ASTHMA

- ***airflow obstruction** that **varies markedly**, both spontaneously and with treatment.*

- ***inflammation** in the airways that makes them **more responsive** than nonasthmatics to a wide range of triggers*

- *excessive narrowing with consequent reduced airflow and symptomatic wheezing and dyspnea.*

PREVALENCE

- 10–12% of adults and 15% of children
- Asthma can present at any age, with a peak age of 3 years.
- In childhood, twice as many males as females are asthmatic, but by adulthood the sex ratio has equalized
- many with asthma become asymptomatic during adolescence but that asthma returns in some during adult life, particularly in those with persistent symptoms and severe asthma
- Adults with asthma, including those with onset during adulthood, rarely become permanently asymptomatic

DEFINITION

- Asthma is a ***chronic inflammatory disorder*** of the airways

- In susceptible individuals, inflammation causes recurrent episodes of ***wheezing, breathlessness, chest tightness, and coughing***, ***particularly at night or in the early morning***

DEFINITION

a chronic inflammatory disorder of the airways

inflammation causes recurrent episodes of

I. ***wheezing***

II. ***Breathlessness***

III. ***chest tightness***

IV. ***Coughing***

particularly at night or in the early morning

These episodes are usually associated with---------- ***widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment***

The inflammation also causes an associated ***increase in bronchial hyperresponsiveness*** *to a variety of stimuli*

DEFINITION

Asthma is defined by

1. ***The history of respiratory symptoms that vary over time and in intensity, together with***
2. ***variable expiratory airflow limitation***

- Symptoms and airflow limitation may ***resolve spontaneously*** or in response to medication
- Asthma is usually associated with ***airway hyperresponsiveness*** to direct or indirect stimuli
- chronic airway inflammation ***usually persist***, even when symptoms are absent or lung function is normal, but may normalize with treatment
- Airflow limitation may later become ***persistent.***

Test *before treating*, wherever possible as it is often more difficult to confirm the diagnosis afterwards

DEFINITION

- The ***pattern*** of symptoms is important, as respiratory symptoms may be due to acute or chronic conditions other than asthma

Typical

Respiratory symptoms of wheeze, shortness of breath, cough and/or chest tightness:

- Patients (especially adults) experience ***more than one*** of these types of symptoms.
- Symptoms are often ***worse at night*** or in the early morning.
- Symptoms ***vary over time and in intensity***
- Symptoms are ***triggered*** by viral infections (colds), exercise, allergen exposure, changes in weather, laughter, or irritants

decrease the probability

- Isolated cough with no other respiratory symptoms
- Chronic production of sputum
- Shortness of breath associated with dizziness, light-headedness or peripheral tingling (paresthesia)
- Chest pain
- Exercise-induced dyspnea with noisy inspiration

- No feature is unique to asthma
- no feature is universal in patients with the condition.

- For example, *all tests of airway caliber may be normal between attacks*, even in patients whose attacks are sudden and severe.
- *Bronchial responsiveness* may be normal over most of the year in patients with seasonal asthma, and bronchial hyperresponsiveness is often found in people with *allergic rhinitis* but without asthma.

ETIOLOGY

- ***Atopy*** is the major risk factor for asthma
- nonatopic individuals have a very low risk of developing asthma.
- Patients with asthma commonly suffer from other atopic diseases, particularly allergic rhinitis, which may be found in over 80% of asthmatic patients, and atopic dermatitis (eczema).

- ***Infections***

it is uncertain whether they play a role in etiology

There is some association between respiratory syncytial virus infection in infancy and the development of asthma

atypical bacteria such as *Mycoplasma* and *Chlamydophila*, have been implicated in the mechanism of severe asthma

- ***Genetic Considerations***

familial association of asthma

high degree of concordance for asthma in identical twins

different genes

severity of asthma is also genetically determined

asthma is polygenic

Genetic polymorphisms may also be important in determining the response to asthma therapy

- ***Diet***

The role of dietary factors is controversial.

low in antioxidants such as vitamin C and vitamin A, magnesium, selenium, omega-3 polyunsaturated fats (fish oil)

high in sodium and omega-6 polyunsaturates

Obesity is also an independent risk factor for asthma, particularly in women

- ***Air Pollution***

Most evidence argues against an important role for air pollution as asthma is no more prevalent in cities with a high ambient level of traffic pollution than in rural areas with low levels of pollution

There is some evidence that maternal smoking is a risk factor for asthma

- ***Allergens***

triggers of asthma symptoms

implicated in allergic sensitization

Exposure to house dust mites in early childhood is a risk factor for allergic sensitization and asthma

- ***Occupational Exposure***

relatively common and may affect up to 10% of young adults

Intrinsic Asthma (approximately10%)

negative skin tests

normal serum concentrations of IgE

(nonatopic or intrinsic asthma)

later onset of disease (adult-onset asthma)

commonly have concomitant nasal polyps, and may be aspirin-sensitive

more severe, persistent asthma.

ASTHMA TRIGGERS

- ***Allergens***

Inhaled allergens

early response

Inhaled allergens activate mast cells with bound IgE directly leading to the immediate release of bronchoconstrictor mediators, resulting in the early response that is reversed by bronchodilators

late response

airway edema and an acute inflammatory response with increased eosinophils and neutrophils that are not very reversible with bronchodilators.

- ***Virus Infections***

rhinovirus, respiratory syncytial virus, and coronavirus are the most common triggers of acute severe exacerbations

- ***Pharmacologic Agents***

increased cholinergic bronchoconstriction

Beta-adrenergic blockers commonly acutely worsen asthma, and their use may be fatal

Angiotensin-converting enzyme inhibitors

Aspirin may worsen asthma in some patients

- ***Exercise***

hyperventilation,

increased osmolality in airway lining fluid

triggers mast cell mediator release

begins after exercise has ended, and recovers spontaneously within about 30 minutes

EIA is worse in cold, dry climates than in hot, humid conditions.

It may be prevented by prior administration of β_2-agonists and antileukotrienes, but is best prevented by regular treatment with ICS

- ***Physical Factors***

Cold air and hyperventilation

Laughter

hot weather

strong smells or perfumes

- ***Food*** little evidence
- ***Air Pollution***

sulfur dioxide,

ozone

nitrogen oxides

Occupational Factors

Occupational asthma is characteristically associated with symptoms at work with relief on weekends and holidays

- ***Gastroesophageal Reflux***

is common in asthmatic patients

increased by bronchodilators. Although acid reflux might trigger reflex bronchoconstriction,

it rarely causes asthma symptoms,

- ❑ antireflux therapy fails to reduce asthma symptoms in most patients.

- ***Stress***

psychological factors can induce bronchoconstriction through cholinergic reflex pathways

DIAGNOSIS

Making the diagnosis of asthma is based on identifying both:

I. ***characteristic pattern of respiratory symptoms***

II. ***Variable expiratory airflow limitation***

Box 1-2. Diagnostic criteria for asthma in adults, adolescents, and children 6–11 years

1. HISTORY OF VARIABLE RESPIRATORY SYMPTOMS	
Feature	*Features that support the diagnosis*
Wheeze, shortness of breath, chest tightness and cough (Descriptors may vary between cultures and by age)	• Generally more than one type of respiratory symptom (in adults, isolated cough is seldom due to asthma) • Symptoms occur variably over time and vary in intensity • Symptoms are often worse at night or on waking • Symptoms are often triggered by exercise, laughter, allergens, cold air • Symptoms often appear or worsen with viral infections
2. CONFIRMED VARIABLE EXPIRATORY AIRFLOW LIMITATION	
Feature	*Considerations, definitions, criteria*
2.1 Documented expiratory airflow limitation	At a time when FEV_1 is reduced, confirm that FEV_1/FVC is reduced (it is usually >0.75–0.80 in adults, >0.90 in children[13])
AND	
2.2 Documented excessive variability in lung function* (one or more of the following):	The greater the variations, or the more occasions excess variation is seen, the more confident the diagnosis. If initially negative, tests can be repeated during symptoms or in the early morning.
• Positive bronchodilator (BD) reversibility test	*Adults*: increase in FEV_1 of >12% and >200 mL (greater confidence if increase is >15% and >400 mL). *Children*: increase in FEV_1 of >12% predicted Change measured 10–15 minutes after 200–400 mcg salbutamol (albuterol) or equivalent, compared with pre-BD readings. Positive test more likely if BD withheld before test: SABA ≥4 hours, twice-daily LABA 24 hours, once-daily LABA 36 hours
• Excessive variability in twice-daily PEF over 2 weeks	*Adults*: average daily diurnal PEF variability >10%* *Children*: average daily diurnal PEF variability >13%*

• Significant increase in lung function after 4 weeks of anti-inflammatory treatment	*Adults*: increase in FEV_1 by >12% and >200 mL (or PEF† by >20%) from baseline after 4 weeks of treatment, outside respiratory infections
• Positive exercise challenge test	*Adults*: fall in FEV_1 of >10% and >200 mL from baseline *Children*: fall in FEV_1 of >12% predicted, or PEF >15%
• Positive bronchial challenge test (usually only for adults)	Fall in FEV_1 from baseline of ≥20% with standard doses of methacholine, or ≥15% with standardized hyperventilation, hypertonic saline or mannitol challenge
• Excessive variation in lung function between visits (good specificity but poor sensitivity)	*Adults*: variation in FEV_1 of >12% and >200 mL between visits, outside of respiratory infections *Children*: variation in FEV_1 of >12% in FEV_1 or >15% in PEF† between visits (may include respiratory infections)

LUNG FUNCTION

DEMONSTRATE THE TEST

RIGHT TECHNIQUE

- DEMOGRAPHIC DETAILS
- SUBJECT POSITION
- DEMONSTRATE TEST
- PERFORM TEST
- ACCEPTABILITY & REPETABILITY
- RECORD VALUES

Explain the procedure to the patient

Demonstrate the procedure to the patient

Give 1 or 2 trial runs with the mouth piece

Important to communicate well for Subject Training

RIGHT EQUIPMENT

SUBJECT CO-OPERATION

RIGHT TECHNIQUE

RIGHT INTERPRETATION

PERFORM THE TEST

PHASE - 1

Nice deeeeeeep inhalation

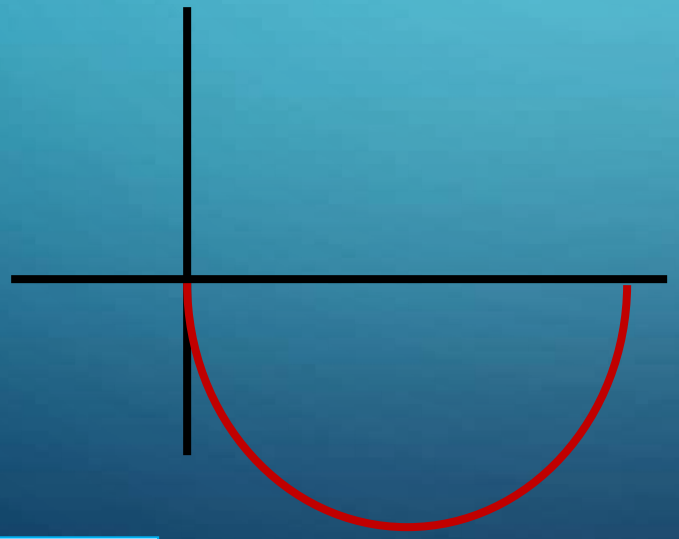
Fill your chest with as much air as you can

FVC,

FEV1,

PEFR

FEF25-75



- RIGHT TECHNIQUE
- DEMOGRAPHIC DETAILS
- SUBJECT POSITION
- DEMONSTRATE TEST
- PERFORM TEST
- ACCEPTABILITY & REPETABILITY
- RECORD VALUES

RIGHT EQUIPMENT

SUBJECT CO-OPERATION

RIGHT TECHNIQUE

RIGHT INTERPRETATION

RIGHT TECHNIQUE

- DEMOGRAPHIC DETAILS
- SUBJECT POSITION
- DEMONSTRATE TEST
- PERFORM TEST
- ACCEPTABILITY & REPETABILITY
- RECORD VALUES

PERFORM THE TEST

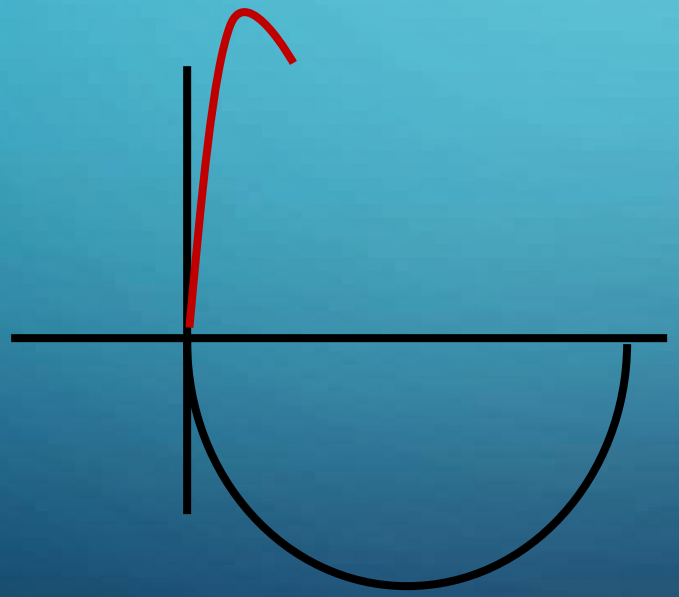
PHASE - 2

Blast

Blow as fast as you can……

Blast maximum……

PEFR, FEV1



RIGHT EQUIPMENT

SUBJECT CO-OPERATION

RIGHT TECHNIQUE

RIGHT INTERPRETATION

RIGHT TECHNIQUE

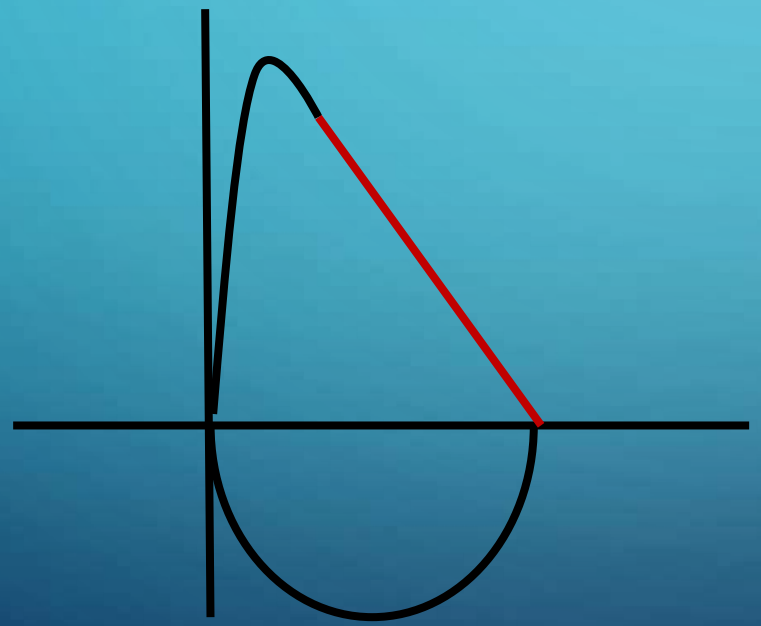
- DEMOGRAPHIC DETAILS
- SUBJECT POSITION
- DEMONSTRATE TEST
- PERFORM TEST
- ACCEPTABILITY & REPETABILITY
- RECORD VALUES

PERFORM THE TEST

PHASE - 3

Continue to remove as much air as possible

FVC+ FEF25-75



RIGHT EQUIPMENT

SUBJECT CO-OPERATION

RIGHT TECHNIQUE

RIGHT INTERPRETATION

RIGHT TECHNIQUE

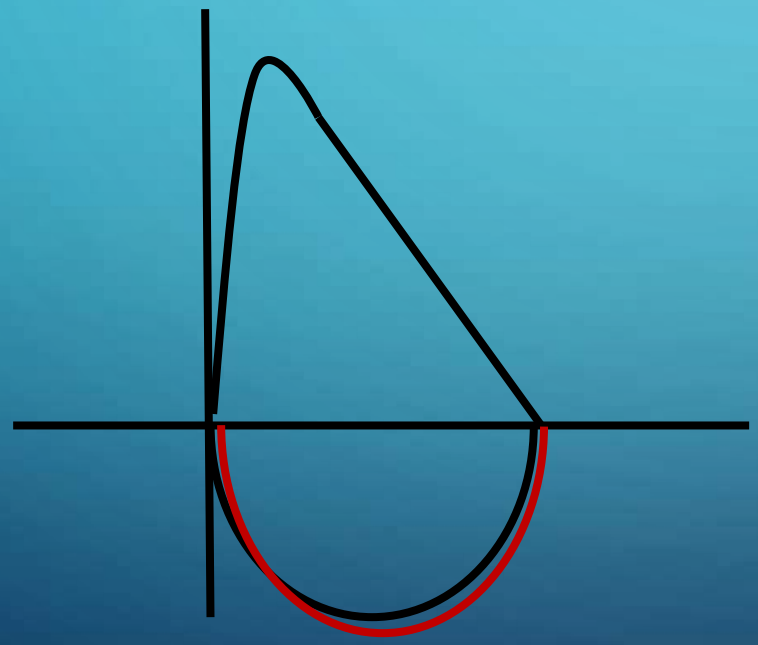
- DEMOGRAPHIC DETAILS
- SUBJECT POSITION
- DEMONSTRATE TEST
- PERFORM TEST
- ACCEPTABILITY & REPETABILITY
- RECORD VALUES

PERFORM THE TEST

PHASE - 4

Take deep inspiration

(Inspire as much air as was blown out)



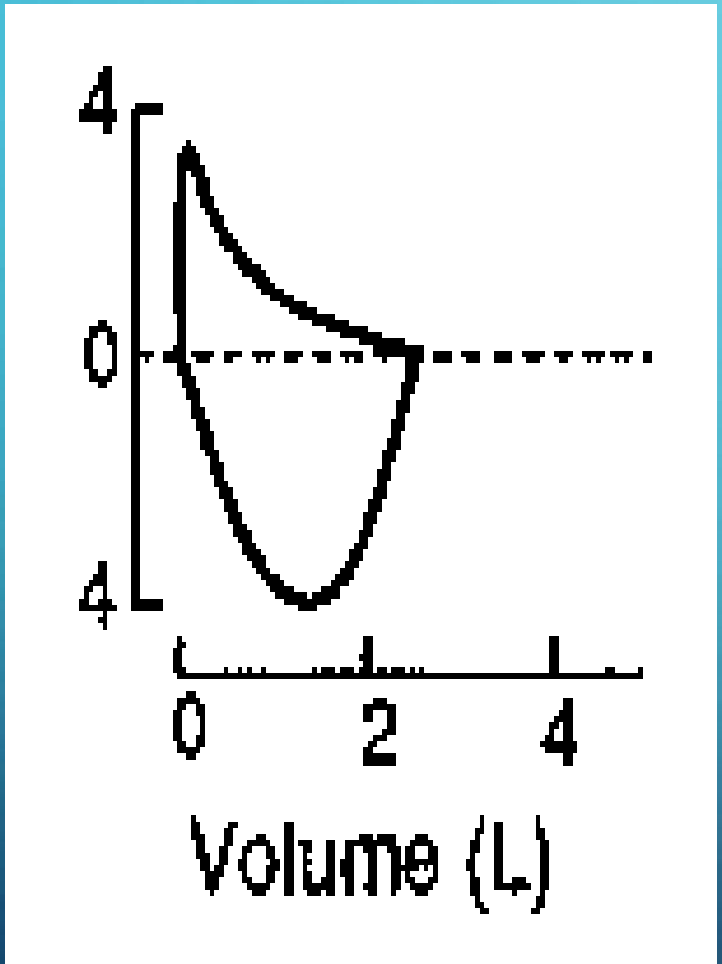
RIGHT EQUIPMENT

SUBJECT CO-OPERATION

RIGHT TECHNIQUE

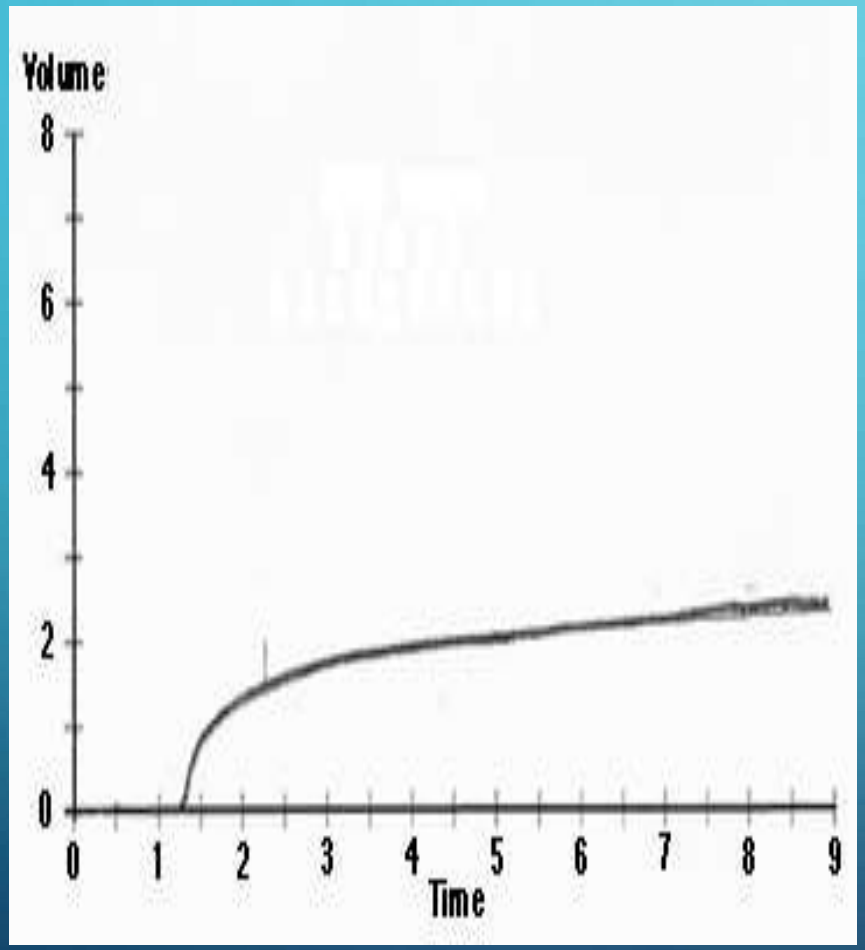
RIGHT INTERPRETATION

OBSTRUCTIVE DISORDERS



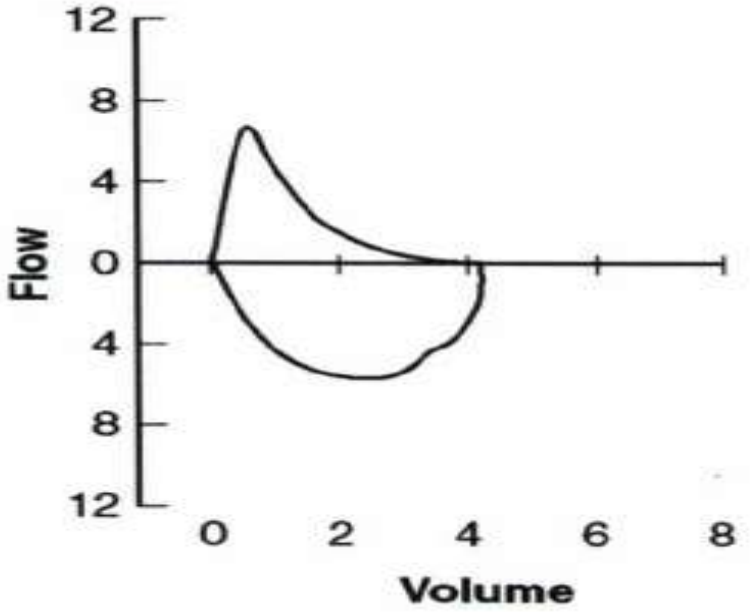
- Characterized by a limitation of expiratory airflow
  - Examples: asthma, COPD
- Decreased: FEV_1, FEF_{25-75}, FEV_1/FVC ratio (<0.8)
- Increased or Normal: TLC

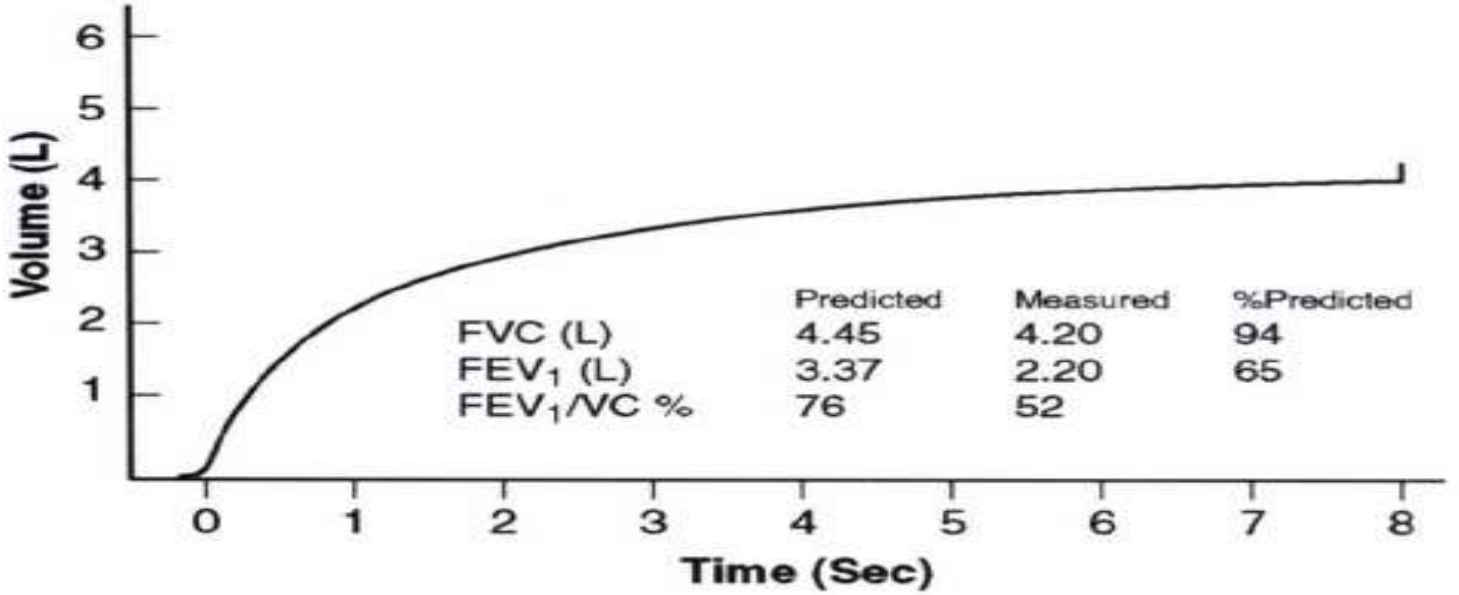
SPIROMETRY IN OBSTRUCTIVE DISEASE



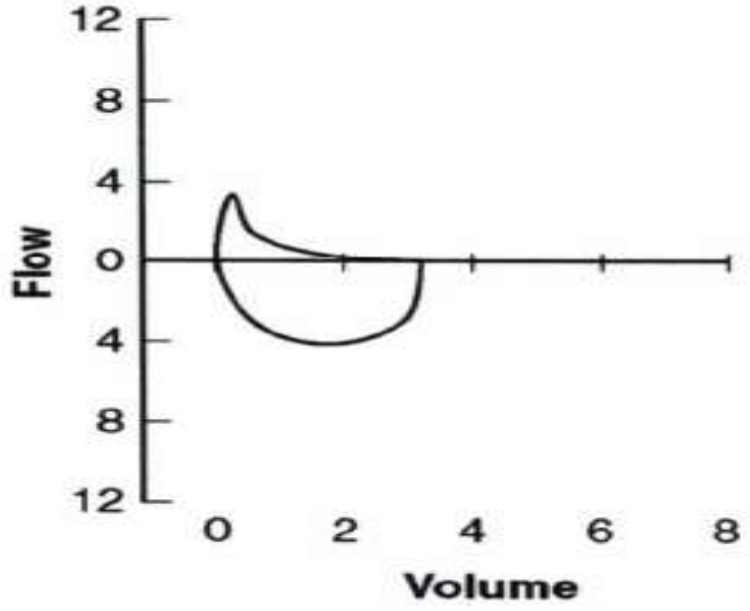
- Slow rise in upstroke
- May not reach plateau

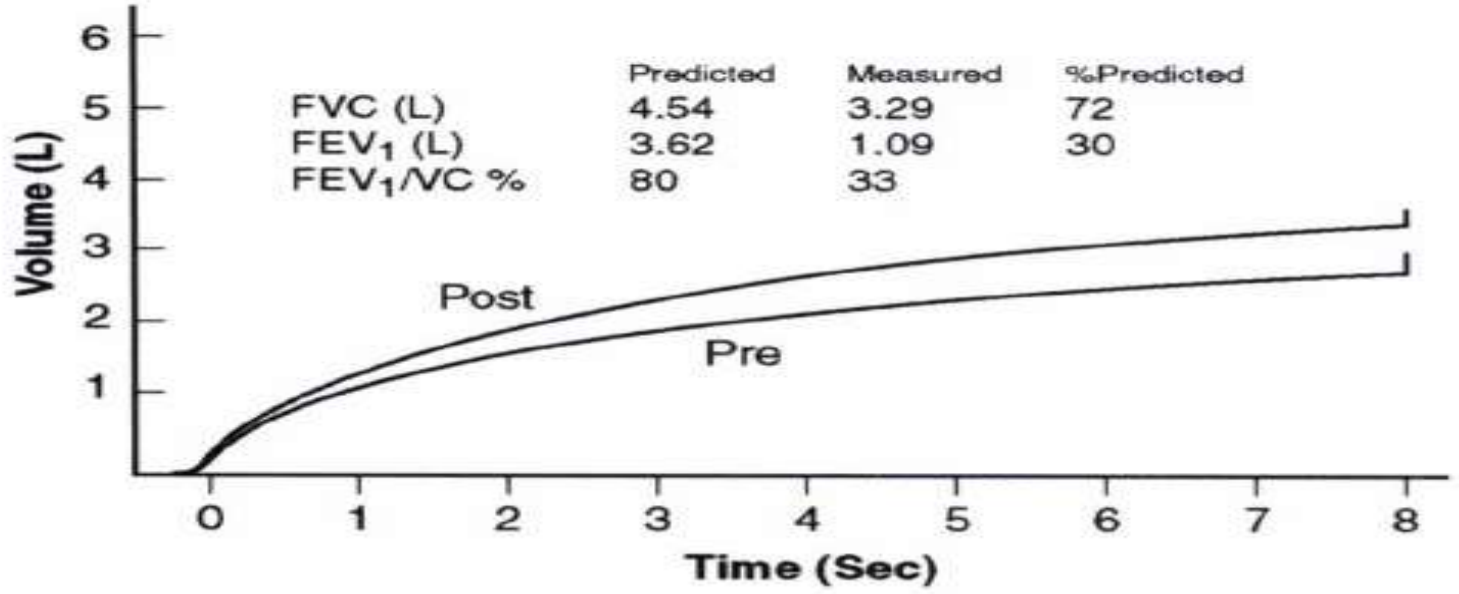
B. Moderate Airflow Obstruction

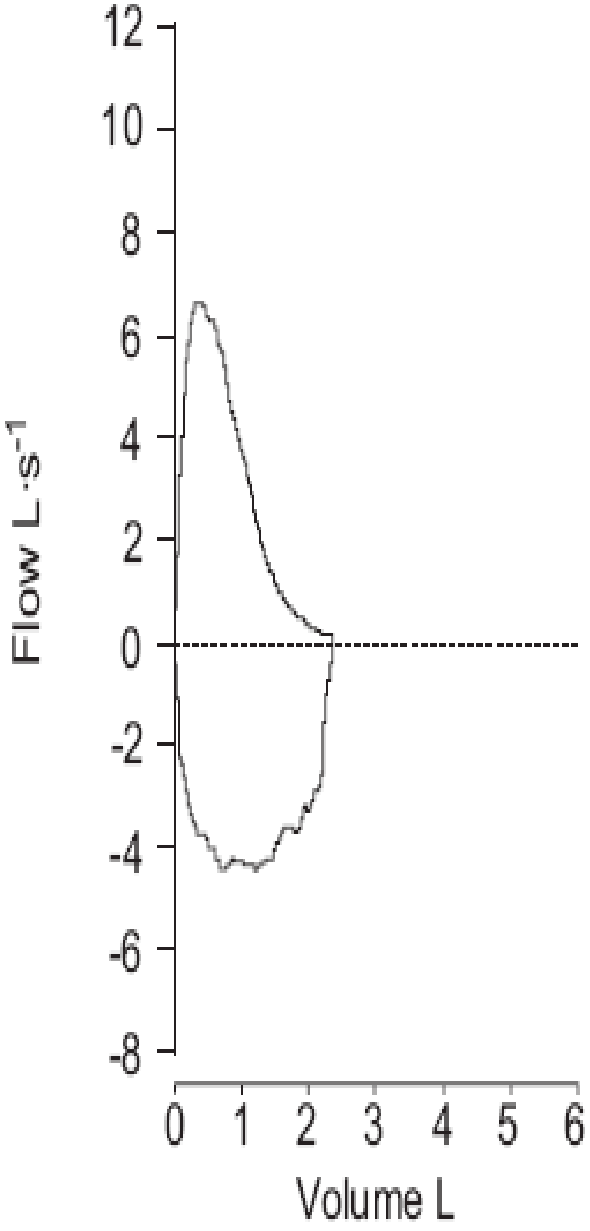


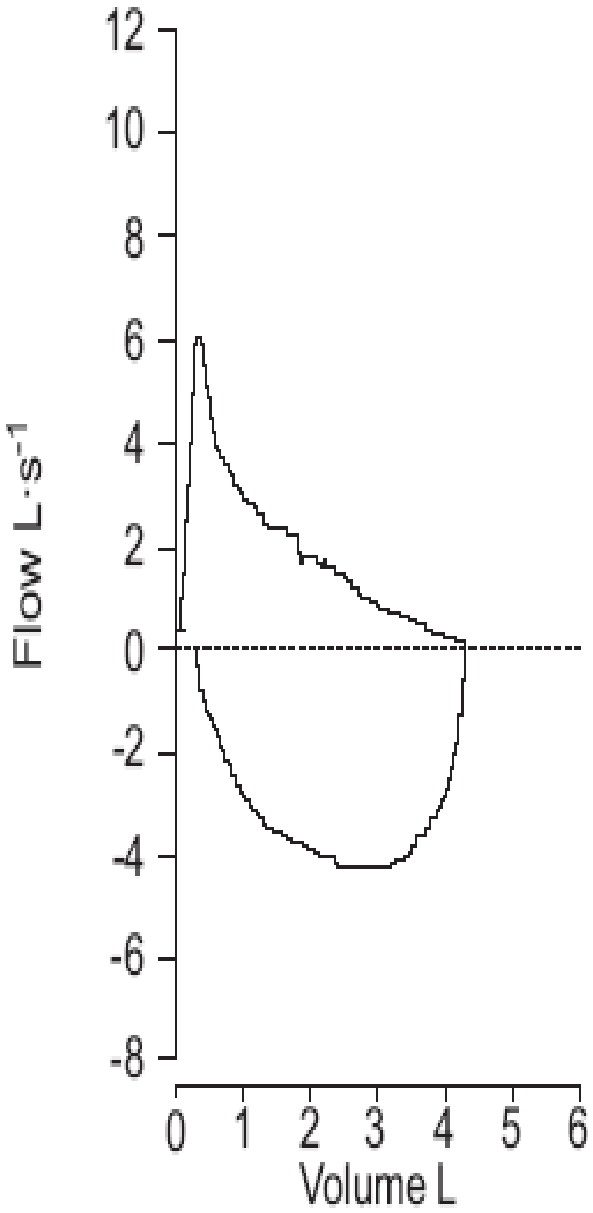


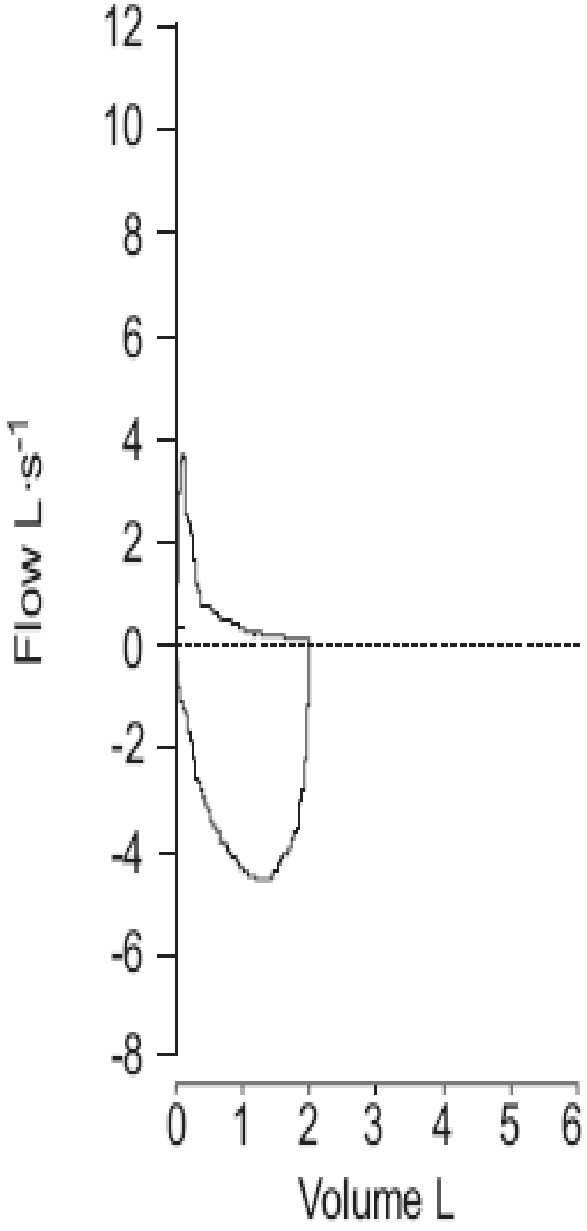
C. Severe Airflow Obstruction






Flow L·s-1
12
10
8
6
4
2
0
-2
-4
-6
-8
0 1 2 3 4 5 6
Volume L


Flow L·s-1
12
10
8
6
4
2
0
-2
-4
-6
-8
0 1 2 3 4 5 6
Volume L


Flow L·s-1
12
10
8
6
4
2
0
-2
-4
-6
-8
0 1 2 3 4 5 6
Volume L

DIFFERENTIAL DIAGNOSIS

- Upper airway obstruction
- stridor localized to large airways.
- foreign body
- Left ventricular failure
- Eosinophilic pneumonias
- systemic vasculitis, including Churg-Strauss syndrome and polyarteritis nodosa
- Chronic obstructive pulmonary disease (COPD)

TREATMENT

Table 254-2 Aims of Asthma Therapy
• Minimal (ideally no) chronic symptoms, including nocturnal
• Minimal (infrequent) exacerbations
• No emergency visits
• Minimal (ideally no) use of a required β_2-agonist
• No limitations on activities, including exercise
• Peak expiratory flow circadian variation <20%
• (Near) normal PEF
• Minimal (or no) adverse effects from medicine

bronchodilators

- rapid relief of symptoms (relaxation of airway smooth muscle)
- little or no effect on the underlying inflammatory process
- are not sufficient to control asthma
- β_2-adrenergic agonists, anticholinergics, and theophylline
- β_2-agonists are by far the most effective.

- ***controllers***(inhibit the underlying inflammatory process).
  - Inhaled Corticosteroids
  - Systemic Corticosteroids
  - Antileukotrienes
  - Cromones

$_2$-Agonists

- activate $_2$-adrenergic receptors
- relaxes smooth muscle cells
- inhibits certain inflammatory cells, particularly mast cells

Table 254-3 Effects of β-Adrenergic Agonists on Airways
• Relaxation of airway smooth muscle (proximal and distal airways)
• Inhibition of mast cell mediator release
• Inhibition of plasma exudation and airway edema
• Increased mucociliary clearance
• Increased mucus secretion
• Decreased cough
• No effect on chronic inflammation

Short-acting $_2$-agonists (SABAs)

- albuterol and terbutaline
- duration of action of 3–6 hours
- used as needed for symptom relief
- Increased use of SABAs indicates that asthma is not controlled
- useful in preventing EIA if taken prior to exercise.

Long-acting $_2$-agonists (LABAs)

- salmeterol and formoterol
- duration of action over 12 hours and
- twice daily
- should not be given in the absence of ICS therapy as they do not control the underlying inflammation
- improve asthma control and reduce exacerbations when added to ICS
- Side Effects
- Tremor
- palpitations
- small fall in plasma potassium

Anticholinergics

- Muscarinic receptor antagonists
- ipratropium bromide
- prevent cholinergic nerve-induced bronchoconstriction and mucus secretion.
- much less effective than $_2$-agonists in asthma therapy
- may be given by nebulizer in treating acute severe asthma
- should only be given following $_2$-agonists

Theophylline

- inhibition of phosphodiesterases
- doses required for bronchodilation commonly cause side effects
- at lower doses has anti-inflammatory effects
- additional bronchodilator in patients with severe asthma
- Side Effects
- vomiting, and headaches
- Diuresis and palpitations
- cardiac arrhythmias, epileptic seizures
- side effects are related to plasma concentration(rarely observed at plasma concentrations below 10 mg/L)
- metabolized by CYP450 in the liver

Systemic Corticosteroids

- treatment of acute severe asthma
- OCS are as effective
- 1% of asthma patients may require maintenance treatment with OCS

Antileukotrienes

- Cysteinyl-leukotrienes are potent bronchoconstrictors, cause microvascular leakage, and increase eosinophilic inflammation
- Antileukotrienes (montelukast and zafirlukast)
- modest clinical benefit in asthma
- less effective than ICS
- less effect on airway inflammation
- useful as an add-on therapy
- less effective than LABAs

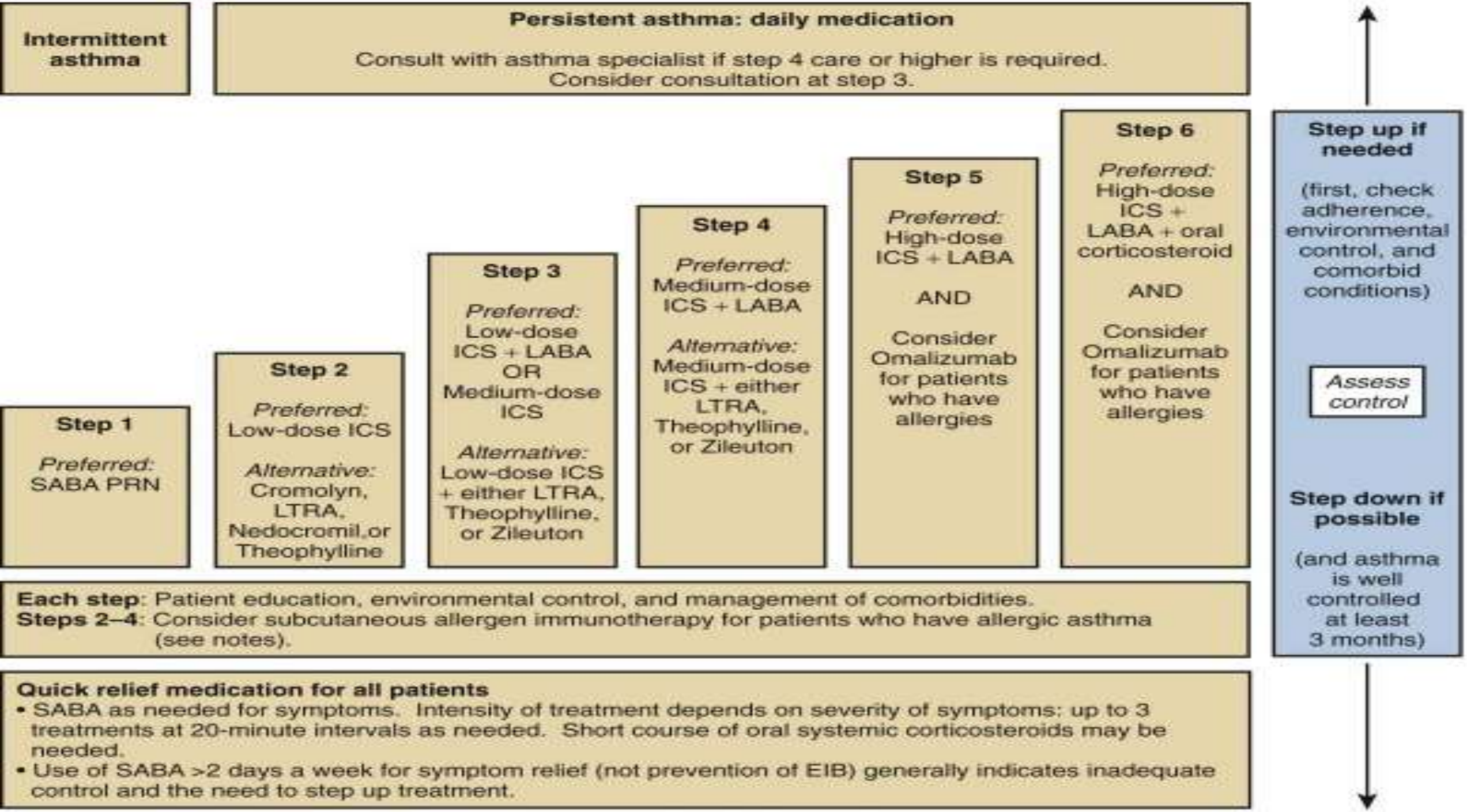
Cromones(Cromolyn sodium and nedocromil sodium)

- inhibit mast cell and sensory nerve activation
- effective in blocking trigger-induced asthma
- EIA
- allergen- and sulfur dioxide–induced symptoms
- little benefit in the long-term control of asthma due to their short duration of action

MANAGEMENT OF CHRONIC ASTHMA

Classifying asthma severity in youths greater than or equal to 12 years of age and adults

Components of severity		Classification of asthma severity (youths ≥12 years of age and adults)			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment Normal FEV_1 /FVC: 8-19 yr 85 percent 20-39 yr 80 percent 40-59 yr 75 percent 60-80 yr 70 percent	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3-4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting beta $_2$ -agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not >1x/day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80 percent predicted • FEV_1 /FVC normal	• FEV_1 ≥80 percent predicted • FEV_1 /FVC normal	• FEV_1 >60 but <80 percent predicted • FEV_1 /FVC reduced 5 percent	• FEV_1 <60 percent predicted • FEV_1 /FVC reduced >5 percent
Risk	**Exacerbations requiring oral systemic corticosteroids**	**0-1/year (see footnote)**	**≥2/year (see footnote)**		
		Consider severity and interval since last exacerbation			
		Frequency and severity may fluctuate over time for patients in any severity category			
		Relative annual risk of exacerbations may be related to FEV_1			


Intermittent asthma
Persistent asthma: daily medication
Consult with asthma specialist if step 4 care or higher is required.
Consider consultation at step 3.
Step 1
Preferred:
SABA PRN
Step 2
Preferred:
Low-dose ICS
Alternative:
Cromolyn, LTRA, Nedocromil,or Theophylline
Step 3
Preferred:
Low-dose ICS + LABA
OR
Medium-dose ICS
Alternative:
Low-dose ICS + either LTRA, Theophylline, or Zileuton
Step 4
Preferred:
Medium-dose ICS + LABA
Alternative:
Medium-dose ICS + either LTRA, Theophylline, or Zileuton
Step 5
Preferred:
High-dose ICS + LABA
AND
Consider Omalizumab for patients who have allergies
Step 6
Preferred:
High-dose ICS + LABA + oral corticosteroid
AND
Consider Omalizumab for patients who have allergies
Step up if needed
(first, check adherence, environmental control, and comorbid conditions)
Assess control
Step down if possible
(and asthma is well controlled at least 3 months)
Each step: Patient education, environmental control, and management of comorbidities.
Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).
Quick relief medication for all patients
• SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
• Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.

ACUTE SEVERE ASTHMA

- increasing chest tightness, wheezing, and dyspnea that are often not or poorly relieved by their usual reliever inhaler

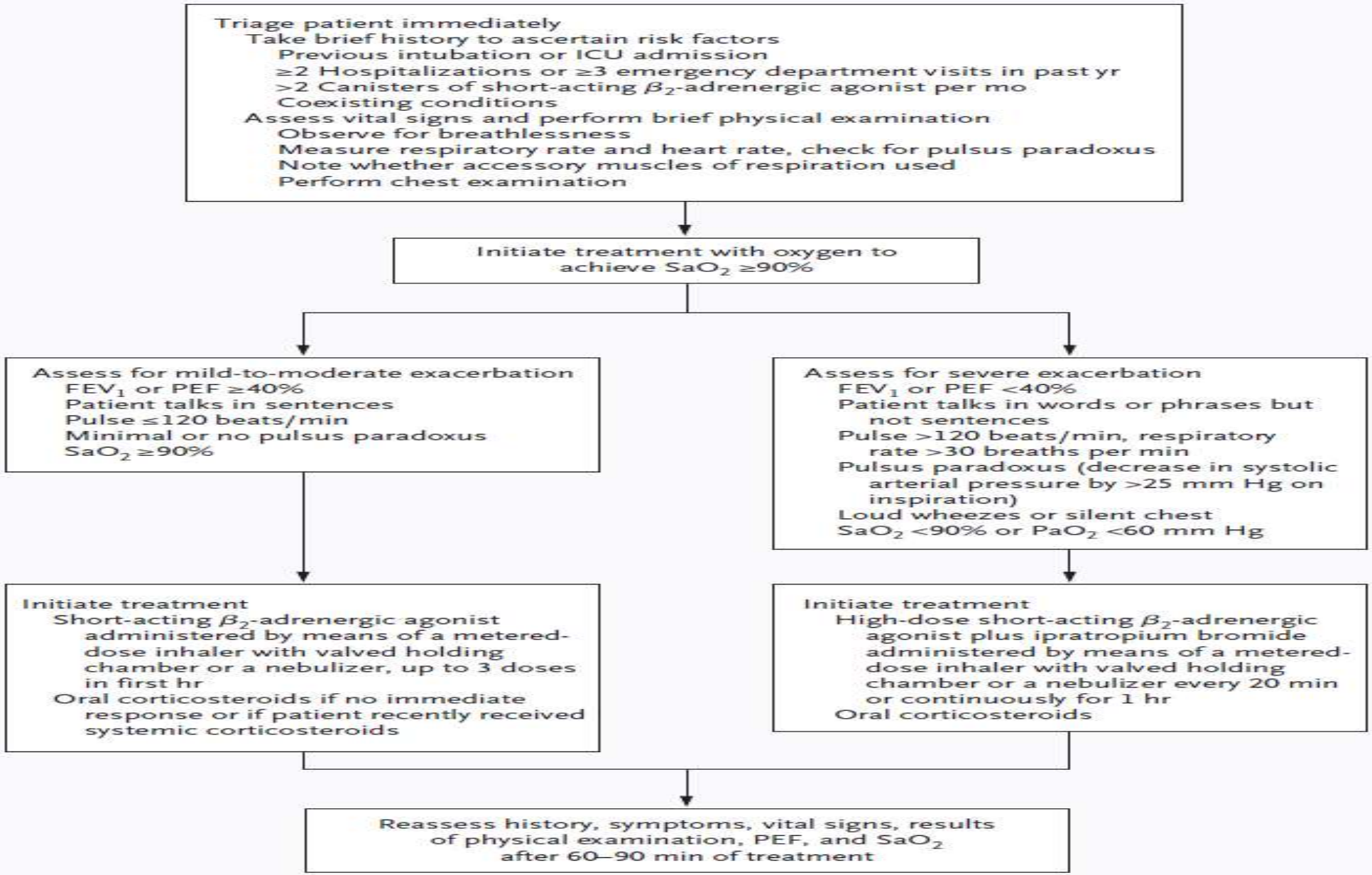


Figure 1. Initial Assessment of a Patient Presenting to the Emergency Department with Asthma.

Adapted from the National Asthma Education and Prevention Program Expert Panel Report 3.[3] FEV_1 denotes forced expiratory volume in 1 second, ICU intensive care unit, $PaCO_2$ partial pressure of arterial carbon dioxide, PaO_2 partial pressure of arterial oxygen, PEF peak expiratory flow, and SaO_2 arterial oxygen saturation.

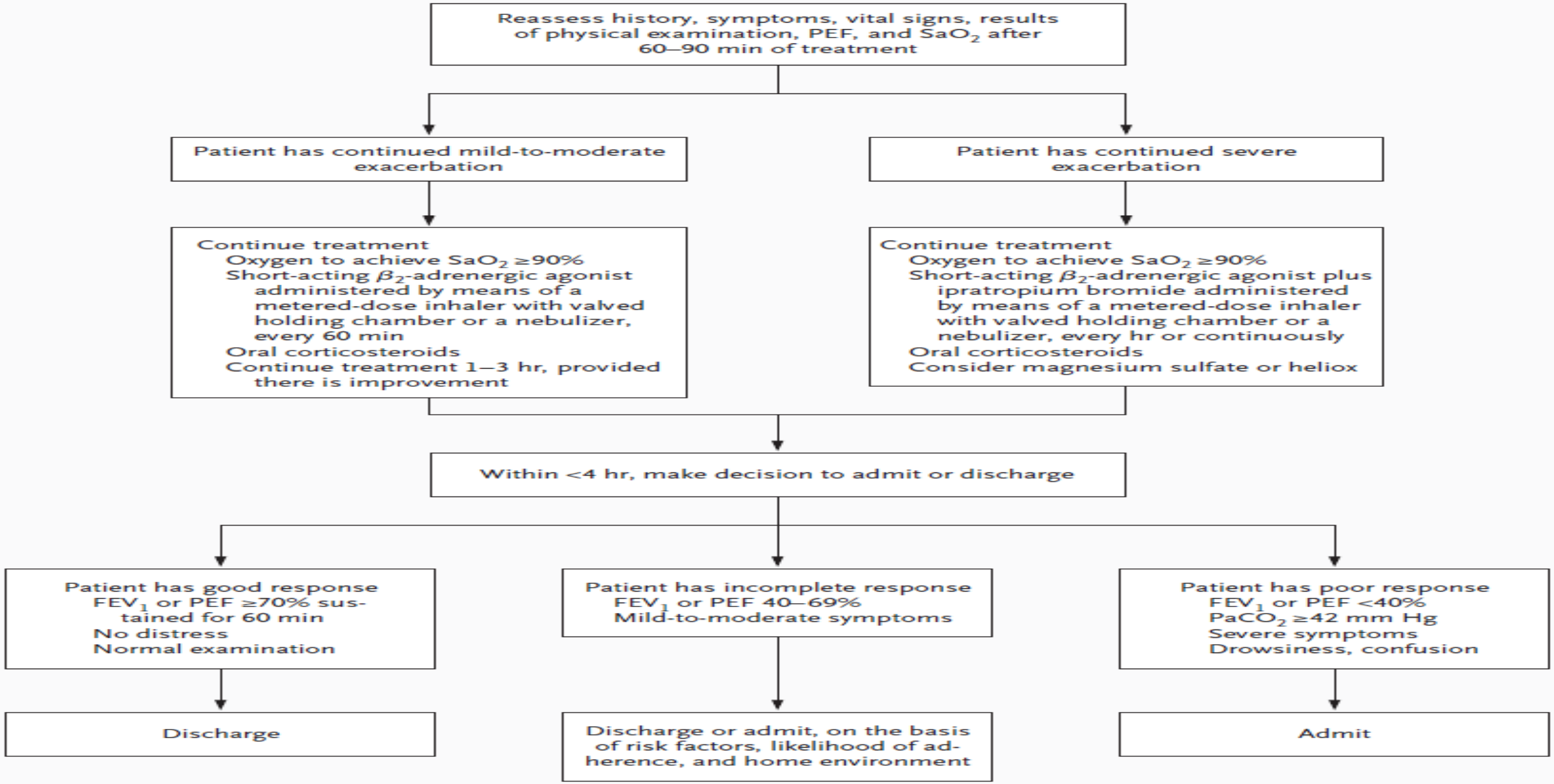


Figure 2. Continued Management of Asthma in the Emergency Department.

Adapted from the National Asthma Education and Prevention Program Expert Panel Report 3.[3] Heliox is a mixture of helium and oxygen, usually 79% and 21%, respectively, whose density is about one third that of air. FEV_1 denotes forced expiratory volume in 1 second, $PaCO_2$ partial pressure of arterial carbon dioxide, PEF peak expiratory flow, and SaO_2 arterial oxygen saturation.