Ceylon College of Physicians

CLINICAL PRACTICE GUIDELINES

ASTHMA

MANAGEMENT GUIDELINES

In Collaboration with

Sri Lanka College of Pulmonologists

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I. Introduction

II. Evidence Base

III. Executive summary

Chapters

1. Diagnosis of Asthma
2. Investigations
3. Stepwise management of asthma
4. Selecting a delivery device
5. Assessing asthma control
6. Follow up and monitoring of asthma
7. Severe Asthma
8. Management of acute asthma
9. Delivery of asthma care services
10. Asthma COPD Over-Lap (ACO)
11. Work related asthma
12. Exercise induced asthma and exercise induced bronchoconstriction
13. Non pharmacological management
14. Management of Asthma in special situations

I. Introduction

Asthma is one of the most common non-communicable diseases worldwide. Undiagnosed and uncontrolled asthma gives rise to limitation of physical activity, loss of productivity, unscheduled utilization of healthcare services and preventable mortality.

World Health Organizations (WHO) estimates, 300 million people suffer from asthma and claim it is the most common chronic disease among children. Sri Lankan data from International Study of Asthma and Allergy in Childhood (ISAAC) survey shows a prevalence of asthma among adolescents is around 17-23%.

Sri Lanka has about 200,000 admissions for asthma to state hospitals each year.

In recent times, major advances have been made in the understanding and management of asthma. The knowledge of the inflammatory process, the heterogeneity, phenotypic clusters and endotypes of asthma has helped in the advancement of diagnostic tools and development of new therapeutic options.

In developing countries asthma care is a major challenge despite expansion of health care system.

The present guideline is an up to date and comprehensive document on asthma care. It is based on most recently updated (2017) and published International Guidelines with levels of evidence and grading.

The chapters on the approach to patients with difficult to treat asthma, asthma in special situations, exercise induced asthma, occupational asthma and on how to organize delivery of asthma care will make this a practice oriented comprehensive document.

Every effort has been made to make the document user friendly and readable.

DR Amitha Fernando

Consultant Respiratory Physician

II. LEVELS OF EVIDENCE

1++	High quality meta-analyses, systematic reviews of RCT (Randomized Control Trials), or RCTs with a very low risk of bias
1+	Well conducted meta-analyses, systematic reviews, or RCT with a low risk of bias
1 -	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2 –	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series or expert opinion

GRADES OF RECOMMENDATION

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A

At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B

A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+

C

A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++

D

Evidence level 3 or 4; or extrapolated evidence from studies rated as 2

GOOD PRACTICE POINTS

- ✓ Recommended best practice based on the clinical experience of the guideline development group

Abbreviations

ABG - Arterial blood gas

ABPA - Allergic Bronchopulmonary Aspergillosis

ACO - Asthma COPD overlap

ACQ - Asthma Control Questionnaire

ACT - Asthma Control Test

BDP-HFA - Beclomethasone dipropionate-hydro-fluoro-alkane

BMI - Body Mass Index

BUD - Budesonide

CIC - Ciclesonide

COPD - Chronic Obstructive Pulmonary Disease

DPI - Dry powder inhaler

EAA - Extrinsic Allergic Alveolitis

ECG - Electrocardiogram

ENT - Ear Nose Throat

ETS - Environmental Tobacco Smoke

FE_{NO} - Exhaled nitric oxide concentration

FEV1 - Forced expiratory volume in one second

FP - Fluticasone propionate

FVC - Forced vital capacity

GERD - Gastro Oesophageal Reflux Disease

HMW - High Molecular Weight

ICU - Intensive Care Unit

IOC - International Olympic Committee

ILD - Interstitial Lung Disease

IgE - Immunoglobulin E

IM - Intramuscular

LMW - Low Molecular Weight

LTRA - Leukotriene receptor antagonists

MDI - Metered dose inhaler

MF - Mometasone furoate

NIV - Non-invasive ventilation

pMDI - Pressured metered dose inhaler

NSAID - Non-steroidal anti-inflammatory drug

OA - Occupational Asthma

PaCO2- - Partial arterial pressure of carbon dioxide

PaO2 - Partial arterial pressure of oxygen

PEFR - Peak expiratory flow rate

RADS - Reactive Airway Dysfunctional Syndrome

RCT - Randomised controlled trial

SABA - Short acting beta agonist

TA - Triamcinolone acetate

TPE - Tropical pulmonary eosinophilia

WEA - Work Exacerbated Asthma

III. Executive Summary

1. Diagnosis of asthma

In the majority, the diagnosis of asthma is made on clinical grounds.

- The clinical approach to a patient with asthma would include; arriving at a clinical diagnosis, excluding other possible differential diagnoses, assessing aggravating and relieving factors, assessing severity and assessing for accompanying asthma related co-morbidities. B
- It is important that all patients suspected of having asthma should have spirometry studies done to demonstrate airway obstruction and reversibility, at the time of diagnosis or during illness.

2. Management of asthma

- The aim of treatment is to achieve good asthma control with pharmacological and non-pharmacological approaches.
- In asthma that is intermittent Inhaled short acting beta agonists (SABA) is preferred as it has more rapid onset of action and less adverse effects. A
- In Persistent Asthma the main stay of treatment is inhaled-corticosteroids (ICS). A
- Long acting beta agonists (LABA) when given should always be prescribed with ICS preferably in a combination inhaler.
- All patients on regular ICS should also be prescribed SABA as rescue medication.

2.1 Selecting a delivery device

It is vital, selecting an inhaler device that delivers inhaled medication to the lung in an optimal manner.

2.2 Assessing asthma control

Assessing level of asthma control and severity is important in stepwise management asthma.

Once good asthma control is achieved stepping down asthma treatment can be considered to find the lowest preventer / controller dose with fewer side effects.

2.3 Non-pharmacological management of asthma

In primary and secondary prevention of asthma, avoiding triggers (e.g. environmental factors including cigarette smoke) could improve asthma control and reduce the requirement for pharmacotherapy.

4. Severe asthma

Need to be reassessed for the diagnosis, treatment and evaluation for coexisting co morbidities.

5. Follow up and monitoring of asthma

Need to have written, structured follow up plan and provided with his/her own self-management plan.

6. Asthma COPD Overlap (ACO)

The assessment features if suggestive of both asthma and COPD, the recommendation is to start treatment as for asthma.

7. Work related Asthma

Patients who have recurring childhood asthma or new onset adult asthma need to be assessed for work related exposure.

8. Asthma in special situations

Asthma in Pregnancy: Well controlled asthma is associated with good outcome in pregnancy and important for the well-being of both the mother and her baby.

Asthma in Surgery: Multidisciplinary team approach may be needed to prevent complications during and after surgery in asthma patients.

9. Management of Acute Asthma

- Recognition of an exacerbation is important to determine the severity of the attack and the nature of treatment required.
- Oxygen should be given urgently in all hypoxemic patients with first line agent, inhaled β2 agonists.
- Early use of systemic steroids, in correct doses, reduces morbidity and mortality.

Chapter 1

Diagnosis of Asthma

Asthma is a chronic inflammatory disease characterized by variable and often reversible air flow obstruction. The airway inflammation persists even in the absence of symptoms and the airway remains hyper-responsive to a wide range of triggers.

This description remains true for the majority of asthmatics. However, asthma is known for its varying clinical presentations, disease progression, accompanying co-morbidities and response to treatment.

Therefore, asthma is now considered a complex heterogeneous disease with distinct clinical phenotypes and underlying endotypes.

It is important for clinicians to be familiar with these concepts so that a more individualized patient centred management can be adopted.

Clinical approach to a patient suspected of Asthma includes following steps.

1.1 Arriving at a clinical diagnosis
1.2 Excluding other possible differential diagnoses
1.3 Assessing aggravating and relieving factors
1.4 Assessing severity
1.5 Assessing for asthma related co-morbidities

1.1. Arriving at a Clinical Diagnosis

In the majority the diagnosis of asthma is made on clinical grounds.

B

Symptoms of asthma include,

- Cough
- Wheeze
- Breathlessness and limitation of physical activity
- Chest tightness

In the majority of asthmatics these symptoms are characterized by their,

- Episodic nature.
- Variability with a diurnal pattern.
- Being triggered by certain known factors.
- Being relieved spontaneously.
- Response to oral or inhaled bronchodilator medication and / or steroids

Asthma may be associated with,

- Allergic rhinitis and/or eczema.
- Childhood asthma or atopy
- A family history of asthma or atopy.

✓ It is important that all patients suspected of asthma should have spirometry studies done to demonstrate airway obstruction and reversibility, at the time of diagnosis or during illness.

D

Asthma variants

- Exercise induced asthma

  In this group of asthmatics, the symptoms are related to exercise.

- Occupational asthma

  In this group of asthmatics, the symptoms of asthma occur due to occupational exposures.

- Cough variant asthma

  In this group of asthmatics, the cough may be the only symptom of asthma and this is accompanied by demonstrable airway hyper-responsiveness.

1.2 Excluding other possible differential diagnosis

1. COPD (Chronic Obstructive Pulmonary Disease) and ACO (Asthma COPD Overlap)

   This is dealt with under the chapter on ACO.

2. Bronchiectasis

   This is characterized by cough productive of sputum, postural cough, haemoptysis and infective exacerbations.

   Radiological changes are important in definitive diagnosis.

   Asthmatics with radiological evidence of bronchiectasis should be screened for Allergic Broncho-Pulmonary Aspergillosis (ABPA).

3. Pulmonary Tuberculosis

   A history of low grade evening pyrexia and constitutional symptoms should prompt exclusion of pulmonary tuberculosis.

   All patients suspected of tuberculosis should have 3 sputum smears inclusive of an early morning sample for acid fast bacilli.

4. Tropical Pulmonary Eosinophilia (TPE)

   This condition mimics asthma. The chest radiographic changes may be of miliary mottling or reticulonodular shadows. There can be elevated ESR, absolute eosinophil count are in excess of 3000 cell/$mm^3$with a high filarial antibody titre.[1]

5. Interstitial Lung diseases (ILD)

   Interstitial lung diseases are often diagnosed late and need detailed evaluation.

   Careful auscultation of lung bases will reveal the characteristic "end-inspiratory crackles (Velcro crackles)", this should prompt referral to a Respiratory Physician for

   further evaluation.

6. Primary Pulmonary Arterial Hypertension

   The diagnosis of pulmonary hypertension is often delayed. Exertional syncope is an early symptom that should arouse clinical suspicion.

7. Cardiac Causes

   Detailed assessment of the cardiovascular system is important to differentiate cardiac causes is needed when clinically indicated.

8. Upper Airway Obstruction

   Upper airway obstruction due to extrinsic and intrinsic compression can present as inspiratory stridor.

There are several conditions that may mimic asthma.

- Vocal Cord Dysfunction
- Hyperventilation syndromes
- Gastro-oesophageal reflux
- Hyper eosinophilic syndrome
- Churg-Strauss Syndrome (Eosinophilic polyangiitis)
- Dysfunctional breathing

1.3 Assessing Aggravating and Relieving Factors

B

Collecting information on aggravating factors at home, work place or at school is mandatory.

As much as 9-15% of patients with new adult onset asthma is related to work place exposures. A detailed occupational history is mandatory in all asthmatics.

- ✓ Information on smoking or exposure to environmental tobacco smoke (ETS) is mandatory and bio-mass fuel exposure should also be obtained.[2,3]

1. 4 Assessing Severity

The degree of severity depends on the frequency of asthma symptoms and classified as

a) Intermittent asthma and

b) Persistent Asthma.

a) Intermittent Asthma

- Day time symptoms are < 2 per week
- Night time symptoms are < 2 per month
- No limitation of daily activity
- No severe asthma attacks needing hospitalization or ICU care
- Rescue medication (short acting bronchodilators) use < 2 per week

If "yes '" to all of the above classified as Intermittent Asthma

b) Persistent Asthma

	Day time symptoms	**Night time symptoms**	***Use of rescue medication**
Mild Persistent	> 2 times/week , may affect daily activity	> 2 times / month but < 1 time /week	> 2 times per week but not daily
Moderate Persistent	Daily symptoms, activity affected	> 1 time per week	Daily use of rescue medication
Severe Persistent	Continuous symptoms	Frequent	Frequent

Reference: Quick Reference Charts for the Classification and Stepwise Treatment of Asthma (Adapted from 2007 NHLBI Guidelines for the Diagnosis and Treatment of Asthma Expert Panel Report 3)

*Rescue Medication = SABA (Short acting beta-agonist bronchodilators), LABA (Long acting bronchodilators with rapid action – formoterol)

1.5 Assessing for possible asthma related co-morbidities

- Allergic rhino-sinusitis
- Sinusitis
- Gastro-oesophageal reflux diseases
- Psychological conditions –depression, anxiety
- Obesity
- Obstructive Sleep Apnoea

Clinical Examination

- ✓ A detailed examination is needed to exclude other possible differential diagnosis as the clinical examination may be normal in asthma.

- ✓ Recording of BMI, looking for signs of anaemia, finger clubbing, ENT examination and cardio-vascular system examination is essential

Chapter 2

Investigations

2.1 Investigations to be done at the time of diagnosis

a) Full-Blood Count - may show eosinophilia

b) Chest Radiograph

This may be normal or show hyper-inflated chest with signs of air-trapping and flattened diaphragms.

✓ It is useful to obtain a chest radiograph in all asthmatics at the time of diagnosis to exclude other differentials.

c) Spirometry

This test is performed to demonstrate the presence and severity of airflow obstruction in adults.

FEV1/FVC ratio normally is > 0.75 – 0.8

- In well controlled asthma or those with milder forms of asthma
  FEV1/ FVC ratio may be normal.
  At least once during diagnostic process when FEV1 is low, the FEV1/FVC ratio should be documented as less than 0.75- 0.8.
- All patients with asthma should have demonstration of air flow limitation with reversibility during their course of illness and repeated during follow up.
  (if clinically indicated)
- Measurement of Peak Flow rates are not a substitute for Spirometry.
- Peak Flow measurement (PEFR) has an important role to play in self-monitoring of asthma control and assessment of occupational asthma.

D

C

Performing spirometry and reversibility testing - *Refer Annexure 1*

Interpretation of the test:

- A post-bronchodilator reversibility test considered positive in FEV1 > 200 ml and increase of >12% suggest asthma.
- A reversibility test of > 400 ml and > 15 % increase in FEV1 strongly favours a diagnosis of asthma.
- PEFR increase of 60 ml and > 15 % after administration of bronchodilator suggests asthma.

2+

2.2 Investigations in special situations

a) Serum IgE levels

Serum IgE levels may be useful in those with atopy and those suspected of Allergic Broncho Pulmonary Aspergillosis(ABPA)

b) Sputum eosinophils

Useful in identifying certain asthma phenotypes and the response to treatment [4,5,6]

c) Exhaled Breath Nitric Oxide (FeNO)[7, 8]

FeNO interpretation - *Refer annexure 2*

d) Skin Prick Tests.

e) Allergen Specific IgE levels

f) Bronchial challenge tests [9,10,11]

- Methacholine
- Histamine
- Mannitol
- Eucapnic voluntary hyperventilation

Chapter 3

Stepwise Management of Asthma

Aim of drug treatment is to achieve good asthma control with the lowest possible drug doses and the fewest possible adverse effects.

Good asthma control is defined as,

- Minimal symptoms during day time and no symptoms at night time
- Minimal need for reliever or rescue medication (need <2/week)
- No exacerbations
- No limitation of physical activity
- Normal lung function (FEV1 and Peak Expiratory Flow >80% of predicted or personal best)

3.1 Management of Intermittent Asthma

As required inhaled Short-Acting Beta 2 agonist bronchodilators (SABA) is used.

Inhaled anti cholinergic Ipratropium is a weaker bronchodilator and has a slow onset of action than SABA.

Theophylline's has mild bronchodilator properties.

- Inhaled SABA is preferred as it has more rapid onset of action and has less adverse effects when compared with oral preparations.

1+

If one needs a SABA > 2days per week, > 10 inhalations per month or runs out of a 200 dose SABA MDI in less than 6 months such a patient is considered to have persistent asthma.

A

- Patients with intermittent asthma can have life threatening acute attacks, thus all patients should be educated to recognize an acute attack and poor control.

✓ These patients should have access to reliever (SABA) medication to use in emergencies.

3.2 Management of Persistent asthma

a) Inhaled corticosteroids

The main stay of treatment of persistent asthma is inhaled-corticosteroids (ICS).[12-15]

A

1+

- Treatment with ICS
  - Reduces symptoms
  - Reduces use of rescue medication
  - Decreases exacerbations
  - Reduces hospital admissions
  - Improves lung function
  - Improves quality of life
  - Reduces mortality

- Principals on initiating ICS
  - Different ICS differ in potency and duration of action.
  - ICS when initiated takes 2-3 weeks to achieve desired results.
  - ICS should be initiated as appropriate for the degree of severity or level of control.

✓ There is no evidence to suggest that starting on a step higher to the degree of severity achieves better or faster control. This may expose patient to potential side effect of medication without any benefit to patient.

- It is recommended to start ICS with twice daily dosing.

1+

✓ All patients on regular ICS should also be prescribed SABA as rescue medication.[16,17,18]

b) **Initiating medication in persistent asthma:**

Drug	**Mild**	**Moderate**	**Severe**
BDP BUD	200-400 mcg/day in two divided doses	400-800 mcg/day in two divided doses	800-1600 mcg / day in two divided doses
Long Acting Beta Agonists (LABA)		Patients who are poorly controlled on low to medium dose ICS, prescribing a combination inhaler with ICS+LABA is preferred.	
Leukotriene receptor modifiers	May be used as oral medication in those who are unwilling to take ICS and those with exercise induced asthma However, ICS remains the treatment of choice.		
Long acting theophylline's	Long acting theophylline's are not an alternative to ICS. In the absence of ICS long acting theophylline's may be used. Long acting theophylline given at night may help to reduce nocturnal and early morning symptoms in patients on ICS. Can be used as add-on medication in those poorly controlled on an ICS+LABA combination.		

1++

- ✓ As ICS takes 2-3 weeks to achieve desired control a short course of oral steroids should be prescribed for symptom control, when initiating treatment.
- ✓ Short term local side effects of dysphonia and oral candidiasis can occur in long term, high doses of ICS. Currently there is no evidence of any effect on bone density.[19]
- ✓ Once control is achieved, maintain the minimum effective dose of ICS for asthma control.

Ciclesonide

Ciclesonide has a 24hour action and is used as a single daily dose, 80-320 mcg daily.

- ✓ Best given as maintenance treatment once control has been achieved with Budesonide or beclomethasone.

c) Principles of prescribing LABA[20-24]

LABA should never be prescribed alone in asthmatics.

Should always be prescribed with ICS, preferably in a ICS+LABA combination inhaler.

ICS in combination inhalers is either budesonide or fluticasone.

LABAs include is salmeterol, formoterol or vilanterol.

A

1++

Salmeterol is long acting and takes 15-20 minutes to act. It is always combined with fluticasone and for optimal benefits should be used in a daily dose of 100 µg (in metered dose inhalers 25 µg, 2 puffs twice daily, in dry powder formulations 50 µg twice daily).

The fluticasone + salmeterol combination is used for maintenance treatment only.

Formoterol has a rapid onset of action (effective in 1-3minutes) and always combined with budesonide. Due to its rapid onset of action, it can be used as a rescue or reliever medication. In rescue situations the maximum dose is up to 72µg/24 hours. For optimum benefits should be used in a daily dose of 18 µg.

Vilanterol 25µg is combined with fluticasone furoate and it's given once daily as it has long active half-life.

d) Leukotriene Receptor Modifiers

Indications

- Prevention of exercise induced asthma.
- Treatment of Aspirin sensitive asthma.
- Leukotriene receptor modifiers have a beneficial effect on allergic rhinitis.
- Add on therapy to ICS when LABAs are not tolerated or control remains poor on ICS+LABA combination. [25,26.]

- ✓ Leukotriene receptor modifiers, when added to ICS are less effective than when LABA's are added to ICS.

e) Theophylline

Theophylline's have bronchodilator, anti-inflammatory and increased effects in diaphragmatic contractility.
Anti-inflammatory effect occurs at a lower dose than its bronchodilator dose

Indications

- They have beneficial effects on nocturnal symptoms and early morning symptoms during acute exacerbations.
- As an add on medication to ICS when other options such as adding LABA or/and increasing ICS dose have failed to achieve desired control.[21]

f) Anticholinergics

Inhaled Short acting anticholinergic is used as an add on bronchodilator. It can be used as a rescue medication in those intolerant to SABA

g) Long-acting inhaled muscarinic antagonist (LAMA -Tiotropium)

A

Tiotropium may be used in moderate to severe persistent asthma which is poorly controlled despite use of an ICS or ICS and LABA. [28-29]

h) Anti-immunoglobulin therapy

1++

B

Anti-Immunoglobulin E (IgE) prevents release of inflammatory mediators by blocking interaction of allergen with IgE on cell surfaces of mast cells and basophils.[30,31]

Omalizumab is a recombinant humanized monoclonal antibody to IgE.

Indications and dosing:

- In patients with moderate to severe asthma who are poorly controlled on ICS+LABA combinations and other add on medications.
- Beneficial effects appear to be more in allergic asthma, with elevated IgE.
- A dose of 150 to 375 mcg is injected subcutaneously every 2-4 weeks to achieve a monthly target of 0.016 mg/kg per IU/ml per month.
- A minimum of 12 weeks of treatment is needed to determine the benefits of therapy.

i) Chromones

Two drugs namely Sodium Cromoglicate and Nedocromil sodium are available as MDIs.

- These are mast cell stabilizers that may reduce early and late phase asthmatic reaction to allergen exposure.
- These may have a role in prevention of exercise induced asthma, particularly in children.

Chapter 4

Selecting a delivery device

Introduction

Selecting an inhaler device that delivers inhaled medication to the lung in an optimal manner is of vital importance.

4.1 Types of delivery devices:

a) Pressurized Metered Dose Inhalers (pMDI) + Spacer Device

b) Dry Powder Inhalers (DPI)

c) Breath-actuated pMDI (BAI)

a) Pressurized Metered Dose Inhalers (pMDI)

These devices can be used to deliver a wide range of inhaled medication. The device delivers a specific amount of medication that is contained in a pressurized canister, in an aerosolized form to the lung.

In addition to the medication itself, the canister contains liquefied gas propellants and stabilizing excipients.

Some devices have dose counters.

- ✓ The number of medicinal doses contained in the canister is stated on the label and box.
- ✓ Once the specified medicinal doses on the canister/box are used up the aerosol contains only propellant and excipients and does not contain medication. Therefore, the date of starting the inhaler should be written down on the canister.

Advantages:

- It is easy to carry. However a spacer may needed if the technique is poor.
- It contains multiple doses.
- When used with a spacer, oropharyngeal deposition is less than with a DPI.

Disadvantages:

- A good co-ordination between pressing on the canister and in the inspiration is needed (Hand-mouth co-ordination).
- Certain amount of dexterity is needed.
- The propellant is cold and can lead to a cough reaction in some patients (called cold Freon effect).

c) Dry Powder Devices (DPI)

These devices use the patient's own inspiratory effort.

An inspiratory effort of 30-60 L/min is required for the drug delivery.

Devices include rota halers (cause a spinning effect to capsule when loaded and inhaled), accu-haler (devices that are pre-loaded) and turbo-halers (breath activates a turbo-device, inspiratory effort of 30 L/minute is adequate).

Pre-loaded devices may have dose counters.

Advantages

- Technique is simpler (Hand mouth co-ordination is less than that for pMDI)
- No cold Freon effect.
- Drug deposition in lungs of a turbo-haler is equal to that of a pMDI with a spacer.

Disadvantages

- Requires a good inspiratory effort.
- Oropharyngeal deposition may lead to changes in voice, not suited for individuals in occupations that involve a lot of talking.
- Improper storage of capsule may lead to damage and can cause inadequate drug delivery.

d) Breath-actuated pMDI (BAI)/ Autohaler

pMDI delivers medication to the lung in an aerosolized form and depends on patient's inspiratory effort, rather than a propellant for drug delivery.

Advantages

- Small and portable
- Pre-loaded
- Dose not require a degree of hand-mouth co-ordination as pMDI hence user friendly.
- Cold Freon effect is less than that of a pMDI

Disadvantages

- Costly
- Inspiratory effort required

4.2 Factors to consider when selecting inhaler device

a) Patient factors

- Patients comfort and ability to use the device
- Dexterity (skill)
- Life style
- Occupation
- Ease to teach/learn

b) Device factors

- Cost
- Portability
- Need for Spacer

✓ The best investment on patient care would be the time spent on inhaler technique.

During follow up clinic visits assess the inhaler technique with patient's medication and own device.

Check the compliance (cross check dose counter)

Check care of inhaler device (cleaning, storing must be taught)

c) Selecting a Spacer

Spacers are holding chambers which assist patients to use their pMDI.

Spacers differ in shape (Oval, cylindrical), material used (static surfaces, non-static surfaces) valve systems (visible moving valve or whistling valves) and volume.

Spacers are classified as,

- large volume (> 550 ml) and
- small volume (149 ml) spacers.

Factors to take into consideration when selecting Spacers.

a) Volume

Drug delivery does not depend on the volume of the spacer device. For routine use, large volume spacer has no advantage over a small volume spacer.
Use of large volume spacer helps in drug delivery in an acute attack.

b) Shape

Oval shaped spacers are considered to be better, as they conform better to the shape of aerosol plume released when pMDI is activated.

c) Material used

Non static material spacers minimize the drug deposition in the inner wall.

d) Valve Spacers

Presence of valve may prevent moisture in breath getting into the spacer.

e) Portability

Large volume spacers are cumbersome to carry around.

- ✓ After 1-2 years of use the spacer device should be replaced.
- ✓ A mask will be needed along with spacer in children 5 years and younger.

Chapter 5

Assessing Asthma Control

Introduction

Classification of asthma based on level of control and severity is not a static process and can be subject to change over time.

Level of asthma control

Level of asthma control			
Characteristics	**Controlled** (All of the following)	**Partly Controlled** (Any one present in any week)	**Uncontrolled**
Day time symptoms	None/ < twice per week	> twice a week	Three or more features of partly controlled asthma present in any week
Limitation of activities	None	Any	
Nocturnal symptoms /awakenings	None	Any	
Need for reliever/rescue medication	None/ < twice a week	>twice per week	
Lung Function (PEF or FEV1)	Normal	< 80% predicted or personal best (if known)	
Exacerbations	None	One or more per year	One in any week

Control is assessed over the past four weeks.
Exacerbations are assessed over a year.

Asthma Control Test (ACT) Score and level of control can provide a useful guide ***(annexure 3)***

➢ Approach to patient with partially controlled or uncontrolled asthma

✓ use the following check list and attend to correctable factors.

- Check compliance in use both in prescribed dose and frequency.
- Check if the patient taking SABA alone without using preventer (ICS) / preventer +controller combination (some patients opt to using SABA alone as they experience symptom relief)
- Check inhaler technique.
- Ask about smoking / exposure to environmental tobacco smoke.
- Look for triggers at home, work place and school.
- Ask of hobbies that may involve potential triggers of asthma.
- Check medication patient may be on (beta-blockers, aspirin, Non-steroidal anti-inflammatory drugs –NSAIDs)
- Look for treatable co-morbidities (allergic rhinitis, sinusitis, gastro-oesophageal reflux etc.)
- Detailed occupational history looking for occupational agents
- Check if patient is on medication as appropriate for degree of severity.

Adjust the medication as appropriate for degree of control.

	Degree of control	
Degree of severity	**Controlled**	**Partially Controlled or Uncontrolled**
Mild Persistent (Step 2) Current Medication 200-400 mcg/day BUD/BDP in two divided doses	Continue maintenance treatment	Step up ICS dose to next step
Moderate Persistent (Step 3) Current Medication 400-800 mcg/day BUD/BPD in two divided doses	Continue maintenance treatment	Patients who are poorly controlled on low to medium dose ICS, prescribing a combination inhaler with ICS+LABA is preferred. Other options are, Leukotriene receptor modifiers in patients who are intolerant or do not do well on LABA +ICS combination. Long acting theophylline in patients who cannot afford ICS+LABA combination or Leukotriene receptor modifiers

		Degree of control
Degree of control	**Controlled**	**Partially Controlled or Uncontrolled**
Severe Persistent (Step 4) Current Medication 800-1600 mcg / day BUD/BPD in two divided doses or Medium dose ICS/LABA	Continue maintenance treatment	*Patients who remain poorly controlled Add Long-acting inhaled muscarinic antagonist (Tiotropium) Add Leukotriene receptor modifiers in patients who are intolerant or do not do well on LABA +ICS combination. Add Long acting theophylline's in patients who cannot afford ICS+LABA combination or Leukotriene receptor modifiers
Very Severe (Step 5)	Continue maintenance treatment	*Patients who remain poorly controlled Add Lowest dose continuous oral steroids Anti-IgE treatment Refer indications for Anti-IgE treatment

Those patients who remain poorly controlled on > 2000 mcg of BDP/BUD or equivalent dose of fluticasone and/or ICS+LABA combinations will need review and management by a Respiratory Specialist.

Stepwise Approach to Adjusting Treatment

Step 1

These patients have infrequent symptoms, and/or low use of SABA.

If symptoms become more persistent or symptoms develop on exercise or has had an attack of asthma needing emergency care, patient should be prescribed low dose inhaled steroid.

Patients who are unwilling to use regular ICS and have exercise induced symptoms a Leukotriene receptor modifier is an option.

Step 2

These patients are on low dose ICS (BUD/BPD 200-400mcg/day) in two divided doses).

If uncontrolled or poorly controlled, therapeutic options are,

On low dose to medium dose ICS

Dose Level	CIC	BDP-HFA	FP	BUD	MF	TA
Low	80-160 mcg	100-200mcg	100-200 mcg	200-400 mcg	110-220	400-1000

Preferred Option

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Step up dose to;

Dose Level	CIC	BDP-HFA	FP	BUD	MF	TA
Medium	160-320 mcg	200-400 mcg	200-400 mcg	400-800 mcg	220-440	1000-2000

Other options to low dose ICS

- A Leukotriene receptor modifier is an option.
  This is less effective than increasing ICS dose and more expensive.
- Long acting theophylline's;
  less effective than ICS, more side effects and drug interactions.

Step 3

These are patients on 400-800 mcg/day BUD/BPD or equivalent FP in two divided doses or BDP /formoterol maintenance and reliever therapy

If uncontrolled or poorly controlled,

Therapeutic options

Patients who are poorly controlled on low to medium dose ICS, prescribing a combination inhaler with ICS+LABA is preferred 1++

Preferred option

Add LABA

Patients who are poorly controlled on low to medium dose ICS, prescribing a combination inhaler with ICS+LABA is preferred. A 1++

Choice of LABA

In patients with more than one exacerbation in the last year BUD/formoterol for maintenance and reliever is more effective than FP/salmeterol and as needed SABA as reliever.

When used as a reliever formoterol up to 72 mcg of can be used per day.

Other options include,

Leukotriene receptor modifiers

In patients who are intolerant or do not do well on LABA +ICS combination.

Long acting theophylline

In patients who cannot afford ICS+LABA combination or Leukotriene receptor modifiers these drugs may have a place.

Step 4 (Severe)

Patients are poorly controlled on 800-1600 mcg / day BUD/BPD in two divided doses or low dose ICS/LABA

Therapeutic options

High dose ICS/LABA (FP/Salmeterol) maintenance therapy.

Or

Add

Long-acting inhaled muscarinic antagonist (LAMA-Tiotropium)

Add

Leukotriene receptor modifiers

In patients who are intolerant or do not do well on LABA +ICS combination.

Add

Long acting theophylline

Which option to choose

High dose ICS/LABA will have more side effects with little extra benefit

Long-acting inhaled muscarinic antagonist (LAMA) (Tiotropium)and these have similar efficacy to LABA with good safety profiles.

Those who are intolerant to LABA, LAMA can be added to medium or high dose ICS.

Leukotriene receptor modifiers

> In patients who are intolerant or do not do well on LABA +ICS combination these oral drugs could be added. They have good safety profiles but are expensive.

In Step 4 one may have to try one or more of these options to achieve control of symptoms

Step 5

These patients remain uncontrolled despite ICS/LABA + one or more add on options in Step 4

Therapeutic options

continuous oral steroids given at the lowest dose.

Anti-IgE treatment

Recommendation

Step 4 and 5 will need review and management by a Respiratory Specialist.

Stepping down treatment

Stepping down asthma treatment can be considered once good control has been achieved and maintained for 3 months.[32]

This enables to find the lowest preventer / controller dose that is required to achieve control at the minimal possible side-effects.

How to step down

Reduce the ICS dose first by 25%-50%.

Once ICS dose is 500 mcg of BDP / BUD (250mcg of FP) per day, LABA can be withdrawn.

If possible reduce the BDP/BUD dose around 50 mcg -100 mcg per day with good control continue at least for 2 years.

There is no definite guideline on how long maintenance treatment should be continued, it is generally believed that even after achieving control bronchial hyper-reactivity remains positive for two years or more.

Chapter 6

Follow Up and Monitoring of Asthma

1. Minimum standard of care for an asthma patient

- The diagnosis should be effectively communicated.
- Diagnosis of asthma and objective spirometry measures should be documented.
- Complete assessment for co-morbidities.
- Should be assessed for possible triggers at home (including exposure to bio-mass fuels), school, workplace etc.
- Detailed documented occupational history.
- Should be evaluated for smoking and exposure to environmental tobacco smoke.
- Need for a documented drug history including non-asthma medications.
- Should have access to educational material on asthma, asthma triggers, use of inhalers.
- Should be trained to recognize and use the different types of prescribed inhaler medication and the delivery devices.
- Should be educated on care of inhaler devices and medication.
- Should be able to recognize symptoms of an acute attack of asthma.
- Should be able to recognized symptoms of poorly controlled asthma
- Should be educated on self-monitoring based on symptoms (using validated tools such as the Asthma Control Test –ACT) and / or based on Peak Expiratory Flow measurements
- Each patient need to be provided with his/her own self-management plan.
- An organized written follow up plan.

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2. **Objectives of follow up visit**

- If preventer / controller medication is introduced for the first time these patients need to be reassessed in two weeks and a second follow up visit in one month for assessment of control, check inhaler technique etc.
- In patients established on preventer/ controller medication follow up visit can be organized in 1-3 months depending on severity of asthma.
- Patients with poor control of asthma and multiple co-morbidities should be seen at least once a month, preferably in a specialist led clinic.
- All asthmatics who smoke should have access to smoking cessation services.

3. Structured assessment in a follow up clinic visit should include

- Information on symptoms of asthma during last 4 weeks (day time symptoms, night time symptoms, effect on activities of daily living and use of rescue medication (SABA oral/inhaled, theophylline's).
- Acute exacerbations needing unscheduled doctor visits, nebulization oral / IV steroids, hospitalizations etc.
- Compliance (if more than two doses missed per week compliance is poor)
- Use of medication (preventer, preventer + controller combination) in both the prescribed dose and frequency
- Inhaler technique
- Care of inhaler devices and medication
- Awareness of triggers and avoidance of triggers
- Reassessment of co-morbidities.
- ACT scores, PFR charts and asthma symptom diaries if available.
- Provision of asthma education leaflets
- Reassessment on patient's ability to recognize poor control and acute exacerbations.
- Provision and review of self-management plan

4. Objective measurements in assessment

- Sputum eosinophil counts[33,34,35]
- Spirometry at the time of diagnosis and annually[36,37]
- FeNo (in Specialist led clinics)

5. Referral / followed up in Respiratory Physician led specialized clinics

- Patients with severe/difficult to control asthma (Refer section on severe asthma)
- Patients with asthma and overlap syndromes (COPD, obstructive sleep apnoea)
- Patients with morbid obesity and asthma
- Patients with suspected fungal sensitization
- Asthma patients complicated with bronchiectasis
- Occupational asthma

6. **Components of written asthma self- management plans** [39-47] ***(annexure 4)***

- Documentation of regular medication with dosage, frequency, under headings of preventer, Preventer + controller and Reliever or rescue medication.
- Recognize good control, poor control, a "traffic light system" using green, yellow and red could be used to denote level of control.
- Objective methods using Peak Expiratory Flow recording of percentage (%) predicted from individual best could be used

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Chapter 7

Severe Asthma and Uncontrolled asthma

Definition

Asthma that requires,

- Therapy recommended for GINA steps 4 and 5 in the previous year.
- Systemic corticosteroids for most of the previous year to prevent asthma from becoming "uncontrolled".

Uncontrolled asthma is defined as ≥ 1 of the following

- Poor symptom control implies ACT score <20 or "uncontrolled" by GINA guidelines.
- Frequent severe exacerbations (requiring > 2 bursts of oral corticosteroid for > 3 days in the previous year).
- Exacerbations (≥1 hospitalization, ICU stay or mechanical ventilation in the previous year)
- Airflow limitation (FEV1 <80% predicted after withholding both short and long acting bronchodilators provided FEV1/FVC < 0.75-0.8).
- Asthma control that worsens on tapering high-dose ICS or systemic steroid or requiring biologics.

Reasons for poor asthma control

- Incorrect diagnosis
- Inadequate therapy
- Poor compliance with treatment
- Poor inhaler technique
- Continued exposure to triggers (occupational agents, environmental tobacco smoke, bio-mass etc.)
- Co-morbidities that are not properly assessed and treated (rhinitis, sinusitis, GERD, obstructive sleep apnoea, vocal cord dysfunction, obesity, psychological disturbance)
- Overlap syndromes (COPD, ACO)
- Smoking
- Aspirin sensitivity
- Fungal sensitization.
- Other phenotypes (e.g. Steroid resistant asthma)

✓ Approach to patients with severe asthma

- Confirm diagnosis of asthma, exclude other differential diagnoses.
- Optimize stepwise guideline defined treatment.
- Correction of poor compliance.
- Correction of poor inhaler technique.
- Re-assess for asthma triggers, occupational agents, drugs that worsen asthma control and implement strategies to minimize / control exposures.
- Detail assessment of comorbidities and treatment.
- Investigate for overlap syndromes
- Smoking cessation
- Exclude Aspirin sensitivity (triad of aspirin sensitivity, nasal polyps and asthma)
- Asses for fungal sensitization (evaluate for fungal sensitization and Allergic Broncho-Pulmonary Aspergillosis-ABPA)

Investigating Patients with severe asthma

1. **Lung Function tests**

   - Spirometry with reversibility testing after appropriately withholding bronchodilators
   - Lung function tests with lung volumes and diffusion studies
   - Serial Peak flow monitoring

2. **Radiographs**

   - Chest radiograph
   - Sinus radiographs / Sinus CT scans
   - HRCT –High Resolution CT Scans of chest (to exclude interstitial lung disease)
   - Contrast CT chest to exclude structural abnormalities

3. **Cardiac investigations**

   - Trans-thoracic echo-cardiograph (to exclude valvular heart disease and pulmonary hypertension)
   - Right heart Catheterization (assessment of Pulmonary Hypertension)

4. Assessing for specific sensitization

- Fungal sensitization for ABPA - (Allergic Broncho-Pulmonary Aspergillosis).
- Occupational sensitizers
- Skin prick Test
- Bronchial challenge tests

5. Assessing asthma phenotype

Asthma can be phenotype according to their cytokine profiles
(E.g. Th2-high and Th2-low asthma). The treatment can be guided according to the specific biomarkers.

- Serum IgE
- Sputum eosinophils
- Exhaled Breath Nitric Oxide (FeNO)

6. Assessment of co-morbidities

- Gastro-oesophageal reflux disease (GERD)
- Upper Gastro-intestinal pH studies
- Barium Swallow
- Upper GI endoscopy
- Assessment for obstructive sleep apnoea (Polysomnography)
- ENT- assessment for Vocal cord dysfunction (may mimic asthma or co-exist with asthma) and vocal cord palsy.
- Bronchoscopy
- Airway tumours
- Carcinoid tumours

Chapter 8

Management of Acute Asthma

8.1 Recognition of Acute Asthma

Asthma exacerbations (attacks of acute asthma) are associated with progressive increase in asthma symptoms (shortness of breath , cough, wheeze, chest tightness or any combination of these).

8.2 Severity evaluation

Recognition of an exacerbation is important and should be determined as to whether it is mild, moderate, severe or life-threatening.[111-116]

Mild - Moderate asthma	Increasing symptoms PEF >50-75% best or predicted No features of acute severe asthma	
Acute severe asthma	Any one of: PEF 33–50% best or predicted respiratory rate ≥25/min heart rate ≥110/min inability to complete sentences in one breath	
Life-threatening asthma	Any one of the following in a patient with severe asthma:	
	Altered conscious level Exhaustion Arrhythmia Hypotension Cyanosis Silent chest Poor respiratory effort	PEF <33% best or predicted SpO2 < 92% PaO2 < 8 kPa (60mmHg) 'normal' PaCO2 (4.6–6.0 kPa) (34.5- 45 mmHg)

8.3 Risk factors for developing fatal asthma[104-110]

a) Previous near fatal asthma
b) Previous admission with asthma, especially if within past 12 months.
c) Requirement of more than 3 classes of asthma medication
d) Heavy use of short acting β_2-agonists
e) Non adherence with regular asthma therapy
f) Failure to attend for regular follow up after an exacerbation
g) Self-discharge from hospital following an exacerbation
h) Using or recently stopped oral steroids
i) Psychological issues
j) Drug/ Alcohol abuse
k) Obesity
l) Learning difficulties

8.4 Initial assessment

The initial assessment is done

- for the diagnosis of an acute attack of asthma
- to determine the severity of the attack and the nature of treatment required.
- delay in treatment and under-dosing in an asthma attack can adversely affect outcomes

Clinical assessment

Altered consciousness, collapse, severe breathlessness (unable to complete sentences in one breath), tachypnoea, silent chest, cyanosis, tachycardia or accessory muscle use.

Absence of above does not exclude a severe attack.[111-116]

PulseOximetry

This is to determine the oxygenation and the need for arterial blood gas (ABG) and monitoring treatments.

The aim of oxygen therapy is to maintain SpO2 94–98%.

- ✓ In hypoxic and disproportionately ill patients it is important to consider an alternative diagnosis e.g. pneumothorax or pneumonia.[117]

PEFR or FEV_1

This is important

- in recognizing the degree of severity
- the appropriateness or intensity of therapy
- decisions about management in hospital or at home. PEFR expressed as a percentage of the patient's previous (<2 yrs.) best value is most useful
    - ✓ PEFR is more convenient in the acute situation

Blood Gas

Patients with SpO_2 less than (<) 92% require ABG measurement.
SpO_2 less than 92% is associated with a risk of **hypercapnea** which may go undetected from pulse oximeter. [116-119]
May repeat after 1hr of treatment if initial paO2 <8 (60mmHg)

Chest X-Ray

This is not routinely recommended.
Urgently needed in

- Suspected pneumo-mediastinum or pneumothorax
- Life threatening asthma
- Initial treatment failure
- Requirement for ventilation

Pulsus-paradoxus is an inadequate indicator of the severity of an attack and should not be used

8.5 Acute Treatment of the Adult Asthma Patient during an Exacerbation[120-127]

Oxygen

- Supplementary oxygen should be given urgently in all hypoxemic patients. Target saturation should be to maintain SpO2 of 94-98%
- Delivery of oxygen is via using a face mask, Venturi mask or nasal cannula with adjusted flow rates.
  - ✓ Persistent hypoxemia or hypercapnia indicates the development of life threatening asthma.

An urgent review is needed for the specialist critical care physician/anaesthetic intervention.

Bronchodilators - β2 agonists

First line agent -Inhaled β2 agonists given in high dose repeated administrations can act quickly to relieve bronchospasm with few side effects.

β_2-agonists can be administered by repeated activations of a pMDI (other than life threatening) via an appropriate large volume spacer or by wet nebulisation driven by oxygen.

- ✓ Use of metered-dose inhaler (MDI), with a spacer for bronchodilator therapy produces at least an equivalent improvement in lung function as the same dose delivered via nebulizer. (more cost effective)

Oxygen-driven nebulisers are preferred for nebulising β2 agonist bronchodilators to minimise the risk of oxygen desaturation while using air-driven compressors.

- ✓ For best results a flow rate of 6 l/min is required and when oxygen cylinders are used, a high flow regulator must be fitted.

Mild to moderate

β_2-agonists 2-4 puffs every 20 minutes for first hour, followed by 6-10 puffs every 1 to 2 hours.

No additional medication is necessary if the rapid-acting inhaled β_2-agonist produces a complete response (FEV_1 or PEF returns to greater than 80% of predicted or personal best)

Severe

In the initial poor response to therapy, the continuous nebulisation with β2 agonists is more effective than bolus nebulisation.

Repeat doses of β_2-agonists at 15-30 minute intervals or give continuous nebulisation of salbutamol at 5-10 mg/hour

Higher bolus doses e.g. 10 mg of salbutamol, are unlikely to be more effective.

Evidences are limited in using parenteral β_2-agonists, in addition to inhaled β_2-agonist. However, may have a role in ventilated patients.

Bronchodilators - Ipratropium bromide

In moderate to severe events use of combining nebulised ipratropium bromide with a nebulised β_2-agonist give greater bronchodilation than a β_2-agonist alone. This helps for a faster recovery and shorter duration of hospital stay.

Ipratropium bromide (every 20–30 minutes) may use, in addition to ß agonists for the first two hours of a severe asthma attack.

Dose

Ipratropium bromide (250 micrograms/dose mixed with the nebulised ß agonist solution[128-130]
Frequent doses up to every 20–30 minutes (250 micrograms/dose mixed with 5 mg of salbutamol solution in the same nebuliser can be repeated in first 2-4 hrs

Steroids[131,132,133]

Early use of steroids in acute asthma reduces mortality, relapses, subsequent hospital admission and requirement for β_2 agonist therapy.

If the patient can swallow the steroid tablets are as effective as injected steroids

Dose: Prednisolone 40–50 mg daily or parenteral hydrocortisone 400 mg daily (100 mg six-hourly) are as effective as higher dose for at least five days or until recovery.

- ✓ Nebulised budesonide has no additional benefit in patients receiving large doses of systemic steroids.

Following patients recovery, the steroids can be stopped abruptly after 5-7 days without tapering. (Unless patients need maintenance dose of oral steroids)

Magnesium sulphate
Intravenous magnesium sulphate has bronchodilator effects and reduces hospital admissions in adults with acute asthma who have had little or no response to standard treatment.

Consider giving a single dose of IV magnesium sulphate for patients with:

- acute severe asthma who have not had a good initial response to inhaled bronchodilator therapy

- life threatening or near fatal asthma.
  - ✓ Nebulised magnesium sulphate is not recommended for treatment in adults with acute asthma

Dose: Magnesium sulphate (1.2–2 g IV infusion over 20 minutes) used after senior review.
Repeated doses could cause hypermagnesemia with muscle weakness and respiratory failure. [134-138]

Intravenous Aminophylline
In acute asthma, IV aminophylline is not likely to result in any additional bronchodilation compared to standard care with inhaled bronchodilators and steroids. Side effects for arrhythmias and vomiting need to be assessed.[139]
However, some patients with near-fatal asthma or life-threatening asthma with a poor response to initial therapy may gain additional benefit from Iv aminophylline.

Dose:
IV aminophylline: 5 mg/kg loading dose over 20 minutes unless on maintenance oral therapy, then infusion of 0.5–0.7 mg/kg/hr.

Theophylline or aminophylline blood levels need to be monitored in

1. Hospitalized patients already taking oral aminophylline or theophylline,
2. daily for all patients on aminophylline infusions

Leukotriene receptor antagonist

No evidence the use of Montelukast in acute asthma. [140]

Antibiotics

Viral infections are more likely to precipitate an exacerbation of asthma. Routine prescription of antibiotics is not indicated for patients with acute asthma.[141]

Supportive treatment - Intravenous fluids
Correction of dehydration and correction of electrolyte imbalance is important in acute asthma management.

- ✓ Hypokalaemia can be caused or exacerbated by β_2-agonist and/or steroid treatment. Currently there is no evidence for differing fluid regimes in acute asthma.

Heliox

There is no evidence the use of heliox, (helium/oxygen mixture in a ratio of 80:20 or 70:30) either as a driving gas for nebulisers, as a breathing gas, or for artificial ventilation in adults with acute asthma. [142,143]

Heliox is not recommended for use in patients with acute asthma.

Referral to ICU/HDU

If no improvement or deterioration after initial treatment, review by an anaesthetist and an intensivist should be done in patients with acute severe or life-threatening asthma. This may be suggested by

- deteriorating PEF
- persisting or worsening hypoxia
- hypercapnea
- arterial blood gas analysis showing fall in pH or rising H+ concentration
- exhaustion, feeble respiration
- drowsiness, confusion, altered conscious state
- respiratory arrest

Not all patients admitted to the Intensive Care Unit (ICU) need mechanical ventilation. The need of an intubation/ventilation strategy should be assessed by an anaesthetist or intensivist.

Patient transfer to an ICU should done by a doctor suitably equipped and skilled to intubate if necessary**.**

Non-invasive ventilation

Non-invasive ventilation (NIV) is well established in the management of ventilatory failure caused by extra pulmonary restrictive conditions and exacerbations of COPD. The hypercapnic respiratory failure due to acute severe asthma, invariably need intubation and ventilation. However, NIV may be used while waiting for intubation under senior supervision[144]

Further investigation and monitoring

1. Measure and record PEF 15–30 minutes after starting treatment, and thereafter according to the response
2. Record oxygen saturation by oximetry and maintain arterial SpO_2 at 94–98%.
3. Repeat measurements of blood gas tensions within one hour of starting treatment if:
    - initial PaO is <8 kPa unless SpO is >92%; or
    - initial PaCO is normal or raised; or
    - patient's condition deteriorates.
4. Measure them again if the patient's condition has not improved by 4–6 hours.
5. Measure and record the heart rate.
6. Measure serum potassium and blood glucose concentrations.
7. Measure the serum theophylline concentration if aminophylline is continued for more than 24 hours (aim at a concentration of 10–20 mg/l or 55–110)

Discharge

Patients should have clinical assessment compatible with home management, be on reducing amounts of ß agonist (preferably no more than four hourly) and be on medical therapy they can continue safely at home.

If patients discharged with PEF <75% best or predicted and with diurnal variability >25% are at greater risk of early relapse and readmission. [145,146]

Prior to discharge, trained staff should give asthma education. This include education on inhaler technique and PEF record keeping, with a written PEF and asthma action plan.

A follow-up appointment with a hospital asthma / respiratory service should be made within 4 weeks of the episode.

A detailed discharge letter should be given and patient's primary care practice is informed within 24 hours of discharge.

See annexure 6 - *Check list for the discharge acute asthma patient*

Chapter 9

Delivery of Asthma Care Services

- **Primary care service**
- **Hospital Clinics**
- **Tertiary care referral centres**
- **National/ Provincial referral centres**

Components of dedicated asthma clinic set up at various levels of care

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Primary care level

- General Practitioner, medical officer experienced in Asthma care.
- Nurse, trained in asthma care (such individuals should be familiar with and competent in training in the use of the wide range of inhaler devices and medication).
- Standardized documentation protocols
- Standardized assessment protocols
- Standardized protocols during follow up visits
- Education material (patient information leaflets/ booklets, posters, flip charts, videos on asthma to be played in waiting areas etc.)
- Self-management plan documents.
- Peak Flow meters, disposable mouth pieces
- Spirometers
- Inhaler devices, spacers, inhaler capsules for demonstration
- ACT Score leaflets.
- Computers, electronic health records.

Hospital clinics

- Regular uninterrupted supply of asthma medication
- Quarterly returns on clinic attendance
- Registry on severe asthma patients.
- Drug requesting formats
- Audit tools on good clinical practice

At tertiary care level

- All of above
- Lung function tests
- Facilities for Skin Prick testing
- Measurement of FeNo
- Standardized protocols for doing sputum eosinophil counts
- Facilities to perform Broncho-provocation tests

National / Provincial referral centres

- Facilities to perform bronchial challenge tests
- Evaluation for possible occupational exposures
- Facilities to diagnose and manage asthma in athletes.

Chapter 10

Asthma Chronic Obstructive Pulmonary Disease Over-Lap Syndrome / Asthma COPD Overlap (ACO)

Definition:

ACO is characterized by persistent airflow limitation with overlapping feature of both asthma and COPD.

Comparison of Asthma, COPD and ACO

Clinical features			
Features	**Asthma**	**COPD**	**ACO**
Age of onset	Usually childhood but can occur at any age	Usually >40 years of age.	Usually ≥ 40 years
Symptoms	Mostly episodic and diurnal pattern. Has known triggers and relieving factors	Continuous breathlessness during the day than night and on exertion Evidence of exposure history to tobacco smoke, biomass and known occupational irritants	Persistent but variability is a prominent feature A doctor diagnosis of asthma symptoms on exposure to known triggers is present. Smoking history may be present
Family history	Asthma or atopy usually present		May be present
Associated symptoms	Allergic rhinitis, atopic dermatitis	Cardio-vascular co-morbidities, GERD, Obstructive Sleep Apnoea (OSA)	Increased Body Mass Index(BMI), GERD (Gastroesophageal reflux Disease)

Features	Asthma	COPD	ACO
Progression of symptoms	Often improves spontaneously or with treatment , but later it may result in fixed air flow limitation	Chronic disease process and usually have persistent symptoms , particularly during exercise with "better" and "worse" days	symptom reduction with treatment However, progression is usual.
Exacerbations	Number of exacerbations can be significantly reduced by treatment	Persistent comorbidities contribute to frequent exacerbations	Exacerbations are more frequent utilization of health care resources

Investigations			
	Asthma	**COPD**	**ACO**
Chest Radiograph	Usually normal	Severe hyper-inflation and other changes of COPD	Similar to COPD
CT scan	Normal or evidence of air trapping or small airway disease	Features of emphysema, bullae, small airway disease	Features of air trapping , small airway disease
Airway inflammation	Eosinophils and /or neutrophils	Neutrophils and/or, lymphocytes	Eosinophils and/or neutrophils
DLCO	Normal or slightly increased	Often reduced	Normal or slightly reduced
Airway Hyper responsiveness(AHR)	Not useful on its own to differentiate asthma from COPD, but higher levels favour asthma or ACO.		
Blood eosinophilia	Favours asthma	May be seen during exacerbations	May be seen
Inflammatory biomarkers Test for atopy (specific IgE and/or skin prick tests) FENO	Increases probability of asthma; not essential for diagnosis A high level (>50 ppb) in non- smokers supports a diagnosis of eosinophilic airway inflammation	Confirms to background prevalence; does not rule out COPD Modestly increased or low	Modestly increases probability of ACO not essential for diagnosis normal

Spirometry differential diagnosis			
Spirometry variable	**Asthma**	**COPD**	**ACO**
Normal FEV1/FVC pre or post bronchodilator(BD)	Compatible with diagnosis of asthma	Not compatible with diagnosis of COPD	Not compatible with diagnosis of ACO
Post-BD FEV1/FVC < 0.7	Indicates airflow limitation but may improve spontaneously or with treatment	Required for diagnosis	Usually present
FEV1 ≥ 80 % predicted	Compatible with diagnosis(good asthma control or interval between symptoms)	Compatible with GOLD classification of mild airflow limitation (categories A or B)	Compatible with a diagnosis of ACO)
FEV1 < 80% predicted	Compatible with asthma diagnosis. An independent risk factors for exacerbations	Indicator of severity of airflow limitation and risk of future events (e.g. mortality and exacerbations.	Indicator of severity of airflow limitation and risk of future events(e.g. mortality and exacerbations
Post-BD increase in FEV1 > 12 % and 200 ml from baseline (reversible airflow limitation)	Usual but may not be present when well controlled on controllers	Common and more likely when FEV1 is low but ACO should be considered	Common and more likely when FEV1 is low but ACO should be considered
Post-BD increase in FEV1 > 12 % and 400 ml from baseline(marked reversibility)	Asthma highly likely	Unusual in COPD consider ACO	Compatible with a diagnosis of ACO

Therapeutic approach to ACO

If the diagnosis is of asthma treat according to the asthma guidelines.

If the diagnosis is of COPD treat according to GOLD guidelines.

If the initial assessment has overlapping features of both asthma and COPD the recommendation is to start treatment as for asthma.

Principles of treatment of ACO

If there are features of asthma long acting beta-agonist (LABA) or long acting anti muscarinic (LAMA) bronchodilators should not be used as mono-therapy.

The main stay of treatment is ICS low to moderate doses, with add on treatment with LAMA or LABA.

All patients with ACO should be,

- assessed for exposure to tobacco smoke, bio-mass fuel and occupational risk factors.
- assessed for associated co-morbidities.
- offered smoking cessation if a smoker.
- with self-management plans.
- with an organized follow up plan.
- offered vaccination, if over 65 years

Chapter 11

Work Related Asthma

Work Related Asthma is now the commonest form of occupational lung disease overtaking by far the mineral dust induced pneumoconiosis and organic dust induced hypersensitivity pneumonitis (HP)/ Extrinsic Allergic Alveolitis. (EAA)

Definitions

Work Related Asthma (WRA) can be categorized into

- **Occupational Asthma (OA)** – asthma caused specifically by exposure to an agent present in work place. There are over 250 documented agents responsible for OA.

- **Work Exacerbated Asthma (WEA)** – Also called work aggravated asthma. In work related asthma, pre-existing asthma is made worse by conditions in the work environment.

OA can be sub-divided into;

- **Sensitizer induced OA**

This is characterized by a latency period between first exposure to a respiratory sensitizer at work place and developments of symptoms.

- **Irritant induced OA**

Occurs typically within a few hours of a high-concentration exposure to an irritant such as gas, fume or vapour at work place.

Reactive airway dysfunction syndrome (RADS) is classified as an irritant induced asthma. The causal irritant exposure consists of a single high level inhalation incident.

Types of OA

<u>Sensitizer-induced OA</u>

An immunologically mediated, IgE dependent mechanism like allergic asthma.

This has a sensitizing agent, exposure to the agent, development of immunologically mediated sensitization, a period of latency, repeated exposures, development of inflammation and hyper-responsiveness of airways with clinical manifestations of asthma.

The period of latency to development of symptoms may also vary from between 2-10 years but typically occurs within the first two years of exposure.

Sensitizing agents are of two broad groups

- High molecular weight agents
- Low molecular weight agents

High-molecular weight agents

HMW agents are complex mixtures of polypeptides that act as complete antigens and stimulate IgE synthesis.

The initial sensitizing dose, intensity and duration of exposure may vary from agent to agent according to data available from published literature.

Immunologic tests that measure IgE responses are available in the form of Skin-Prick test and tests that detect allergen specific IgE.

High-molecular weight proteins (5,000 Daltons or greater)		
Sub-groups	Substances	Jobs and industries
Animal-derived substances	Laboratory animals.	Animal handlers/farmers
	Bird proteins	Bird breeders, poultry workers
	Crab/sea food	Food processors
	Mites, insects	Grain handlers, Bakers
Plant-derived substances	Flour and grain dust, plant enzymes	Bakers, Pastry chefs, Grain handlers
	Tea Dust Camomile tea dust, negative for black and lemon tea	Tea blender, shifter, maintenance worker in tea packing plant Skin Prick test, Specific IgE (Immunocap)available.
	Cinnamon, cinnamic aldehyde	Cinnamon crusher, Specific Skin-Prick and IgE test available

	Natural rubber latex gloves	Health care workers
	Substances	Job and industries
	Bacterial enzymes, fungal proteins.	Detergent makers, pharmaceutical industry
	Vegetable gums	Printers
	Wood dust, cotton dust	Carpenters, Textile workers
	Fluxes, colophony	Solders, electronic industry

Low-molecular weight agents (LMW)

Some LMW chemicals, such as acid anhydrides, platinum salts, persulfates, and reactive dyes may combine with endogenous proteins and act as haptens stimulating IgE production.

Skin testing does not adequately assess the response to LMW antigens

Serologic tests have limited utility in the diagnosis of isocyanate-induced asthma, but they are preferred to skin tests in the diagnosis of OA due to acid anhydrides.

Low-molecular weight /chemical sensitizers

Sub-groups	Substances	Jobs and industries
	Amine dyes	Cosmetic industry, Hair dressers, Rubber workers.
	Plasticizers, spray paints, adhesives, foams	Auto-spray painting varnishing, Woodworking
	Metals Platinum salts, cobalt	Welding, plating, metal refining
		Platinum refineries, metal grinding

a) Irritant induced asthma

This is also called OA, formally called Reactive Air-way Dysfunction (RADS) without latency and is non-immunologically mediated. Workers develop asthma like syndrome immediately following exposure to an agent known to have strong irritant properties. e.g. chlorine, ammonia.

This results in air-way injury and inflammation which is non-immunologically mediated.

Approach to Occupational Asthma

Step 1

Medical, Occupational history and directed physical examination

Symptoms are similar to non-occupational asthma. Some may have cough alone or nocturnal cough. Symptoms may be preceded by or associated with nasal allergies, eye irritation / itching.

> All adults with new onset asthma, reappearance of childhood asthma, or unexplained deterioration of known asthma should have a detailed occupational history documented.

Symptoms of asthma,

- Frequently worsen at work or at night after work
- Improve on days off / holidays.
- Recur on return to work.
- Worsen progressively towards the end of the workweek.

The patient may note specific activities or agents in the workplace that reproducibly trigger symptoms.

> Allergic Nasal symptoms are important and should be treated seriously as evidence suggests risk of OA is increased in such workers.

Smokers appear at increased risk of developing OA.

Step 2

Evaluation for reversible airway obstruction and/or Nonspecific bronchial hyper-responsiveness (NBR)

A post work shift spirometry is preferred with reversibility testing on a day with symptoms

Positive test- A FEV1 value of $\geq$ 12% and a 200ml increase in FEV1 20 minutes after administration of a beta-2-agonist Broncho-dilator.

> Or

Peak Flow Meter; a 60 ml increase in post-bronchodilator Peak Expiratory Flow (PEF)
In patients without clear evidence of airflow limitation on spirometry, a quantitative testing for Non-specific Bronchial Hyper-reactivity(NBR) using methacholine or histamine should be done.
Reversibility testing may be negative in 5-40% individuals with a positive NBR test.

Therefore, a negative reversibility test does not exclude the diagnosis of OA.

Step 3

Serial Peak Expiratory Flow Measurements (PEF) at and away from work

Serial PEF measurements are recorded every two hours, during waking hours, when exposed to the suspected agents on symptomatic days.

The measurements should be continued for at least 16 consecutive days (e.g. two five-day work weeks and 3 weekends off) if the patient can safely tolerate continuing to work.

PEF measurements are recorded in a diary along with notation of work hours, symptoms, use of bronchodilator medications, and significant exposures

Step 4

Immunologic assessment

Skin Prick Test and specific IgE estimations are useful in identifying HMW allergens but less characterized in identifying LMW allergens.

For most occupational allergens of interest immunological tests are not commercially available.

The presence of specific IgE at work place identifies sensitization does not necessarily indicate with OA.

Step 5

Specific challenge tests, work place challenge tests

Specific bronchial challenge testing using an exposure chamber and standardized exposure levels has been labeled the "gold standard" for diagnosis of OA[48]

Work place challenges require cooperation of the employer and much technician time with a mobile spirometer.

Both of these procedures carry some risk of precipitating a severe asthmatic attack, and should therefore be done under close supervision of specialists experienced with the procedures.
Diagnostic criteria of Occupational Asthma are given in ***annexure 5.***

Management of OA

Management of OA includes medical and preventive interventions for individual patients, as well as public health measures in workplaces identified as high risk for OA.[49-57]

Chapter 12

Approach to patient with Exercise Induced Asthma and Exercise Induced Bronchoconstriction

Exercise Induced Asthma (EIA) is defined as reversible transient narrowing of airways which occurs during or after vigorous physical activity with an individual in a previous diagnosis of asthma.

Exercise Induced Broncho constriction (EIB) is defined as the development of reversible transient narrowing of airways which occurs during or after vigorous physical activity with an individual **without** a previous diagnosis of asthma.

The bronchoconstriction on vigorous physical activity is present in more than 10% of the general population and approximately 90% of those with a diagnosis of asthma.

Clinical diagnosis

The symptoms of EIA and EIB are similar. Certain endurance sports, like cross-country running, swimming and certain environmental conditions like dry-cool weather predispose to EIB.

EIA can occur during vigorous physical activity in an asthmatic and may indicate underlying poor asthma control.

Symptoms

Symptoms typically occur during exercise, peaks 5-10 minutes after exercise and may last 30 minutes to one hour. A late response may be seen over a period of 24 hours

Symptoms include one or more of the following

- Shortness of breath
- Cough during exercise
- Chest tightness during or after exercise
- Wheeze

Atypical symptoms

- Fatigue
- Drop in performance in an athlete
- Difficulty in keeping up with peers
- Drop in exercise capacity
- Abdominal discomfort

✓ Non-Respiratory causes with similar presentations should be excluded.

Differential Diagnosis

- Vocal cord dysfunction
- Exercise induced hyperventilation syndromes
- True reduction in physical fitness

Symptoms due to these conditions however subside soon after stopping exercise

Following conditions should be considered in a patient not responding to empiric treatment with inhaled beta-2 agonists,

- Cardio-vascular conditions - conduction defects and cardiomyopathies, valvular heart disease Pulmonary Arterial Hypertension

- Pulmonary conditions -Interstitial lung disease, chest wall deformities / scoliosis/pectus and tracheobronchomalacia

✓ Exclude cardio-vascular and other pulmonary conditions

Self-reported symptoms are a poor predictor of EIB and should not be used alone in the diagnosis.

Diagnostic testing

- Spirometry **C**
  - Spirometry with reversibility testing should be performed to rule out chronic persistent asthma
  - Resting spirometry is normal in EIB, it may be even supra-normal in elite athletes.

- Broncho-Provocation tests **A**

  Indications
  - Athlete who is a national player/national player representing at international events will need documentation of objective testing as certain medication used in treatment will need prior approval**.**

  - Athlete who do not respond to an empirical trial of treatment with beta-agonists before exercise.

Two main types

1. **Direct Broncho-provocation tests**

These tests are performed at the site (field test) in which the athlete develops symptoms. This can be performed by using hand-held spirometers.

2. **Indirect Broncho-provocation tests**

These are performed under laboratory conditions using pre-defined protocols

Test	Description	Advantages	Disadvantages
Laboratory based Exercise challenge <u>Involves</u> • standard treadmill, • cycle ergometer, • free-running, • step-testing in a pulmonary laboratory.	An exercise challenge should be of sufficient intensity to raise the athletes heart rate to 90%(minimum of 6 min after starting the test) This should be maintained for at least 2–4 min. FEV 1 is measured before exercise, 5-10 and 30 minutes after exercise A positive challenge is defined as one that produces at least a 10% reduction in FEV1 from baseline	More sensitive and specific	Need to control inspired gases and humidity Needs to monitor heart rate and minute ventilation

Inhalation Challenge tests **(Indirect)** **Eucapnic Voluntary hyper ventilation**	Subject hyperventilates a standard preparation of cold dry air for at least 6 min. Spirometry is performed before and after hyperventilation FEV 1 is measured before exercise, 5, 10 and 30 minutes after exercise A positive challenge is defined as two or more that produces at least a 10% reduction in FEV1 from baseline	Highly sensitive and specific Recommended by the International Olympic Committee (IOC)	Need to control inspired gases and humidity Need to monitor minute ventilation Relatively expensive

Following are not recommended by IOC

Mannitol (currently under review)

Hypertonic saline

Direct Challenge tests

Histamine

Methacholine

Management

Remains the same for both EIA and EIB.

In EIA underlying asthma should be optimally controlled.

EIA patients should be advised on

- Importance of warming up before exercise
- Using pre Exercise beta2-agonists
- Minimizing development of symptoms by reducing allergen exposure.

Pharmacological Management 1++

SABA are the first line of treatment (including prevention) in both EIA/EIB.

LABA(Formoterol) can be used to treat EIB but should not be used in patients with EIA unless patient is already on ICS. A

Leukotriene receptor modifiers 1++

These agents have an onset of action within two hours and continued preventive benefits up to 24 hours after single oral dose in EIB. A

Mast Cell stabilizers

Chromones, Sodium Cromoglicate MDI, Nedocromil sodium MDI. May have a role in prevention of exercise induced asthma, particularly in children 1++ C

ICS

These are the mainstay of treatment in patients with persistent asthma and exercise induced asthma. There is a paucity of evidence for the regular preventive use of ICS in EIB. A

Other agents

Ipratropium may provide some protection against EIB but not as effective as SABA. A

SABA are the first line of treatment in the prevention and treatment of EIA/EIB.SABA should be used 15 minutes before exercise

Non –Pharmacological treatment

Pre-exercise warming up

Pre-exercise warm up may attenuate EIB. However, not been shown to be helpful in elite and cold weather athletes.

Heat exchange masks

Designed to limit cold air exposure during exercise in athletes with EIB. May not be practical in competition.

Nutrition

Low sodium diet 1-three weeks prior to competition and omega 3 fish oils may reduce the incidence of EIB

Environmental Control

It is recommended that all asthma patients avoid their environmental triggers that might increase airway hyper-reactivity and, thereby, increase susceptibility to exercise-induced symptoms.

Chapter 13

Non-Pharmacological Management of Asthma

Avoiding triggers (e.g. environmental, dietary) will improve asthma control and reduce the requirement for pharmacotherapy. However, the evidence is lacking as there are no well controlled interventional studies available.

Primary Prevention

Primary prevention includes interventions before the detection of asthma to reduce its incidence.

a) Allergen Exposure

Early life exposure to allergens (aeroallergens and ingested food allergens) may lead to allergic sensitisation and so potentially increase the risk of subsequent asthma, particularly in children at high-risk (children with a parental history of asthma or atopy). [58-61]

b) House dust mite

House dust mite aeroallergen avoidance or pet ownership avoidance is not recommended for the primary prevention. [62-64] 1+ A

c) Food allergens

Maternal food allergen avoidance during pregnancy and lactation is not recommended for preventing childhood asthma.[65-67] 1+ A

d) Breast feeding

Breast feeding may have potential protective effect in relation to early asthma. [68,69] 2+ C

e) Infant Milk formulae

Avoidance of modified infant milk formulae has no benefit in primary prevention of childhood asthma. [70,71] 1+

f) Fish Oil

Use of fish oil during pregnancy has no benefit on prevention of childhood asthma. [72-75] 1+

g) Weight reduction

Weight reduction is recommended in obese patients to reduce subsequent respiratory symptoms consistent with asthma.[76, 77] 2- C

h) Probiotics

Use of dietary probiotics in pregnancy will not reduce the incidence of childhood asthma. [78] 2+

i) Smoking

Smoking parents and parents-to-be are linked with increase wheezing in infancy and increase risk of persistent asthma in their children.[79-83]

2+ B

j) Immunisation

All childhood immunisations should proceed normally as there is no evidence of an adverse effect on the incidence of asthma. [84,85]

1++ B

Secondary Prevention

Interventions introduced after the onset of asthma to reduce its impact on control of asthma

a) House dust

Exposure to house dust can act as a trigger in sensitised asthmatic individuals. Physical and chemical methods of reducing house dust mite levels at home (including acaricides, use of mattress covers, vacuum-cleaning, heating, ventilation, washing, air-filtration and ionisers) may not be effective as secondary prevention. [86]

1++ A

b) Animal allergens

Allergens particularly from cat and dog, are potent provokers of asthma symptoms. Removal of pets from homes are paradoxical. They are either no benefit for asthma or does not induce tolerance on continued high exposure. [87-90]

B

c) Fungal Allergens

Fungal exposure has been strongly associated with hospitalisation and increased mortality in asthma.
A multifaceted approach is more likely to be effective on mites, mould allergens and indoor pollutants. The use of a mechanical ventilation system to may reduce humidity and increase indoor air exchange (cross ventilation).

d) Smoking

Direct or passive exposure to cigarette smoke adversely affects quality of life, lung function, need for rescue medications for acute episodes of asthma and long-term control with ICS.[91-94]

2+ B

e) Electrolytes (Na, Mg), Fish Oil, Antioxidants (Vit C, Vit E)

Supplementation has no benefit in secondary prevention in Asthma management.
However observational studies in both adults and children shown that a high intake of fresh fruit and vegetable is associated with less asthma and better pulmonary function.[95-98]

f) Weight reduction

Weight loss in overweight patients should be encouraged. If successful, it may lead to improvement in asthma symptoms in addition to other many health benefits. [99,100]

g) Air Ionisers

1++

Air ionisers are not recommended for the treatment of asthma.[101]

A

h) Breathing exercises

1++

Physiotherapist carried breathing exercises and hyperventilation reduction techniques (preferably combined with Behavioural therapy programmes) can improve asthma symptoms, quality of life and reduce bronchodilator requirement in adults with asthma.

A

But it may have little effect on lung function. [102]

i) Physical exercise

Physical exercise will increase oxygen consumption, maximum heart rate, and work capacity significantly. But it has no effect on PEF, FEV1, forced vital capacity (FVC) or ventilation at maximal exercise capacity (Vmax). Physical exercise can be promoted as a part of a general approach in improving lifestyle and rehabilitation.[103]

Chapter 14

Asthma in special situations

Asthma in Pregnancy

Good control of asthma during pregnancy is important for the health and well-being of both the mother and her baby. Well controlled asthma is associated with a good outcome in pregnancy.

The disease course can vary from improvement to deterioration. However, pregnant women with asthma have an increased chance for acute asthma requiring hospital admission. Monitoring and making appropriate adjustments in therapy may be required to maintain lung function and, hence blood oxygenation that ensures oxygen supply to the foetus.

The obstetric team should be involved in asthma care, including monitoring of asthma status during prenatal visits.

Asthma treatment in pregnancy

The treatment is assumed to be the same in pregnant women as in non-pregnant women with the stepwise therapy approach.

The medications used to treat asthma are safe in pregnancy the risk of harm to the foetus from under-treated asthma exceeds risk from the medications used to control asthma.

β2 agonists - SABA, LABA or LAMA can be used as in normal asthma patients.

Inhaled steroids - Exposure to inhaled steroids has no significant association with major congenital malformations or adverse perinatal outcome. Use of inhaled steroids can be done as in a normal asthma patient.

Oral steroids - Use of oral corticosteroids in the first trimester may slightly increase rates of cleft lip and palate though this is not well established. Hence oral steroid can be used when indicated during pregnancy for severe asthma.

Steroid tablets should never be withheld because of pregnancy if there is an indication to use.

Leukotriene receptor antagonists - Data on the safety of the Leukotriene receptor antagonists are limited. However, it may be continued in mothers who have demonstrated significant improvement in asthma control with these agents prior to pregnancy not achievable with other medications.

Theophylline - This has no increase in congenital malformations or adverse perinatal outcome. Oral and intravenous theophylline's can be used as normal during pregnancy.

Labour and peri-partum

During labour endogenous steroid production is increased hence the acute asthma attacks are rare. However, use of regular medications is recommended.

Use of Prostaglandin F2α can induce bronchoconstriction and may be used with extreme caution.

If Caesarean section is required, a regional blockade is preferable to general anaesthesia.

Breast feeding mothers can continue asthma medications during lactation.

Asthma in Surgery

Patients who have asthma are at risk for developing complications during and after surgery. These complications include acute bronchoconstriction triggered by intubation, hypoxemia, possible hypercapnia, impaired effectiveness of cough, atelectasis, respiratory infection and reactions to some anaesthetic agents.

Review of an asthmatics history and the appropriate preoperative preparations can significantly reduce the risk of adverse outcomes.

- ✓ One-week prior assessment is necessary in an elective major surgery.
- ✓ Clear evaluation of Aspirin and NSAIDs drug sensitivity to minimise the drug induced asthma.

If PEF is >80% predicted with minimum symptoms step-up treatment of asthma may not require to prior surgery.

Multidisciplinary team approach may be needed for better outcome in poorly controlled asthmatics.

Treatment options prior to surgery are based upon the level of the severity of the disease.

- **Short-term “step up” in the treatment regimen**

Controlled asthmatics may only need a short-acting β-2 agonist just prior to surgery.

Additional short acting β-agonists are indicated regardless of disease level.

If there is evidence of poor control, (Mild to moderately controlled) or > 20% variability in Peak Expiratory Flow Rate (PEFR), consider add/step up (doubling) the dose of inhaled steroids 1 week prior to surgery.

If control is poor, consider review by a physician, and a one-week course of oral prednisolone (20–40 mg daily).

Perioperative systemic corticosteroids can be used safely to suppress production of inflammatory cytokines.

For patients receiving oral systemic corticosteroids during the 6 months prior to surgery and for selected patients on long-term high-dose ICS, 100 mg hydrocortisone should be given every 8 hours intravenously during the surgical period, the dose rapidly reduced within 24 hours after surgery.

Annexure

Annexure 1

Performing a spirometry and demonstrating airway reversibility

Prerequisites:

Patient must be clinically stable and not having an exacerbation.

Should avoid SABA 6 hrs prior to the test

LABA 12 hrs prior to the test

Theophylline's 24 hrs prior to the test

Smoking, should be stopped 24 hrs prior to the test

Should not be under the influence of alcohol

No heavy meal or coffee 2 hrs prior to the test

No tight clothing at the time of performing

How test is done

Baseline Spirometry (or PEFR)

Nebulize with salbutamol (2.5 mg) or 4 puffs MDI via Spacer.

Repeat test after 15 minutes of bronchodilator

Annexure 2

	Low	**Intermediate**	**High**
FeNO (ppb) >12 years of age	< 25	25-50	>50
<12 years of age	<20	20-35	>35
Consider as significant increase in FeNO	Increase > 10 ppb from last measurement		> 20% increase from last measurement

Ppb= parts per breath

Inhaled Corticosteroid dose equivalents

BUD- budesonide

BDP-HFA – beclomethasone dipropionate(HFA) (Fine particulate, the equivalent dose is half that of, BUD)

FP- Fluticasone propionate – is twice as potent as BUD, equivalent dose is half that of BUD.

CIC –Ciclesonide is given once daily and has a 24 hrs of action.

MF – Mometasone furoate

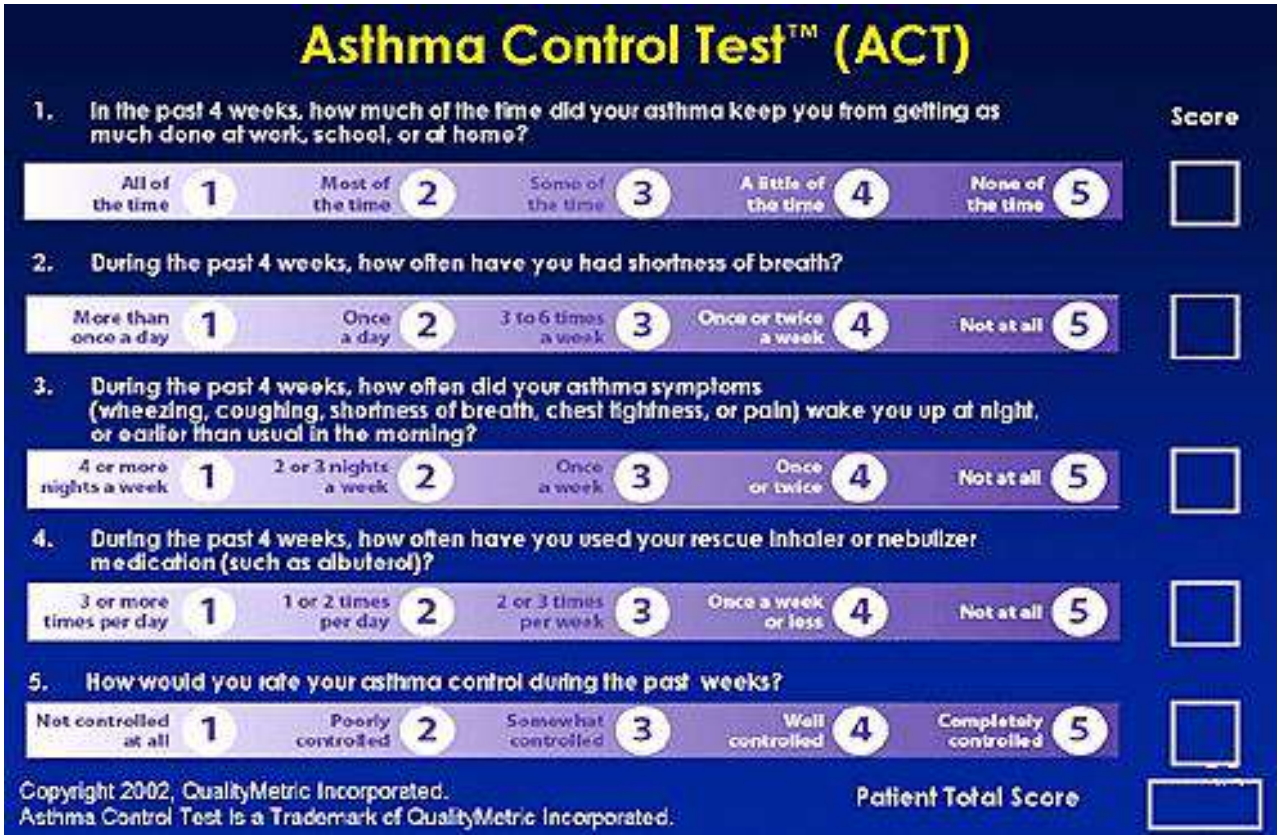
TA- Triamcinolone acetate

Dose equivalence of ICS

Dose Level	**CIC**	**BDP-HFA**	**FP**	**BUD**	**MF**	**TA**
Low	80-160 mcg	100-200mcg	100-200 mcg	200-400 mcg	110-220	400-1000
Medium	160-320 mcg	200-400 mcg	200-400 mcg	400-800 mcg	220-440	1000-2000
High	>320 mcg and above	> 400 mcg	> 400 mcg	> 800 mcg	>440	>2000

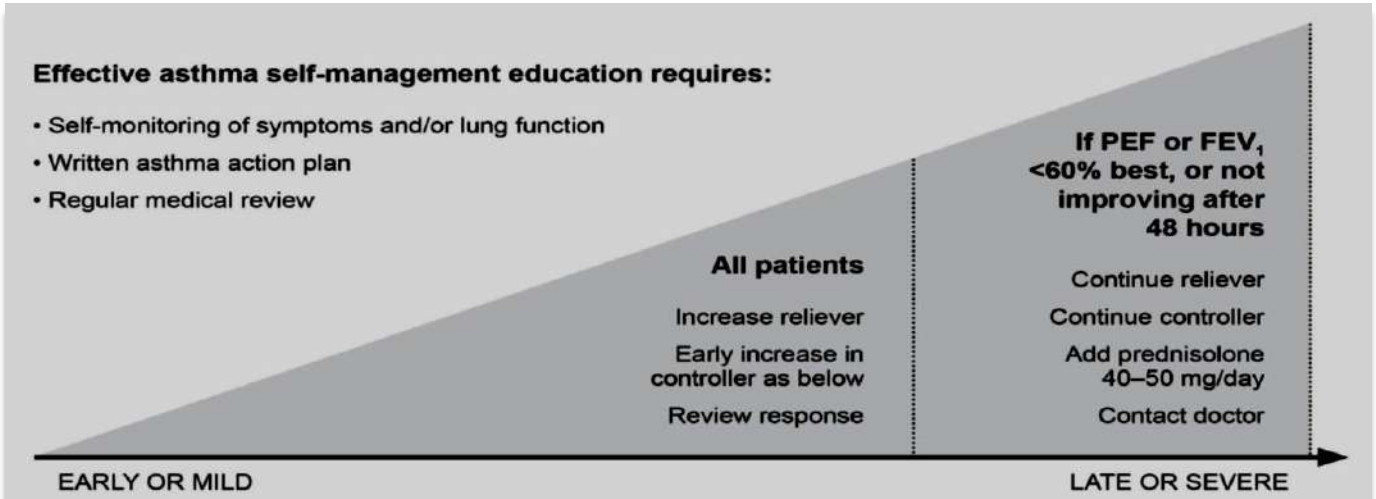
Annexure 3

Asthma Control Test (ACT) Score and level of control



If the score is 19 or less , asthma may not be controlled as well as it could be

Annexure 4



Medication	Short-term change (1-2 weeks) for worsening asthma	Evidence Level
Increase usual reliever:		
Short-acting $beta_2$-agonist (SABA)	Increase frequency of SABA use For pMDI, add spacer	A A
Low dose ICS/formoterol *	Increase frequency of reliever use (maximum formoterol total 72 mcg/day)	A
Increase usual controller:		
Maintenance and reliever ICS/formoterol *	Continue maintenance ICS/formoterol and increase reliever ICS/formoterol as needed* (maximum formoterol total 72 mcg/day)	A
Maintenance ICS with SABA as reliever	At least double ICS; consider increasing ICS to high dose (maximum 2000 mcg/day BDP equivalent)	B
Maintenance ICS/formoterol with SABA as reliever	Quadruple maintenance ICS/formoterol (maximum formoterol 72 mcg/day)	B
Maintenance ICS/salmeterol with SABA as reliever	Step up to higher dose formulation of ICS/salmeterol, or consider adding a separate ICS inhaler (to maximum total 2000 mcg/day BDP equivalent)	D
Add oral corticosteroids (OCS) and contact doctor		
OCS (prednisone or prednisolone)	Add OCS for severe exacerbations (e.g. PEF or FEV_1 <60% personal best or predicted), or patient not responding to treatment over 48 hours	A
	Adults: prednisolone 1 mg/kg/day (maximum 50 mg) usually for 5–7 days. *Children:* 1–2 mg/kg/day (maximum 40 mg) usually for 3–5 days.	D
	Tapering is not needed if OCS are prescribed for <2 weeks	B

BDP: beclometasone dipropionate; FEV_1: forced expiratory volume in 1 second; ICS: inhaled corticosteroid; PEF: peak expiratory flow; SABA: short-acting $beta_2$-agonist. Options are listed in order of evidence.

*ICS/formoterol maintenance and reliever regimen: low dose budesonide or beclometasone with formoterol. This regimen is not approved for children <12 years in many countries.

Annexure 5

American College Of Chest Physicians Criteria for diagnosis of Occupational Asthma

A. Physician diagnosed asthma and/or physiological evidence of air-way hyperresponsiveness.

B. Occupational exposure precede onset of symptoms.

C. Association between symptoms and work.

D. Exposure and /or physiological evidence of relation of asthma to workplace environment.

Diagnosis requires all 4 (A-D) and one or more of D2-D5, likely OA requires only D1

D1 Workplace exposure to agent reported to give rise to OA.

D2. Work-related changes in FEV1 or PEF.

D3. Work-related changes in serial testing for non-specific bronchial responsiveness (e.g. methacholine challenge)

D4. Positive specific bronchial challenge test.

D5. Onset of asthma with a clear association with a symptomatic exposure to inhaled irritant at work place (generally RADS).

Criteria for diagnosis of RADS (should meet all 7)

1. Documented absence of preexisting asthma-like complaints.

2. Onset of symptoms after a single exposure incident or accident.

3.Exposure to gas, smoke, fumes, vapor or dust with irritant properties present in high concentrations.

4.Onset of symptoms within 24hrs after exposure with persistence of symptoms for at least 3 months.

5.Symptoms consistent with asthma, cough, wheeze, dyspnea.

6. Presence of airflow obstruction on pulmonary function tests and /or presence of non-specific bronchial responsiveness (testing should be done shortly after exposure)

7. Other pulmonary diseases ruled out.

Criteria for diagnosis of Work-Aggravated Asthma (WAA)

1. Meets criteria A and C of OA.

2. Pre-existing asthma or history of asthmatic symptoms (with active symptoms during the year prior to start of employment or exposure of interest).

3. Clear increase in symptoms or medication requirement, or documentation of work-related changes in PEF or FEV1 after start of employment or exposure of interest.

Annexure 6

Check list for the discharge acute asthma patient

1. Ensure to monitor and manage the asthma at home
2. Assess the inhaler technique and provide the reliever medications
3. If PEF < 50% on presentation, prescribe oral prednisolone 40-50 mg/day for 5 days
4. To make an appointment with their usual primary care physician within 2–4 weeks
5. Consider arranging referral to a consultant/respiratory physician with acute severe asthma presentation.
6. Provide the action plan – 7. instructions when and how to reduce reliever dose 8. instructions on preventer use 9. own written asthma action plan
10. 7. provide a copy of the discharge summary to the primary care physician

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