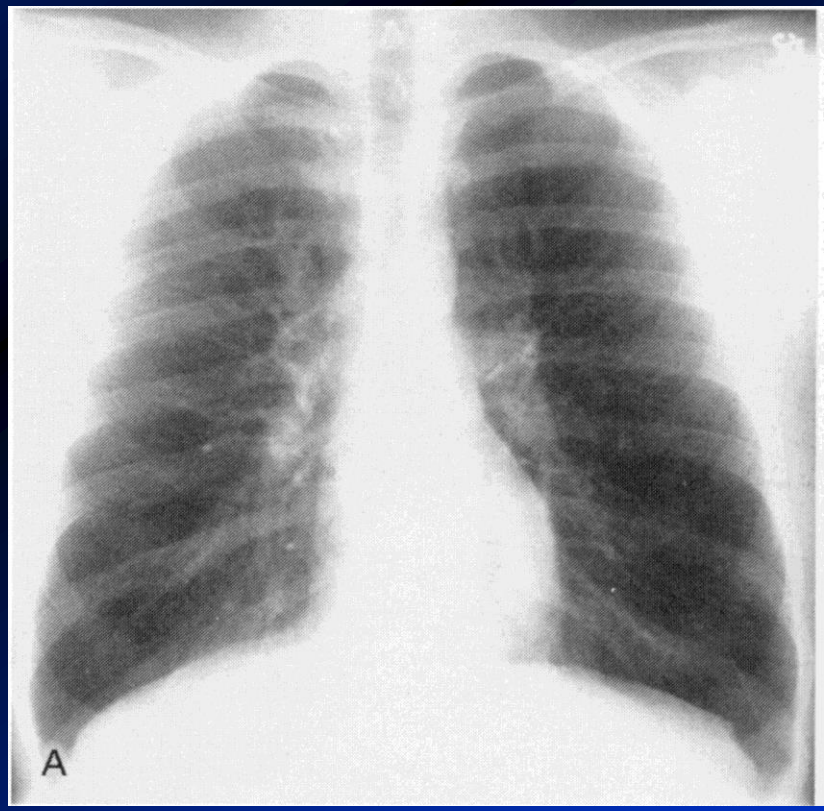
Interpretation(NICE): Moderate Obstruct[illegible]

Test	Actual	% Predicted	Predicted (L)
FVC	2.27 L	67	3.36
FEV_1	1.11	43	2.56
FEV_1/FVC	49	63	76
$FEF_{25\%-75\%}$	0.40 L/sec	13	2.96
$FEF_{50\%}$	0.37	8	4.29
FEF_{max}	2.35	38	6.12
TLC	4.41 L	87	5.07
FRC	2.81	102	2.75
RV	2.27	132	1.71
VC	2.14	63	3.36
IC	1.60	69	2.32
ERV	0.54	52	1.04
DLCO (mL/min per mm Hg)	13.02	64	20.33

CXR

- Most patients with asthma have normal x-rays.

- Signs of Hyperinflation (Diaphragm is down to the 8th rib anteriorly, MCL-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, $PaCO_2$**

- **Oxygen saturation (O_2 sat)**
  - **Detect the percent of oxyhaemoglobin**
  - **Normal O_2 sat 95 – 99 %**

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 to be reduced to Dexamethazone or oral preparation**
- **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

All of the following are accurate indicators of a severe asthmatic attack 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

Acute severe asthma

1. Anxiety, and SOB ; can not complete one sentence.
2. Use of accessory muscles of respiration

3. Tachycardia ≥ 110 beat/min
4. Tachypnea ≥ 25 breath/min
5. Pulsus paradoxus
6. Bilateral generalized inspiratory and expiratory rhonchi

7. PEF ≤ 50%

Life-threatening asthma

1. Confusion
2. Cyanosis,

3. Bradycardia,
4. Hypotension
5. Silent chest,

6. Pao2<60 ,paco2 ≥ 50
7. PEF < 33%

The cornerstone drug of choice for the control of asthmatic patient is:

(a) Inhaled Corticosteroids
(b) Atropine
(c) Inhaled beta-adrenergic agents
(d) Subcutaneous beta-adrenergic agents

Key Components of Asthma Therapy

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

I- Patient Education in the Clinic

- Explain nature of the disease (i.e. **inflammation**)
- Explain **action** of prescribed drugs
- Stress need for **regular, long-term** therapy
- **Peak flow** reading
- Treatment diary / 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 other causes of poorly controlled asthma include 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 and drug preservatives found in such foods as processed potatoes, dried fruits, beer, 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, morbidity, and health status.**

Emotional Stress

- **Emotional stress may lead to asthma exacerbations, primarily because extreme emotional expressions (laughing, crying, anger, or fear) can lead to hyperventilation and hypocapnia, which can cause airway narrowing.**
- **Panic attacks, which are rare but not exceptional in some patients with asthma, have a similar effect.**

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.

I-Controllers:

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

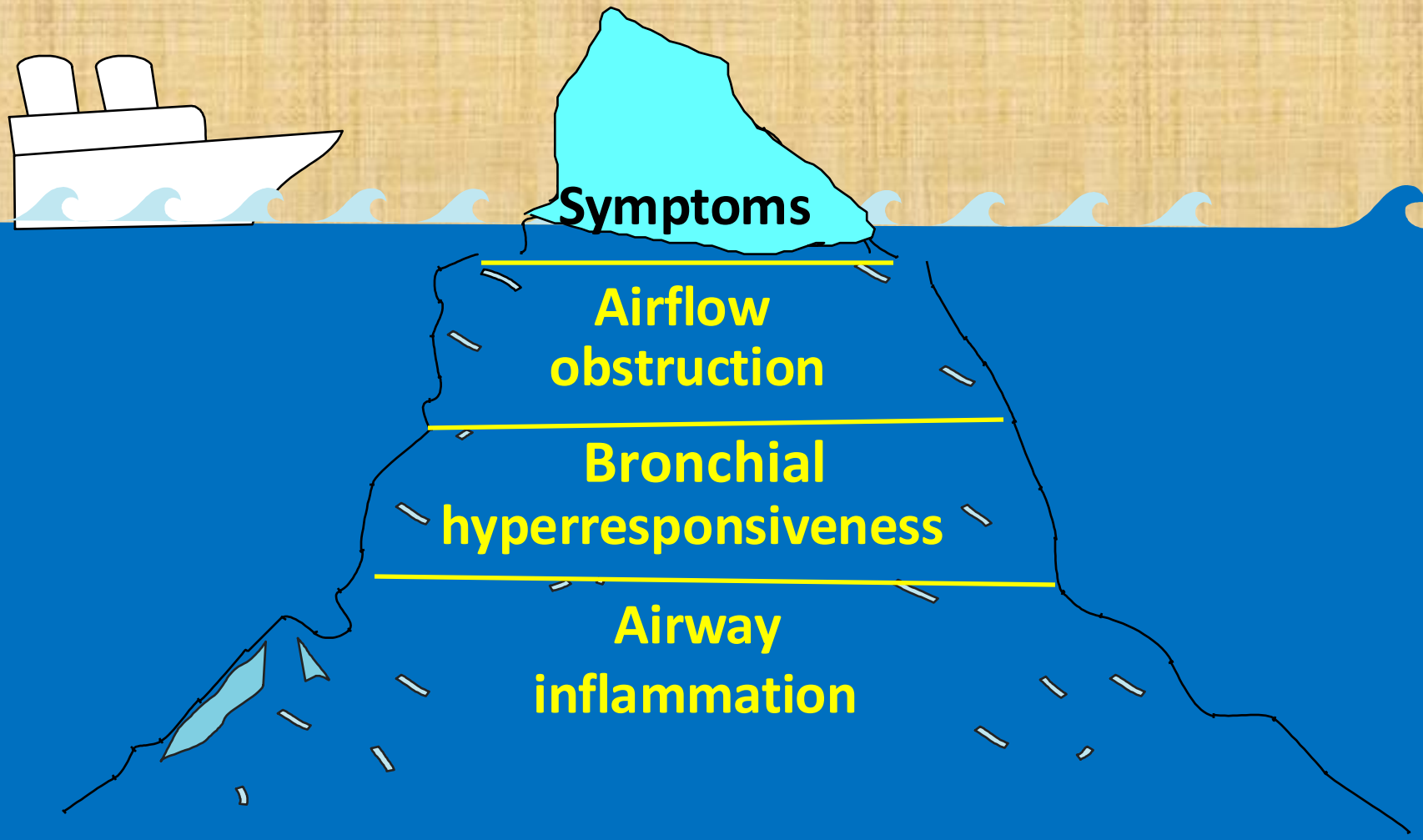
- Controller medications include:
  - Inhaled and systemic glucocorticosteroids,
  - Leukotriens modifiers,
  - Long-acting inhaled B2-agonists, LABA
  - Sustained-release theophylline,
  - Immunomodulators: 1.Omalizumab
    2.Allergen-specific immunotherapy

2-Relievers:

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

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

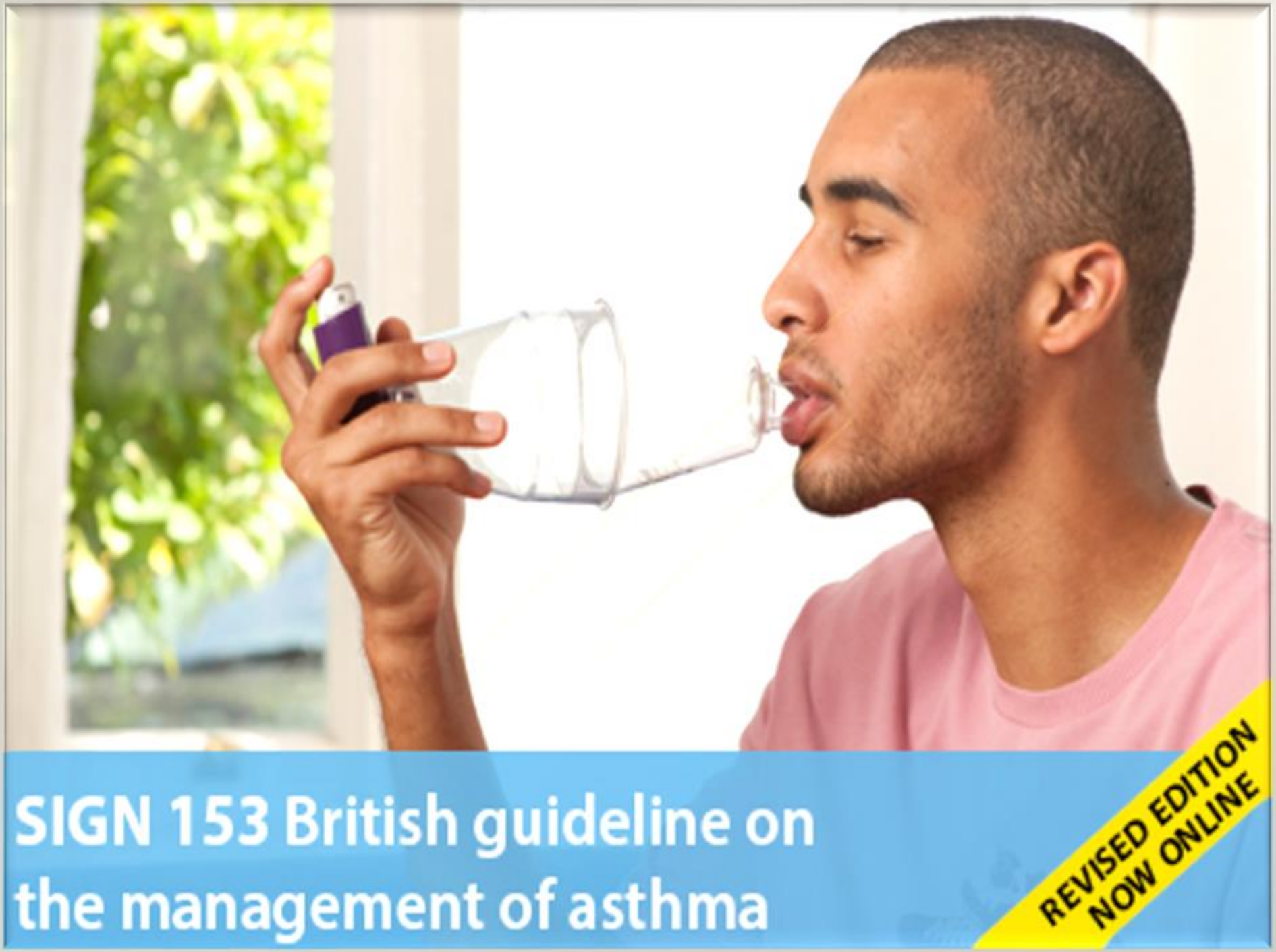
A Lot Going On Beneath The Surface

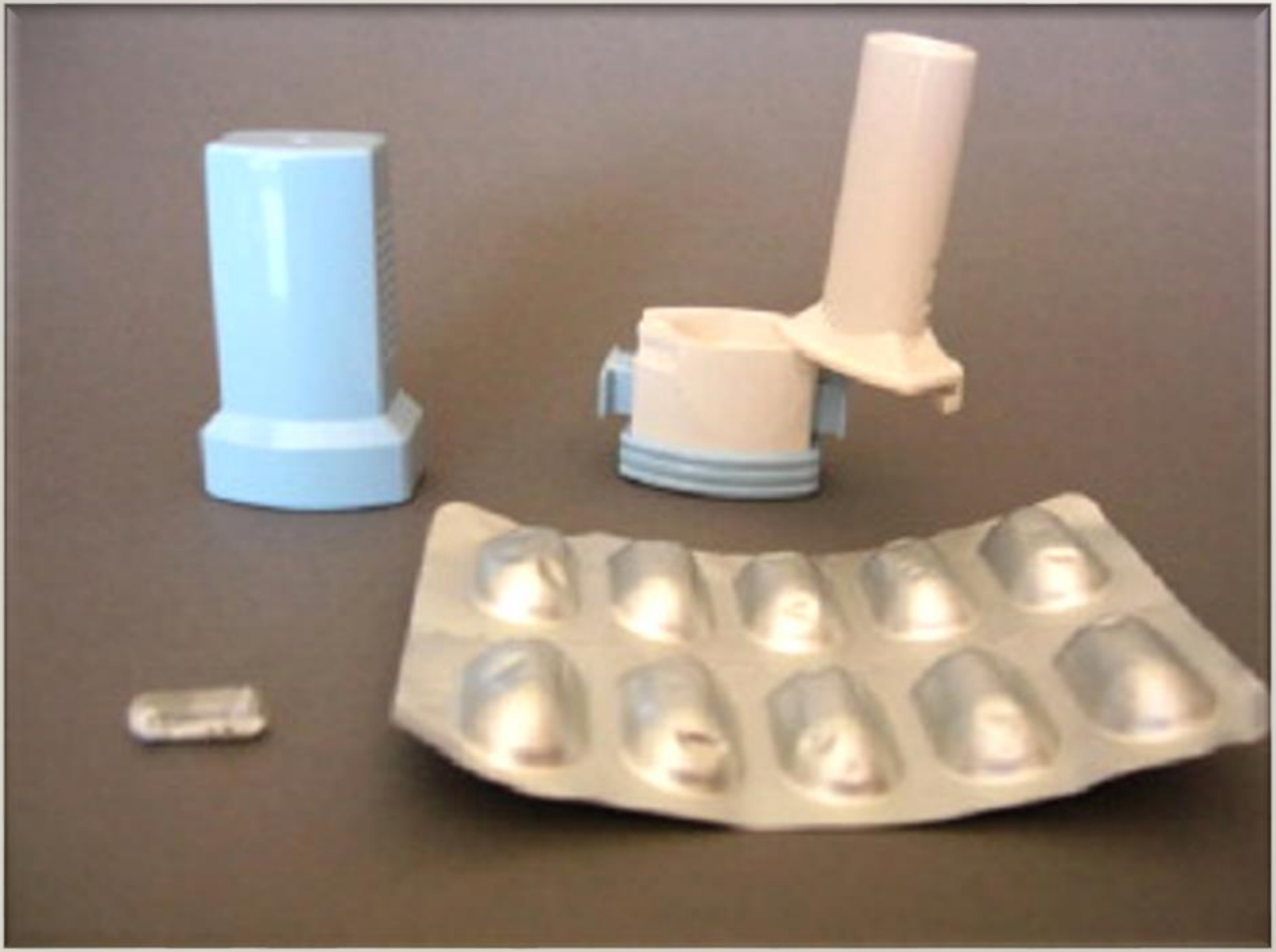


Route of Administration

- **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


Flixotide
Flixotide
Diskus
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

DRUGS USED IN ASTHMA

(Mechanism of action and side effects)

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,

- **However, they do not cure asthma, and when they are discontinued deterioration of clinical control follows within weeks to months in a proportion of patients.**

Inhaled Corticosteroid

- Reduces the synthesis of arachidonic acid by phospholipase A_2
- increases the responsiveness of beta agonists in the airway

- Early use may prevent the severe, progressive inflammatory changes of long-standing asthma

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.

Leukotriens antagonists

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

Methylxanthines

- Bronchodilatation is the most important therapeutic effect

- CNS stimulation, cardiac stimulation, vasodilatation and slight increase in BP (due to release of NE from adrenergic nerves

- **Slow-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

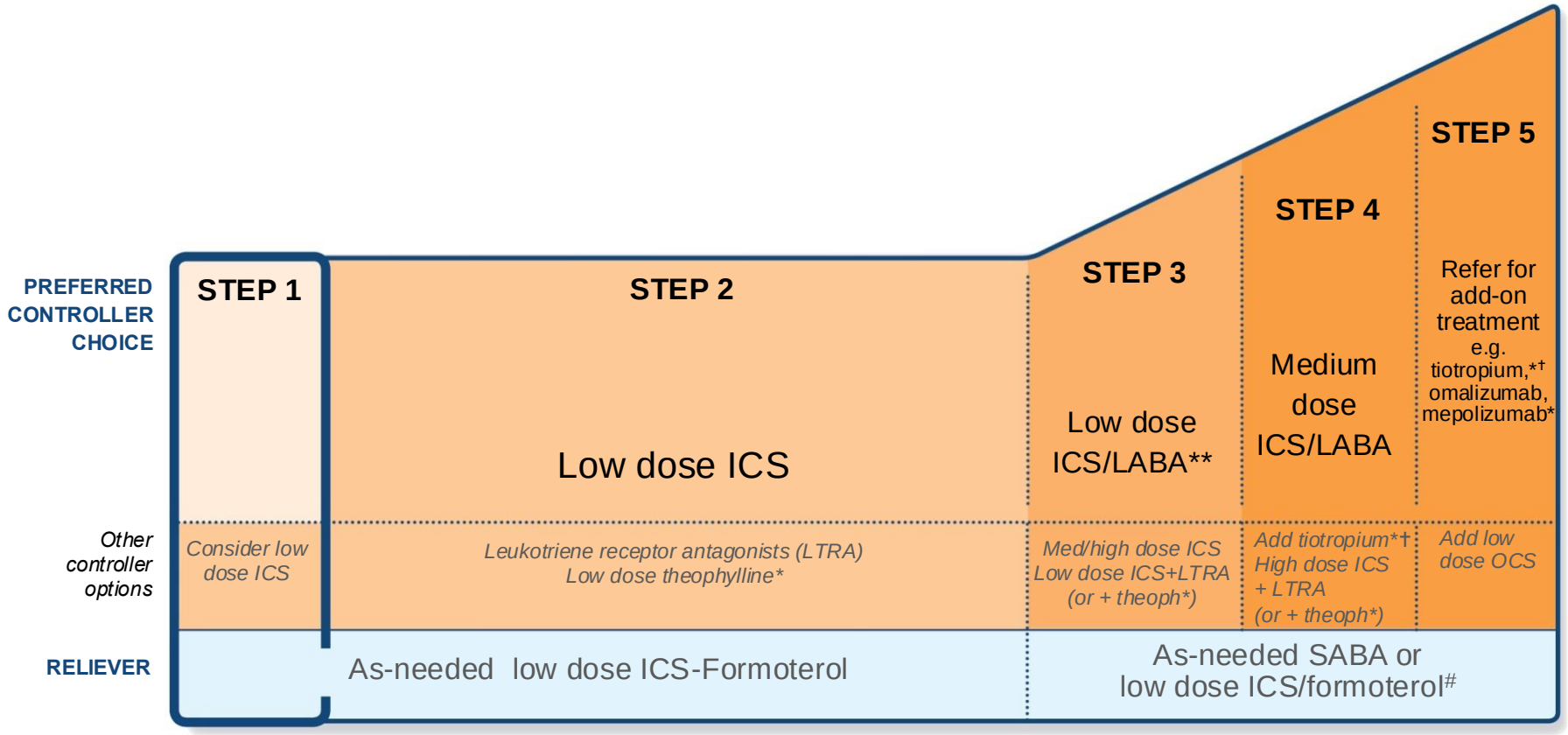
- **Omalizumab**
  - Monoclonal antibody to human IgE
  - management of severe persistent asthma not controlled with maximum therapy.
  - Given parenterally

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.