Guideline *for*
ASTHMA
Management in Nigeria

NIGERIAN
THORACIC SOCIETY

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Abbreviations

AAAA	American Academy of Allergy, Asthma & Immunology
ABG	Arterial Blood Gas
ACCP	American College of Chest Physicians
AOR	Adjusted Odds Ratio
ACQ	Asthma Control Questionnaire
ACSS	Asthma Control Scoring System
ACT	Asthma Control Test
ACTH	Adrenocorticotropic Hormone
ATS	American Thoracic Society
AQLQ	Asthma Quality of Life Questionnaire
ATAQ	Asthma therapy Assessment Questionnaire
BHR	Bronchial Hyper-Reactivity
BTS	British Thoracic Society
CCAG	Canadian Consensus Asthma Guideline
CFC	Chloroflurocarbon
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CXR	Chest X-Ray
DOT	Directly Observed Therapy
DPI	Dry Powder Inhaler
ECG	Electrocardiogram
ER	Emergency Room
FEV_1	Forced Expiratory Volume in 1 Second
FRC	Functional Residual Capacity
FVC	Forced Vital Capacity
GINA	Global Initiative for Asthma
ICS	Inhaled Corticosteroids
ICU	Intensive Care Unit
IgE	Immunoglobulin E

IM	Intramuscular
IOS	Impulse Oscillometry
ISAAC	International Study of Asthma and Allergies in Childhood
IV	Intravenous
kPa	kiloPascal
LABA	Long Acting Beta$_2$ Agonist
LTRA	Leukotriene Receptor Antagonist
MDI	Metered Dose Inhaler
mmHg	Millimetres of Mercury
NAEPPR	National Asthma Education and Prevention Program
NHLB	National Heart, Lung, and Blood Institute
NIAID	National Institute of Allergy and Infectious Diseases
NICE	National Institute of Clinical Excellence
NIV	Non-Invasive Ventilation
NSAID	Non-Steroidal Anti-inflammatory Drug
NTS	Nigerian Thoracic Society
PAAPs	Personalised Asthma Action Plans
PAQLQ	Paediatric Quality of Life Questionnaire
PEF	Peak Expiratory Flow
PEFR	Peak Expiratory Flow Rate
PICU	Paediatric Intensive Care Unit
pMDI	Pressurised Metered Dose Inhaler
QoL	Quality of Life
RR	Risk Ratio
RV	Residual Volume
SABA	Short-acting Beta$_2$ Agonist
SATS	South African Thoracic Society
SIGN	Scottish Intercollegiate Guidelines Network
TLC	Total Lung Capacity
URTIs	Upper Respiratory Tract Infections
VHCs	Valve Holding Chambers
WHO	World Health Organisation

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Preface

The guideline for the management of Asthma in Nigeria was initiated at the annual general meeting of the Nigerian Thoracic Society in Uyo November, 2015. The management of Asthma in Nigeria over the decades has involved different therapeutic regimes and approaches. Therefore there was this very compelling need to streamline various treatments plan to meet the international standard of practices worldwide.

The challenge of managing Asthma is still enormous because of the diverse approaches to it by many patients; some of whom still adopt unorthodox or traditional methods of treatment. Thus, the need to put together a concise method of treatment of this highly prevalent non communicable disease cannot be over emphasised.

The various contributors to the First Edition of guideline for the management of Asthma in Nigeria have put down very simplified approach to the management of this condition that will cut across all strata of health care delivery both at urban and rural settings. Similarly, the management of acute exacerbation of this condition which is often fatal in Nigerian hospitals has been simplified and made easy for medical practitioners to adopt. It is gratifying that the content which is now available in print Nigeria will be widely used by medical practitioners in the treatment of Asthma.

I wish to express my sincere gratitude to the Chairman of the steering committee, Prof. G. E. Erhabor and other very distinguished members of the committee for the painstaking nature and explicit contribution to the development of the guideline.

I also appreciate other members of the Nigerian Thoracic Society for their solidarity and support for this novel project of developing a guideline for the treatment of asthma.

Finally, I wish to thank the editorial advisers and the publisher for their wonderful cooperation towards the successful publication of this book.

I really appreciate everybody that has contributed to the realization of this project in a timely manner as was envisaged.

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INTRODUCTION

1.1 Why a National Asthma Guideline for Nigeria?

Several international guidelines on asthma have been published. Some of these include: British Thoracic Society (BTS) Asthma Guideline[1], American College of Chest Physicians (ACCP) Guideline,[2] Canadian Consensus Asthma Guideline[3], the National Asthma Education and Prevention Program (NAEPPR) Guideline,[4] the South African Thoracic Society (SATS) Guideline,[5] and the Global Initiative for Asthma (GINA) Guideline.[6]

Available evidence shows that asthma is still poorly understood, under-diagnosed and poorly managed in most part of the developing world.[7]Currently, there is no existing National Guideline for asthma in Nigeria. Although there have been a previous attempt to develop a National Asthma guideline for Nigeria, this has been inconclusive.

In view of recent advances in the understanding of asthma and its management, there is a need to develop a document which will reflect the current state-of-the -art and adapt this to the peculiarities of Nigeria.

Guidelines educate health care providers on evidence-based practice and recent advances in the management of diseases. They serve as a means of comparing practice in different regions of the world and ensuring standardization.

Guidelines not only help in the training of health care practitioners on evidence-based approach to the management of disease conditions, they also help the government and other stake holders to decide on essential drug lists for individual countries.

This National Guideline on Asthma has taken cognizance of the peculiarities and challenges of the local reality and will serve as a reference document for health care providers and other stake holders.

Beyond reading however, it is hoped that there will be good adherence to this guideline in our day to day practice.

1.2 Dedication and Acknowledgements

We dedicate this book to all the founding Fathers of respiratory medicine in Nigeria. Without their invaluable support, this document would not have been published.

We want to thank most profoundly Prof. Babatunde Onadeko, Past President of Nigerian Thoracic society (NTS), a great teacher and mentor whose intellectual contribution to Respiratory Medicine in Nigeria is unparalleled. He has been the prime mover of this initiative.

We want to thank Prof. Emmanuel Bandele, Past President of NTS who has shown relentless zeal to make sure this document is published and has demonstrated great enthusiasm towards respiratory medicine in Nigeria. We are thankful to Prof. Elegbeleye of blessed memory who has contributed immensely to respiratory medicine in Nigeria.

We appreciate Prof. Femi Pearse and Prof. Elebute who are the pioneers of research and clinical care in respiratory medicine in Nigeria. We thank Prof Awotedu for his mentorship and enthusiastic work in respiratory medicine. Our appreciation also goes to Prof Oluboyo who is a past executive of the NTS who has shown interest in pushing the frontiers of respiratory medicine forward through research. Space will not permit us to talk about the numerous Senior colleagues, Paediatric Pulmonologists, Chest Physicians, Cardiothoracic Surgeons and everyone who contributed immensely to making this document a great success. We hope that their work will continue to resound after them. This document cannot be said to complete without acknowledging the great work done by the Global Initiative on Asthma (GINA). We have borrowed and adapted quite a lot of resources from the GINA whose guideline continues to be a reference point for the care of asthma globally. We are also thankful for all the written documents and asthma materials from the ATS, ACCP, ERS, NICE, and the BTS/SIGN.

This document is by no means prescriptive and does not replace the objective assessment of the clinician but it is a guide to help augment his clinical judgment with established facts. Knowledge is ever evolving and by the time this document comes out of the press, some of its recommendations might even have become obsolete. We however hope to continually revise the document so that it will remain relevant to current practice.

We are aware that there is a big gap between the science of medicine and the actual practice of it particularly in regions of the world with limited resources. This is because some asthma medications and devices are unaffordable and in many cases unavailable. This is not a call for

complacency but an opportunity for the clinicians, the government and other stake holders to continue to seek ways of improvising, adapting and encouraging technological advancement which should be steered towards managing this disease that has send many Nigerians to untimely death.

1.3 How the Guideline was Developed

We followed the internationally recommended procedure for developing guidelines. Contributors were chosen from various regions of the country based on their area of expertise, published work and experience in the management of asthma.

The guideline was subjected to local and international peer-review. Editorial work was carried out by the secretariat of the Asthma Guideline Drafting Committee and professional editors before the final version was

Table 1: Description of levels of evidence used in this guideline [8]

Evidence Level	Sources of Evidence	Definition
A	Randomized controlled trials (RCTs) and meta-analyses. Rich body of data.	Evidence is from endpoints of well-designed RCTs or meta-analyses that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.
B	Randomized controlled trials (RCTs) and meta-analyses. Limited body of data.	Evidence is from endpoints of intervention studies that include only a limited number of patients, post hoc or subgroup analysis of RCTs or meta-analysis of such RCTs. In general, Category B pertains when few randomized trials exist, they are small in size, they were under-taken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.
C	Nonrandomized trials. Observational studies.	Evidence is from outcomes of uncontrolled or non-randomized trials or from observational studies.
D	Panel consensus judgment	This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above listed criteria.

published.

1.4 Levels of Evidence and Recommendations

The strategies recommended in these guidelines are classified according to the Evidence Category in Table 1 and denoted as "Evidence A, B, C and D."

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2

DEFINITION **OF ASTHMA**

2.1 Definition of Asthma

Asthma is difficult to define. Different attempts at defining asthma have focused on the various components that characterize the disease, with special emphasis on the inflammatory nature of the condition. A more universally acceptable definition is the one by the Global Initiative for Asthma (GINA), which defines asthma as a **heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation** (GINA 2016).

2.2 Prevalence of Asthma

Asthma affects about 300 million people world-wide, and it is estimated to rise to 400 million by 2025.[1] Although studies on the prevalence of asthma have consistently shown lower levels in rural areas, available data suggests an increase in prevalence in both urban and rural settings.[2]

The International Study of Asthma and Allergies in Childhood (ISAAC), which was conducted with the goal of having a worldwide comparison of asthma symptoms in various regions of the world, estimated the prevalence of Asthma in African adolescents at approximately 14% with variability by country, as follows: Ethiopia 9.1%, Kenya 15.8%, Nigeria 13.0%, South Africa 20.3%, Algeria 8.7%, Morocco 10.4% and Tunisia 11.9%.[3]

Further data from ISAAC suggests that asthma is frequently undiagnosed in African children and when diagnosed, the disease is severe.[4] Poor access to care, sub-optimal treatment, environmental exposures or gene-environment interactions may contribute to this. The wide variation in the prevalence and severity of asthma is partly explained by poverty, climate, exposure to tobacco smoke, infection, air pollution, chemical irritants, helminthic infections, diet, and exposure to allergens such as house dust mite, cockroach, dog and cat dander, and even washing soap. Sensitization to pet allergy, which was uncommon some years ago, is becoming more frequent in urban areas.

It has been previously thought that asthma was rare in Nigeria. However, this was not backed by standardized studies and most were hospital-based.[5,6]

Recent population studies conducted by various investigators across Nigeria estimate the prevalence of asthma to range from 5.12-18.6%. [7-15] The prevalence of asthma differs from region to region depending on the methodology used in carrying out the studies. This varies from the use of questionnaires to the use of lung function testing and challenge test.

2.3 Risk Factors for Asthma

Various risk and precipitating factors have been associated with the development of asthma or its exacerbation. Viral infections, particularly Rhinovirus C, have been implicated in the inception of asthma as well as in triggering asthma exacerbations.[16] Atopy, which is a genetic predisposition to development of IgE-mediated response to common environmental allergens, remains a strong risk factor.[17,18] A strong and significant association have been found between asthma and a damp mouldy bedroom,[19] household pets,[20] cigarette smoke[21], mosquito coil and cockroaches[22,23]. Among the various environmental allergens, house dust mite (dermatophagoide pteronyssimus) allergy is a major contributory cause of asthma .[24,25] Other significant allergens are feathers, dog hair, cat fur, grass pollen, flower pollen, feathers, cow's milk and fish. A strong correlation exists between history and skin test sensitivity for most allergens.[26]

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3

DIAGNOSIS **OF ASTHMA**

3.1 Summary of Practice Points

The following should be taken into consideration in diagnosing asthma;

1 Asthma should be suspected in the presence of recurrent/episodic wheezing, breathlessness, cough, and/or chest tightness with no alternative explanation for these symptoms (Evidence A).

2 Diagnosis of asthma is based on symptoms of cough, chest tightness, breathlessness and wheezing and variable of airflow limitation (Evidence GPP).

3 Spirometry is the recommended method of measuring airflow limitation and reversibility to establish a diagnosis of asthma (in patients over 5 years of age). A normal spirometry when not symptomatic does not exclude the diagnosis of asthma (Evidence A).

4 If spirometry is not available, reversibility may be assessed with PEF meters (Evidence B).

5 In patients with an intermediate probability of asthma, carry out further investigations like atopic testing, bronchodilator reversibility, bronchial hyperresponsiveness challenge. (Evidence GPP)

Diagnosis of asthma is based on clinical evidence of airway obstruction manifesting as variable respiratory symptoms, physiological parameters, history of atopy or a family history of atopy and bronchial hyperresponsiveness. The cardinal symptoms of asthma include a cough, chest tightness, breathlessness and wheezing that vary over time in their occurrence, frequency and intensity (Table 2). Occasionally, the cough may be the only symptom (cough-variant asthma). The symptoms often occur or are worse at night or on waking, and often triggered by certain agents (Table 3) [1-3]. It is important to note that in clinical practice all that wheezes is not asthma. History of improvement in symptoms in response to asthma medication increases the likelihood of asthma. All these features increase the probability of asthma in suspected patients.

The presence of features that suggest an alternative diagnosis e.g. history of fever, sweats, weight loss, chest pain and hemoptysis, no response to the trial of asthma therapy, focal or normal chest examination when symptomatic decreases the probability of asthma (Table 4) [4-7].

In some categories of patients particularly those below the age of five, they have an intermediate probability of asthma, because they lack features to make a firm diagnosis of asthma or to suggest an alternative diagnosis. The steps for the three groups are illustrated in Figure 1.

Physical examination in people with asthma is often normal in between attack, but the most frequent finding is wheezing on auscultation, especially on forced expiration. In a subset of patients with chronic asthma, widespread wheeze could be detected in spite of regular anti-asthmatic drugs. In addition, in patients with the severe attack, they could develop signs of respiratory distress, cyanosis and wheezing may be absent [4,7].

3.2 Physiological Measurements

One of the hallmarks of asthma is the variable of airway obstruction[4-7].

The need for objective measurement of airflow obstruction and variability is central to the diagnosis of asthma. **Spirometry is the recommended method of measuring airflow limitation and reversibility to establish a diagnosis of asthma. A normal spirometry when not symptomatic does not exclude the diagnosis of asthma**. [1,4-7]

Two measurements are particularly useful: the forced expiratory volume in one second (FEV_1) using a spirometer and peak flow rate measured using a spirometer and peak flow respectively. FEV_1 - Forced expiratory volume in one second: The volume of air expired in the first second of the forceful expiration after maximum inspiration. PEF is the maximum peak expiratory flow in units of l/min or l/s. Forced expiratory volume in 1 second (FEV_1) from spirometry is more reliable than peak expiratory flow (PEF) [4,8].

One characteristic of asthma is reversibility. This can be demonstrated by the inhalation of two pulps of a short-acting bronchodilator and measuring the PEF or FEV_1 before and about 15-30 minutes after inhalation: An increase in FEV_1 of >12% and >200 mL is indicative of asthma[4,9]. (Table 5).

When the improvement is less than 12%, a steroid trial should be given. An improvement in FEV_1 of >12% and >200 mL (or PEF by >20%) from baseline after 4 weeks of treatment, outside respiratory infections with steroid trial confirms the presence of asthma [9].

In the most part of the country, spirometer is not readily available and most doctors lack the knowledge of interpretation of test. [10] The use of the simple PEF with reported symptoms before and after a therapeutic trial with as-needed SABA and regular ICS, often together with 4 weeks course of oral corticosteroids, can help to confirm the diagnosis of asthma before long-term treatment is commenced. The use of PEF is less sensitive and specific.[4-7]

In addition, patients with asthma do demonstrate diurnal variation (morning dip). Variability of at least PEF variability >10% in adults and >13% in children of established maximum for each subject is diagnostic of asthma[11-12].

In children or young adults, exercise challenge may be useful. A fall in FEV_1 of >10% and >200 mL from baseline and for children a fall in FEV_1 of >12% predicted, or PEF >15% after 6 minutes intensive exercise is assumed to be diagnostic of asthma[13-14].

The use of provocative tests with histamine and methacholine are not necessary for the routine diagnosis of asthma, but may be useful in doubtful cases where simple tests have failed to confirm the diagnosis[4-7].

Other investigations such as skin prick test and measurements of serum IgE can confirm the presence of atopy and perhaps lend support to the diagnosis in doubtful cases. They do not usually help with the management of Asthma[4-7].

3.3 Differential Diagnosis

Finally in the diagnosis of asthma, asthma mimics should be excluded. Furthermore, any of these alternative diagnoses may also be found together with asthma as comorbidity. The differential diagnosis in a patient with suspected asthma is numerous (Table 6).

Table 2: Bronchial Asthma: Diagnostic Clues

HISTORY
• Cough • Wheeze • Dyspnoea • Chest tightness • ±Mucus production • Family history of asthma
PATTERN OF SYMPTOMS
• Episodic or continuous • Seasonal or perennial • Nocturnal (diurnal variation)
PRECIPITATING FINDINGS
• Associated with common allergens (dust, pollen etc.) • Exposure to allergens at home or school • Occupational exposures
PHYSICAL FINDINGS
• Often normal • Inspiratory/ Expiratory wheeze • Presence of allergic disease (rhinitis, sinusitis, nasal polyps, eczema)
LUNG FUNCTION TEST
• Evidence of airway obstruction (↓PEF ↓FEV_1) • Circadian variation in airway obstruction (morning dips) • Reversibility test – bronchodilators - steroids
OTHERS
• Exercise test • Bronchial hyperreactivity – Histamine/Methacholine challenge test • ±Skin test / RAST • ±Blood / Sputum eosinophilia • ±Bronchoscopy

Adapted from ref 1

Table 3: Asthma Triggers

Environmental allergens	Non-Environmental allergens
Indoor allergens / Pollutants • Domestic Mites • Animal With Furred & Feather • Insects-Cockroach Allergen • Fungi • Tobacco Smoke (Active & ETS) • Wood Smoke • Household Aerosol /Sprays • Volatile Organic Compounds (e.g., Polishes, and cooking oils)	**Drugs** • β blockers • aspirin • NSAIDS • Cocaine • Contrast agents • Dipyridamole • Heroin Food • Milk, Egg, Fish, Shrimp, • Dried Fruits • Beer And Wine • Chocolate
Outdoor Air Pollutants • Pollens • Fungi • Infections (Predominantly Viral) • Cold Air • Hair Spray Paint • Exhaust Fumes • Smoke From any fire • Changes in Temperature • Changes in weather Occupational sensitizers • Chemicals • Latex • Paint	Others • Exercise • Strong Emotional Expression • Laughter • Acid Reflux • Pregnancy • Menopause/menstruation • rhinitis, sinusitis, polyposis

Adapted from ref 3-7

Table 4: Features that decrease the probability of Asthma

Clinical Features
• Chronic production of sputum • Isolated cough • Chest pain • Noisy inspiration • Dizziness, Light-Headedness or Peripheral Tingling • History of fever, chills, sweats, weight loss and haemoptysis • No response to trial of asthma therapy • Focal or normal chest examination when symptomatic • Normal lung function test when symptomatic • Cardiac disease

Adapted from ref 1-7

Table 5: Confirmed variable expiratory airflow limitation

Tests	Diagnostic Criteria
Air flow limitation [8]	the FEV1/FVC ratio < LLN for age < 0.90 in children <0.80 in 20-39 years <0.75 in 40-59 years <0.70 in 60+ years
Positive Bronchodilator (BD) Reversibility Test [9]	Adults: increase in FEV1 of >12% and >200 mL from baseline 10–15 minutes after 200–400 mcg salbutamol inhalation Children: increase in FEV1 of >12% predicted
Positive Bronchodilator (BD) Reversibility Test after 4 weeks trial of controller Treatment[9]	Adults: increase in FEV1 by >12% and >200 mL (or PEF† by >20%) from baseline after 4 weeks of treatment, outside respiratory infections
PEF Variability in twice - daily PEF measurement over 2 weeks [11-12]	Adults: average daily diurnal PEF variability >10% Children: average daily diurnal PEF variability >13%
Exercise Challenge Test [13-14]	Adults: fall in FEV1 of >10% and >200 mL from baseline Children: fall in FEV1 of >12% predicted, or PEF >15%
Bronchial Challenge Test [14]	Fall in FEV1 ⩾20% with standard doses of methacholine or histamine, from baseline or histamine, or ⩾15% with standardized hyperventilation, hypertonic saline or mannitol challenge
Variation in lung functions between visits outside of respiratory infections[9]	Adults: variation in FEV1 of >12% and >200 mL between visits (less reliable) Children: variation in FEV1 of >12% in FEV1 or >15% in PEF† between visits (may include respiratory infections)

Table 6: Diseases which can mimic asthma

Age group	Disease	Clinical Features	Diagnostic Tests
< 5 years	Chronic upper airway cough syndrome Foreign body aspiration Tuberculosis Congenital bronchial dis. Congenital heart disease	Sneezing, itching, blocked nose throat-clearing Sudden symptoms & Unilateral signs Cough > 3 weeks & history of contact Preterm & symptoms since birth Cardiac murmurs	ENT examination Radiography Bronchoscopy AAFB Microscopy Bronchoscopy/CT Echocardiogram
6-11 years	Chronic upper airway cough syndrome Inhaled foreign body Bronchiectasis Tuberculosis Congenital heart disease	Sneezing, itching, blocked nose throat-clearing Sudden symptoms and Unilateral sign A chronic cough, purulent sputum Cough > 3 weeks & history of contact Cardiac murmurs	ENT examination/ Radiography Bronchoscopy CT scan chest AAFB Microscopy Echocardiogram
12-39 years	Chronic upper airway cough syndrome Vocal cord dysfunction Inhaled foreign body Bronchiectasis Tuberculosis Hyperventilation, dysfunctional breathing	Sneezing, itching, blocked nose throat-clearing SOB, inspiratory wheezing (stridor) Sudden symptoms and Unilateral sign Chronic cough, purulent sputum Cough > 3 weeks & history of contact Dizziness, paraesthesia, sighing	ENT examination/ Radiography Stroboscopy Bronchoscopy CT scan chest AAFB Microscopy
⩾ 40 years	COPD Bronchiectasis Cardiac failure Parenchymal lung dis. Pulmonary embolism Central airway obstruction	Chronic cough/sputum A chronic cough, purulent sputum SOB,PND, Oedema, 3rd Heart sound SOB with exertion, Dry cough Sudden SOB, chest pain Dyspnoea, unresponsive to bronchodilators	Spirometry CT scan chest Echocardiogram Lung biopsy CT Angiogram Spirometry

Adapted from ref 3-7

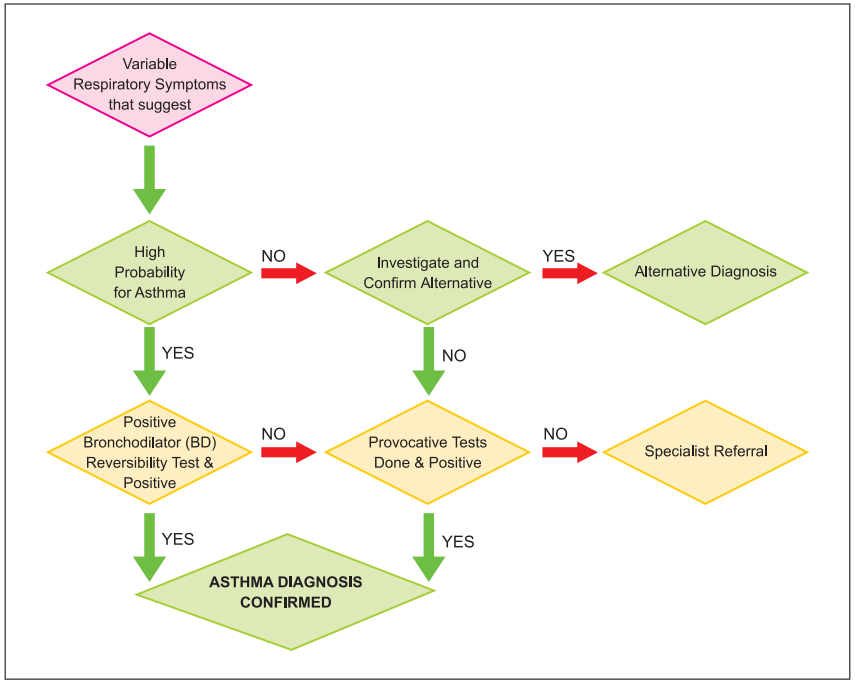

Figure 1: Recommended Step based on Probability of asthma

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MANAGEMENT **OF ASTHMA**

4.0 The Aim of Asthma Management is Control of the Disease[1]

Complete control of asthma is defined as:

- no daytime symptoms
- no night-time awakening due to asthma
- no need for rescue medication
- no asthma attacks
- no limitations on activity including exercise
- normal lung function (in practical terms FEV^1 and/or PEF>80% predicted or best)
- minimal side effects from medication

The cardinal mode of asthma management is the step-wise approach[2] which involves either escalating (step-up) or reducing (step-down) the number of medications or frequency of dosing depending on the degree of asthma control assessed over a period.

The stepwise approach aims to abolish symptoms as soon as possible and to optimize asthma control as early as possible by starting treatment at the level most likely to achieve this. Treatment is usually started at the step most appropriate to the initial severity of their asthma.

Before initiating a new drug therapy, the practitioners should check adherence with existing therapies, inhaler technique,[3,4,5,] advice on eliminating known trigger factors,[6,7] and assess for presence of co-morbidities.[8,9]

4.1 Manage Asthma in a Continuous Cycle

The management of the patient should involve a continuous cycle of assessment, adjustment of treatment and review of response.[10] (Fig. 2)

- **Assess:** This includes establishing the diagnosis of asthma through lung function testing, assessing for symptom control, risk factors, inhaler technique and adherence to medications
- **Adjust:** Adjust asthma medications treatment and treat modifiable risk factors.

- **Review**: Review symptoms, exacerbations, drugs' side effects, patient satisfaction and lung function.

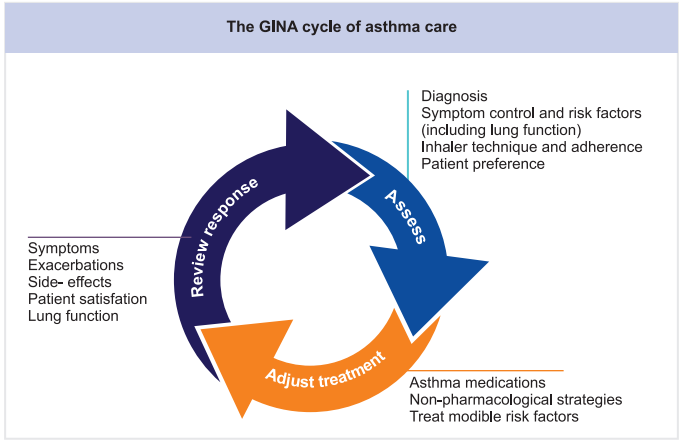

Figure 2: Adapted from GINA guideline 2016[10]

4.2 Classification of Chronic Stable Asthma

Chronic stable asthma is classified as either intermittent or persistent depending on the frequency of symptoms. The persistent is further classified as mild, moderate or severe persistent. The implication of this is mainly for treatment purposes. Table 7 summarizes this.

4.3 Asthma Medications

Maintenance treatment of asthma is determined by severity on presentation, current asthma medication, patient profile and level of control.

A classification of asthma drugs based on current knowledge of their mode of action is presented in the Table 8a and 8b. They may be:

- ***Relievers*** short-acting bronchodilators with rapid onset of action that provide acute relief of symptoms
- ***Controllers*** drugs with anti-inflammatory and/or a sustained bronchodilator action

Table 7: Classification of chronic stable asthma.

Classification	Day Time Symptoms	Night Time Symptoms	Lung Function
Intermittent	Symptoms less than once a week Brief exacerbations	Nocturnal symptoms not more than twice a month	FEV_1 or PEF ⩾ 80% predicted PEF or FEV1 variability < 20%
Mild Persistent	Symptoms more than once a week but less than once a day Exacerbations may affect activity and sleep	Nocturnal symptoms more than twice a month	FEV_1 or PEF ⩾ 80% predicted PEF or FEV1 variability < 20 – 30%
Moderate persistent	Symptoms daily Exacerbations may affect activity and sleep Daily use of inhaled short-acting 2-agonist	Nocturnal symptoms more than once a week	FEV_1 or PEF 60 - 80% predicted PEF or FEV_1 variability > 30%
Severe persistent	Symptoms daily Frequent exacerbations Limitation of physical activities	Frequent nocturnal asthma symptoms	FEV_1 or PEF ⩽ 60% predicted PEF or FEV_1 variability > 30%

Adapted from GINA guideline 2016

Table 8a. Asthma Medications (Relievers)

Relievers	Examples
Rapid-acting inhaled β_2-agonists	Salbutamol Fenoterol Terbutaline
Systemic gluco corticosteroids	Prednisone Prednisolone
Anticholinergics	Ipratropium bromide
Short-acting oral β_2-agonists	Salbutamol
Theophylline	Aminophylline

Table 8b. Asthma Medications (Controllers)

Controllers	Examples
Inhaled glucocorticosteroids	1. Beclomethasone 2. Budesonide 3. Fluticasone 4. Ciclesonide
Leukotriene modifiers	1. Montelukast 2. Zafirlukast
Systemic glucocorticosteroids	1.Prednisone 2.Prednisolone
Long-acting inhaled β2-agonists	1. Salmeterol 2. Formoterol
Theophylline	Sustained-release theophylline Preparations
Cromones	Sodium cromoglycate
Long-acting inhaled anticholnergic	Tiotropium
Anti-IgE	Omalizumab

4.4 Step-Wise Asthma Management

4.4.1 General Principles

The stepwise approach to therapy operates on the premise that the dose, number of medications and frequency of administration should be increased as the situation dictates and decreased whenever this can safely be accomplished.[10]

Initially, treatment should be selected that correlates with the patient's level of asthma severity, but thereafter, treatment should be selected on the basis of current asthma control (or lack of control).[11]

Deciding which step of care is appropriate for a patient depends on whether long-term control therapy is being initiated for the first time or whether therapy is being adjusted.[12] Care is stepped up to regain control, and it is stepped down for patients who have maintained control for a sufficient length of time to determine the minimal amount of medication required to maintain control and/or reduce the risk of side effects. The classification of asthma severity (table 1), provides a guide for initiating therapy for patients who are not currently taking long-term control medications. Once therapy is selected, the patient's response to therapy will guide decisions about

adjusting therapy based on the level of control.[12]

Table 9 is a summary of the step-wise management for chronic stable asthma in adults.

Table 9. Step-Wise Management of Chronic Stable Asthma

Step	Preferred Option	Rationale/Evidence	Other Option
1	**As-needed inhaled short-acting beta$_2$-agonist (SABA)**	This option should be reserved for patients with: infrequent symptoms (less than twice a month) of short duration, and with no risk factors for exacerbations ***(EVIDENCE A)***	Consider adding regular low dose inhaled corticosteroid (ICS) for patients at risk of exacerbations. ***(EVIDENCE A)***
2	**Regular low dose ICS with as-needed inhaled SABA**	Low dose ICS reduces symptoms and reduces risk of exacerbations and asthma-related hospitalization and death ***(EVIDENCE A)***	1. Leukotriene receptor antagonists (LTRA) with as-needed SABA • Less effective than low dose ICS • May be used for some patients with both asthma and allergic rhinitis, or if patient will not use ICS 2.Combination low dose ICS/long-acting beta$_2$-agonist (LABA) with as-needed SABA • Reduces symptoms and increases lung function compared with ICS • More expensive, and does not further reduce exacerbations
3	**– one or two controllers + as needed inhaled reliever**	combination low dose ICS/LABA maintenance with as-needed SABA, OR combination low dose ICS/formoterol maintenance and reliever regimen***(EVIDENCE A)***	Adults/adolescents: Increase ICS dose or add LTRA or theophylline (less effect ive than ICS/LABA) ***(EVIDENCE B)***
4	**Two or more controllers + as-needed inhaled reliever**	combination low dose ICS/formoterol as maintenance and reliever regimen*, OR combination medium dose ICS/LABA with as-needed SABA **(EVIDENCE D)**	Tiotropium by mist inhaler may be used as add-on therapy for patients aged ⩾12 years with a history of exacerbations ***(EVIDENCE D)*** Trial of high dose combination ICS/LABA, but little extra benefit and increased risk of side-effects Increase dosing frequency (for budesonide-containing inhalers) Add-on LTRA or low dose theophylline
5	**Higher level care or add-on therapy**	Preferred option is referral for specialist investigation and consideration of add-on treatment If symptoms uncontrolled or exacerbations persist despite Step 4 treatment, check inhaler technique and adherence before referring • Add-on tiotropium for patients ⩾12 years with history of exacerbations.***(EVIDENCE D)*** • Add-on omalizumab (anti-IgE) for patients with severe allergic asthma. ***(GOOD PRACTICE POINT*** • Add-on mepolizumab (anti-IL5) for severe eosinophilic asthma (⩾12 yrs)	Sputum-guided treatment: This is available in specialized centers; reduces exacerbations and/or corticosteroid dose • Add-on low dose oral corticosteroids (⩽7.5mg/day prednisone equivalent): this may benefit some patients, but has significant systemic side-effects.***(GOOD PRACTICE POINT)*** Assess and monitor for osteoporosis • Immunotherapy (refer patient to specailzed treatment centre) • Bronchial thermoplasty ***(EVIDENCE A)*** (refer patient to specialized treatment centre)

Table 10: Low, medium and high dose inhaled corticosteroids adults and adolescents (⩾12 years)

Inhaled corticosteroid	Total daily dose (mcg) Low	Medium	High
Beclometasone dipropionate (CFC)	200–500	>500–1000	>1000
Beclometasone dipropionate (HFA)	100–200	>200–400	>400
Budesonide (DPI)	200–400	>400–800	>800
Ciclesonide (HFA)	80–160	>160–320	>320
Fluticasone furoate (DPI)	100	n.a.	200
Fluticasone propionate (DPI or HFA)	100–250	>250–500	>500
Mometasone furoate	110–220	>220–440	>440
Triamcinolone acetonide	400–1000	>1000–2000	>2000

4.5 Reviewing Response and Adjusting Treatment[4]

Asthma treatment should be reviewed

- 1-3 months after treatment started, then every 3-12 months
- During pregnancy, every 4-6 weeks
- After an exacerbation, within 1 week

4.5.1 Stepping Up Asthma Treatment

- ***Sustained step-up*, for at least 2-3 months if asthma is poorly controlled**
  - ✓ Important: first check for common causes (symptoms not due to asthma, incorrect inhaler technique, poor adherence)
- ***Short-term step-up*, for 1-2 weeks, e.g. with viral infection or allergen**
  - ✓ May be initiated by patient with written asthma action plan
- ***Day-to-day adjustment***
  - ✓ For patients prescribed low-dose ICS/formoterol maintenance and reliever regimen*

4.5.2 Stepping Down Asthma Treatment

- Consider step-down after good control maintainance for 3 months
- Find each patient's minimum effective dose, that controls both symptoms and exacerbations

4.5.3 General Principles for Stepping Down Controller Medications.

The aim of treatment is to find the lowest dose that controls symptoms and exacerbations, and minimizes the risk of side-effects

- **When to consider stepping down**
  - ✓ When symptoms have been well controlled and lung function stables for ⩾3 months
  - ✓ No respiratory infection, patient not travelling, not pregnant
- **Prepare for step-down**
  - ✓ Record the level of symptom control and consider risk factors
  - ✓ Make sure the patient has a written asthma action plan
  - ✓ Book a follow-up visit in 1-3 months
- **Step down through available formulations**
  - ✓ Stepping down ICS doses by 25–50% at 3 month intervals is feasible and safe for most patients

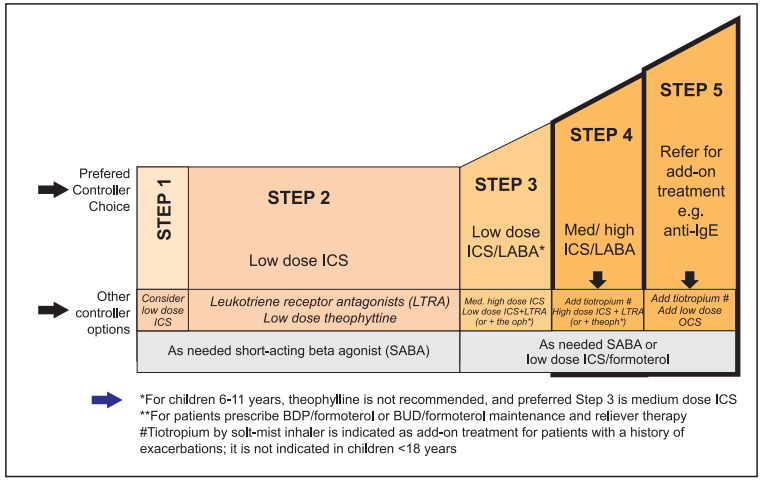

Figure 3. Step – wise management of asthma. ©GINA, 2016

4.5.4 Non-Pharmacological Interventions[4]

Minimizing exposure to allergens and irritants can help to improve symptoms of asthma through reduction in airway inflammation. Failure to control these exposures can make the asthma more difficult to manage.[13] This non-drug approach has been found to be of immense importance in achieving control of asthma and optimizing treatment.

This has been divided into two main aspects:

1. **Primary Prevention** – interventions introduced before the onset of disease and designed to reduce its incidence (check section of Paediatrics asthma guideline)
2. **Secondary Prevention** – interventions introduced after the onset of disease to reduce its impact. These include:

- Avoidance of tobacco smoke exposure
  - ✓ Provide advice and resources at every visit; advise against exposure of children to environmental tobacco smoke (house, car).
- Physical activity
  - ✓ Encouraged because of its general health benefits. Provide advice about exercise-induced bronchoconstriction.

- Occupational asthma
  - ✓ Ask patients with adult-onset asthma about work history. Remove sensitizers as soon as possible. Refer for expert advice, if available.
- Avoid medications that may worsen asthma
  - ✓ Always ask about asthma before prescribing NSAIDs or beta-blockers.
- Remediation of dampness or mold in homes
  - ✓ Reduces asthma symptoms and medication use in adults.
- Allergen avoidance (house dust or animals) have not been found to be effective in management of asthma.[10]
  - ✓ (Not recommended as a general strategy for asthma (Evidence A)
- Others include weight reduction (EVIDENCE C), smoking cessation (EVIDENCE B), acupuncture, (breathing exercises (Evidence A). ***They are only recommended as adjuncts to the regular pharmacotherapy and NOT as monotherapy***

4.6 Asthma Self-Management Plan

Self-management has been defined as the tasks that individuals must undertake to live with chronic conditions,[14] including, having the confidence to deal with medical management, role management and emotional management of their conditions.[15] Self-management education has been found to improve outcomes, reduce costs treatment and improve the quality of life for asthma patients.[16]

Three essential components

- Self-monitoring of symptoms and/or PEF
- Written asthma action plan (see section on acute severe asthma)
  - ✓ Describe how to recognize and respond to worsening asthma
  - ✓ Individualize the plan for the patient's health literacy and autonomy

- ✓ Provide advice about a change in ICS and how/when to add OCS
- ✓ If using PEF, base action plan on personal best rather than predicted
- ■ Regular medical review

SUMMARY OF ASTHMA MANAGEMENT GUIDELINE

- The goal of asthma therapy is to maintain control of asthma with the least amount of medication and hence minimal risk for adverse effects. (Evidence A)
- Assess asthma severity based on measurements of impairment and classify as appropriate. (Evidence A)
- Select treatment that corresponds to the patient's level of asthma severity. (Evidence A)
- Patient adherence and technique in using medications correctly should be assessed. (Evidence B)
- A temporary increase in anti-inflammatory therapy may be indicated to re-establish asthma control. (Evidence D)
- Other factors that diminish control may have to be identified and addressed. (Evidence C)
- A step up to the next higher step of care may be necessary. (Evidence A)
- Consultation with an asthma specialist may be indicated. (Evidence D) If: there are difficulties achieving or maintaining control of asthma; immunotherapy or omalizumab is being considered; the patient requires step 4 care or higher; or the patient has had an exacerbation requiring a hospitalization.

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ASTHMA **CONTROL**

5.1 What Is Asthma Control?

This refers to the control of disease manifestations both in terms of symptoms and laboratory investigations. *(International Consensus Report on Diagnosis and Treatment of Asthma, 1992).* Poor assessment of asthma control is a major cause of suboptimal asthma management worldwide, so the focus is now shifting to an assessment and treatment approach based control. Asthma control implies the following:

- No (minimal*) day-time symptoms
- No limitation of activity
- No nocturnal symptoms
- No (or minimal) need for rescue medication
- Normal lung function
- No exacerbation

Minimal *= Twice or less per week
GINA 2015

Assessment of asthma control takes into consideration the following parameters:

- Nocturnal symptoms / awakening
- Need for rescue / "reliever" treatment
- Lung function (PEF or FEV_1)
- Exacerbation

The assessment of asthma control has become pivotal in the management of asthma. However, several surveys in developed nations have shown that the majority of patients with asthma do not enjoy adequate asthma control. This has been shown by several studies carried out in different regions of the world.

Asthma Insights and Reality Study (AIRE)[1]: This was a study involving 7 European Countries. 2803 were selected for screening and 73880 house hold was selected. The results showed that :

46% of patient reported day time symptoms

30% reported asthma related symptoms

25% reported unscheduled urgent care visit

10% reported one or more emergency room visits

7% reported overnight hospitalization

50% of patients reporting severe persistent symptoms consider their asthma to be completely or well controlled

Other asthma insights and reality surveys in Japan[2], Europe[1], and Asia[3] Pacific have also documented that most patients are uncontrolled.

According to Chapman et al[4], of the 10,428 patients assessed by 354 physicians, 59% were uncontrolled, 19% well-controlled and 23% totally controlled. Physicians overestimated control, regarding only 42% of patients as uncontrolled.

5.2 Levels of Asthma Control

The different levels of asthma control include: controlled, partly controlled and uncontrolled. This is deducted using the parameters listed, depending on the degree and frequency of occurrence of asthma symptoms. The table below summarizes this.

Table 11: Levels of Asthma Control

LEVELS OF ASTHMA CONTROL			
Characteristic	Controlled	Partly controlled (Any present in any week)	Uncontrolled
Daytime symptoms	None (2 or less/ weeks)	More than twice/ week	3 or more features of partly controlled asthma present in any week
Limitations of activities	None	Any	
Nocturnal symptoms/ awakening	None	Any	
Need for rescue/ "reliever" treatment	None (2 or less/ weeks)	None (2 or less/ weeks)	
Lung function (PEV OR FEV_1)	Normal	<80% predicted or personal best (if known) on any day	
Exacerbation	None	Once or more/ year	1 in any week

5.3 Adverse Effects of Poor Asthma Control

Poor asthma control is known to cause several adverse effects. Some of these are:

1. Increased death from asthma[5,6]
2. Chronic airway changes
3. Chronic fatigue
4. Chronic psychological dysfunction
5. Frequent emergency visits
6. Presenteeism (present at work but poor performance)
7. Absenteeism
8. Severe muscular in children
9. Increased cost of asthma treatment

5.4 Assessment of Symptom Control

Several instruments have been developed, tested and validated for several years for their reliability and reproducibility to measure asthma control.

Some of these tools include:

- The Asthma Control Test (ACT) (Nathan et al., 2004)[7]
- The Juniper Asthma Control Questionnaire (ACQ) (Juniper et al., 1999)[8]
- Asthma Therapy Assessment Questionnaire (ATAQ) (Skinner et al., 2004)[9]
- Asthma Control Scoring System (ACSS) (Boulet et al., 2002)[10]

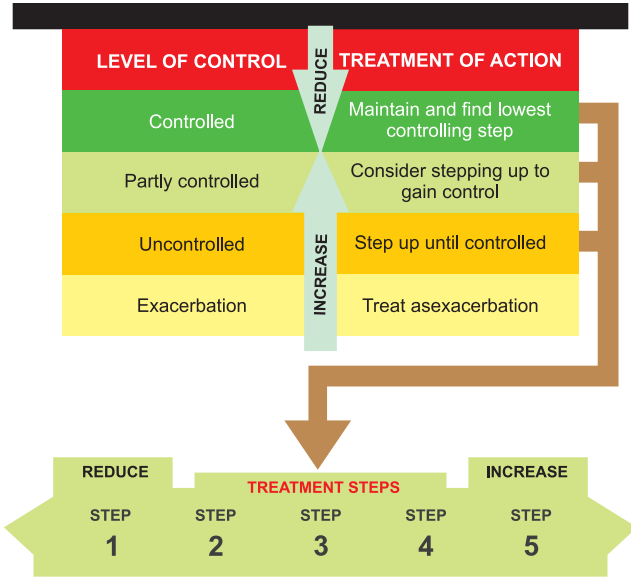
** The simplest form is the ACT.

Table 12 summarizes the different instruments.

Table 12: Summary of different instruments of ACT

ASTHMA CONTROL TEST (1)	ASTHMA CONTROL QUESTIONNAIRE (ACQ) (2)	ASTHMA THERAPY ASSESSMENT QUESTIONNAIRE (ATAQ) (3)
A simple, 5-question tool which asks patients to report, for the prevous 4 weeks, on: 1 Limitations to activities; Shortness of breath, Night-time awakening; Use of rescue medication, and Perception of control; Score ranges between 5 and 25.	7 questionnaire scoring 5 symptoms, FEV, % pred. and daily rescue bronchodilator use. (0 = no impairment, 6= maximum impairment). The ACQ score is the mean of the 7 questions and therefore between 0 (totally controlled) and 6 (severely uncontrolled).	The ATAQ, consists of 4 questions relating to the patient's past month of asthma control and is scored on a scale of 0-4 with a higher score meaning more control issues.
20 - 25: Well-controlled asthma; 16 - 20: Not well controlled asthma; 5 - 15: Very poorly controlled asthma	Score of 0.0 - 0.75 is Well-controlled; 0.75 - 1.25 is grey zone and >1.5 is poorly controlled asthma	0 is Well controlled 1-2 Not well controlled 3-4 Very poorly controlled

Table 13: Different action plans at different levels of control



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6

INHALER DEVICES AND **TECHNIQUES**

6.1 Summary of Practice Points

1. We recommend the use of pMDI + spacer for the delivery of Beta2 agonist and of inhaled corticosteroids in children because it is the most cost effective route of drug delivery and carries less risk of infection compared to the nebulizer. (Evidence A)
2. We recommend the use of pMDI + spacer or DPI in delivering Beta2 agonist in adults because pMDI + spacer is as effective as any DPI in delivering Beta2 agonist in a stable state. (Evidence A)
3. We suggest the use of Nebulizers for patients with severe exacerbations, especially those with alterations of consciousness, severe respiratory distress and those who cannot perform the correct inhalation maneuver. [Evidence GPP]
4. We suggest the use of spacers for adults with poor coordination when using an MDI, children of all ages: (with a mask for those aged up to 2 years and mouthpiece for those aged over 2–5 years) during an acute asthma attack. [Evidence GPP]
5. We suggest that health care professional must choose appropriate inhaler for the patient, taking into consideration the peculiarity of each patient, this is because of some common errors that are peculiar to a special group of patient. [Evidence GPP]
6. We suggest that HCP must always check patients' inhaler technique at each visit and confirm with a checklist. They should not rely on the patient's assurance that they know how to use their inhaler. [Evidence GPP]

6.2 Introduction

The goal of asthma treatment is to achieve and maintain clinical control with minimal side effects of medications. Drug therapy is the mainstay of management and at one point in time, a patient will benefit from some kind of pharmacotherapy.[1]

6.3 Administration of Asthma Drugs

Asthma treatment can be administered in different ways: the most important is the inhalational route. Inhaled asthma medications can be given either singly or in combination inhalers which most often contain glucocorticosteroids and a bronchodilator.[1-5] The advantages of inhaled therapy are that drugs are delivered directly into the airways, producing higher local concentrations, rapid onset of action with significantly less risk of systemic side effects. [6-7]

6.4 Delivery of Inhaled Medications in Aged 5-12 and Adults

The delivery of Beta2 agonist either by pMDI with spacer device or a nebulizer during acute asthma has not shown any significant differences in patients' outcome[8] (Evidence A). Nebulizers are indicated for severe exacerbations, especially those with alterations of consciousness and cannot perform the correct inhalation maneuver with the pMDI and spacer [Evidence GPP]. In stable asthma, the results of studies in children aged 5-12 and adults found no significant differences in patients' outcome between pMDI + spacer and DPI. [9-11]

For the delivery of ICS in stable asthma in children aged 5-12 and adults, the systematic reviews showed that the use of pMDI + spacer is as effective as any DPI for the delivery of inhaled corticosteroids for stable asthma in children aged 5-12 and in adults[8,11] (Evidence A).

There are no robust data to draw conclusions for delivery of Inhaled medications in children under five.

Table 14: Delivery of Inhaled Medications in Aged 5-12 and Adults

Medications	Acute asthma	Chronic stable asthma
Beta2 agonist	pMDI + spacer Nebulizers for severe exacerbations	pMDI + spacer DPI
Inhaled corticosteroids		pMDI + spacer DPI

6.5 Inhalational Devices

Inhalers are handheld devices that deliver drugs directly to the internal lumen of the airways and onto the therapeutic sites. The efficiency of Inhaler devices is determined by the form of the device, formulation of medication, particle size, the velocity of the aerosol cloud or plume (where applicable), and ease of which the device can be used by the majority of patients. [1-5]

The inhaler devices that are available to deliver these asthma drugs include

a. Pressurized metered-dose inhalers (pMDIs) plus spacers or valve holding chambers (VHCs);

b. Breath-actuated pMDIs (BA-pMDIs);

c. Dry powder inhalers (DPIs);

d. Nebulizers; and

e. Soft mist inhalers[1-5]

6.5.1 Types of Inhaler Devices

6.5.1.1 Pressurized Metered Dose Inhalers (pMDI)

MDI devices consist of a metal canister of medicine that fits inside a plastic casing with a mouthpiece. The pressurized canister contains the drug suspended in a mixture of propellants, surfactants, preservatives, flavoring agents, and dispersal agents. The propellant, which comprises about 80 percent of the aerosol was previously a chlorofluorocarbon (CFC) but it has now been replaced by Hydrofluoroalkane (HFA).

6.5.1.2 The Spacer

A spacer is a special extension device that attaches to a pressurised metered-dose inhaler (pMDI, or 'puffer'). Spacers come in different shapes and sizes and are either 'large volume' or 'small volume' depending on how much air they hold.

The large-volume spacers are oval-shaped spacers that usually come in two

pieces that you assemble before use. They can be used by adults and children over 5 years of age. The use of a large volume spacer (holding chamber) improves drug delivery from a pMDI (Evidence A).[8.12]

The small-volume spacers are a tube or cone-shaped spacers and, because they are smaller, they are suitable for children under 5 years of age.

Spacers when used to deliver glucocorticosteroids reduce deposition in the oropharynx, the frequency of dysphonia, upper airway irritating cough, oral candidiasis (Evidence A) and the risk of systemic side effects (Evidence B) [13]. Mouth washing with water (rinsing, gargling) and spitting are effective in reducing the amount of drug swallowed and absorbed systemically.[14]

6.5.1.3 A Dry Powder Inhaler (DPI)

It is a device that contains medicine in a dry powder form. The available DPIs include the Accuhaler, Turbuhaler Aerolizer, Breezhaler, HandiHaler, Rotahaler and Spinhaler devices. The most common of them in Nigeria are Accuhaler and Turbuhaler.

6.5.1.4 Nebulizer

A nebulizer is a device that pushes air or oxygen under pressure through liquid medicine. This converts solutions and suspensions into aerosols. If a nebulizer is used for delivery of ICS, it should be used with a mouthpiece to avoid the medication reaching the eyes.

6.6 Using a Device

Each of the inhaler types has pros and cons that must be considered in the selection of a device for a particular patient (Table 15). **If the devices are used correctly as recommended by the manufacturer, all inhalers are effective and can achieve the same therapeutic effect. There is no evidence of the clinical advantage of one device over another when evaluated over a long period of time.**[15, 16]

6.7 Prescribing Devices in a General Population

There is no robust evidence to recommend an order in which devices should be tested for those patients who cannot use pMDI. Therefore, when prescribing inhaler devices in adults and children, the highlighted factors in Table 16 should play a key role.

Tables 15: Device Advantages and Disadvantages

Device	Indications	Advantages	Disadvantages
PMDI	in ⩾5 years old of any severity and during exacerbations for < 5 years it should be used with a spacer device or a valve holding chamber (VHC) mask	Portable, compact, possess high reproducibility between doses and has less risk of contamination It can be used very quickly	Training and skill are required to coordinate activation of the inhaler and the inhalation. There is a high rate of errors.
Spacer	In patients who have difficulty performing adequate MDI technique particularly in young children and the elderly	It improves lung delivery and response in patients who have poor coordination of actuation and inhalation compared to a pMDI alone. There is reduced possibility of oral candidiasis.	Some are not compact and not portable which limit patient's utilization outside of the home. Many chambers can develop static electrical charge on the inner walls, which reduces the lung delivery.
Valve holding chamber (VHC)	It is indicated in <4 years old. VHC with a face mask.	The VHC improves lung delivery and response in patients who have poor MDI technique.	Many chambers can develop static electrical charge on the inner walls, which reduces the lung delivery.
DPI	In a patient who cannot coordinate inhalation and actuation; may be useful for elderly.	Portable, compact, easier to use and does not require the use of spacer [28] No propellant is needed and it is environmentally friendly.	DPI may be difficult for patients to use because of low inspiratory pressure [4,34]. DPI's cannot be used with spacers; this may be a disadvantage in patients who require large doses of steroids.
Nebulizers	It can be used at any age, and especially for those with severe respiratory distress.	Allows delivery >1 one medication simultaneously. It has the ability to deliver very high doses of drugs that are not available as DPIs or pMDI. No propellant is needed and it is environmentally friendly.	Time-consuming than either an MDI or DPI. High risk of infection less portable, and not compact.

Adapted from ref 1-5

Table 16: Key factors to be considered in prescribing devices

1.1	Patient preference /suitability
1.2	Cost of the device in the locality
1.3	Patient's ability to use the device effectively and whereby the patient is unable to use a device satisfactorily an alternative should be prescribed.
1.4	Level of education

Adapted from ref 1-5

6.7.1 Choice of Device to Use in Special Populations

The choice of device is affected by the patients' cognitive ability and impairment, patients' dexterity, and linguistic barrier. The choice of device to be used in special populations is shown in Table 17.

Table 17: Choice of device to be used in special populations

Populations	Problem	Choice
Children	Cognitive ability Age < 2years	MDI, small volume spacer and face mask or Nebulizers with a facemask
	Age 2-4 years	MDI, small volume spacer and mouthpiece
	Age 5-12 years	MDI, small volume spacer or DPI
Elderly	Cognitive impairment	Assistance by caregiver or family member who knows about the prescribed MDI, small volume spacer
	Dexterity problem e.g. osteoarthritis, stroke	Breath-activated inhaler MDI
Linguistic	Linguistic barriers	Avoid prescribing multiple inhalers because of errors
Mechanically-Ventilated Patients		pMDI and in-line spacer, or by a nebulizer
Non-Invasive Mechanical Ventilation (NIV)		pMDI and a spacer with a face mask or with a nebulizer and facemask

Reference 17-23

6.8 Incorrect Inhaler Technique has Significant Clinical Consequences

Clinical studies conducted in Nigeria and other parts of the world revealed that large proportion of patients showed incorrect technique to either standard pressurised metered dose inhalers (pMDIs) or dry-powder inhalers (DPIs).[24-28] In Nigeria, patients who incorrectly used their inhaler

device were twice more likely to have uncontrolled asthma compared with those who used their device correctly.[28] This result was consistent with three large observational studies, which found out that inhaler mishandling may lead to insufficient drug delivery and poor asthma control, absences from work or school, and asthma-related hospitalization.[28-31]

6.9 Strategies by Health Care Professionals to Help Patients Use Inhalers Correctly

1. Most health care professional do not know correct inhaler technique.[32-34] HCP must **confirm** that their knowledge of correct technique is up to date and must not assume their own technique is always correct to be able to educate the patient.[35] Pharmacists and nurses can assist in providing highly effective inhaler skills training to the patients.[36-37]
2. HCP must always **check** patients' inhaler technique at each visit and confirm with a checklist. They should not rely on the patient's assurance that they know how to use their inhaler.
3. HCP must **correct** patient's technique through verbal instruction, physical demonstration and or video instruction in addition to patient information leaflet from the manufacturer because the manufacturer's instruction sheet alone is ineffective in achieving correct technique.[38]

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7

ASTHMA EXACERBATIONS

7.0 Asthma Exacerbations

Exacerbations of asthma are episodes characterized by a progressive increase in symptoms of shortness of breath, cough, wheezing or chest tightness and progressive decrease in lung function, i.e. they represent a change from the patient's usual status that is sufficient to require a change in treatment.[1] Exacerbations may occur in patients with a pre-existing diagnosis of asthma or, occasionally, as the first presentation of asthma.

7.1 Classification

Asthma exacerbations exist along a continuum. The severity of symptoms and signs, along with the findings on functional lung assessment which are more objective, are used to categorize asthma exacerbations as (see Table 18 below):

- Mild
- Moderate
- Severe
- Life-threatening and
- Near fatal

7.2 Acute Severe Asthma

7.2.1 What Is Acute Severe Asthma?

Acute severe asthma or exacerbation of asthma are episodes characterized by a progressive increase in symptoms of shortness of breath, cough, wheezing or chest tightness and progressive decrease in lung function. They represent a change from the patient's usual status that is sufficient to require a change in treatment.[1]

7.2.2 Epidemiology

The prevalence rate of severe asthma in industrialized countries ranges from 2 - 10%.[2] Trends suggest an increase in both the prevalence and morbidity especially in children less than 6 years.

Factors implicated include urbanization, air pollution, passive smoking and change in exposure to environmental allergens. Annual worldwide death from asthma is put at 250 000, mostly due to preventable causes[3].

In Nigeria, studies have reported a mortality rate of 4.9-6% [4,5] among patients admitted for acute severe asthma. An estimated 75% of admissions for Asthma are avoidable and as many as 90% of the deaths from Asthma are thought preventable. Most deaths occurred before admission to hospital.[6]

Table 18: Asthma Exacerbation - Categorized

MILD	MODERATE	SEVERE	LIFE THREATENING	NEAR FATAL
Symptoms				
Breathlessness-while walking May be agitated	Breathless at rest Usually agitated	Breathless at rest Usually agitated Unable to complete sentences	Dyspneic at rest Drowsy or confused Cyanosed	Features of life threatening asthma
Signs				
Tachypnoea End expiratory wheeze	Tachypnoeic Wheezes throughout exhalation Pulse rate: 100 - 120b/min Pulsus paradoxus may be present (10 – 25mmHg)	Tachypnoeic RR >30c/min Use of accessory muscles of respiration Loud inspiratory and expiratory wheeze Pulse rate >120b/min Pulsus paradoxus >25mmHg (only present in 45% of cases)	Feeble respiratory effort with a RR < 12c/min Silent chest Bradycardiaor hypotension	As in features of life threatening asthma
Physical assessment				
PEF ⩾ 70%	PEF 50-69% of Best of predicted.	PEF 33-⩽50% Arterial blood gas (ABG) analysis shows; -Hypoxemia (PaO_2 <8Kpa) and; -Low $PaCO_2$ (<6.0 Kpa) due to hyperventilation SaO_2 < 92%	Peak expiratory flow <33% of predicted ABG shows PaO_2 < 8Kpa, $PaCO_2$ Normal or < 6.0Kpa SaO_2 < 92%	Elevated $PaCO_2$ (> 6.0 Kpa) Low pH < 7.2

7.3 Patient at Risk for Asthma Exacerbations

The risk of asthma exacerbations is increased under the following instances:

- Poor access to healthcare services;[7]
- Late presentation to the emergency department;[7]
- Previous intensive care unit (ICU) admission [7]
- Underuse of steroids; [8]
- Overuse of short-acting B-2 agonists; [9]
- Patient with food allergy [10]
- Poor perception of asthma symptoms by patients [11]
- Presence of co-morbid conditions such as cardiac disease; [12] and
- Psychosocial factors. [13-16]

7.4 Pathogenesis

The clinical expression of asthma is due to four main pathogenetic mechanisms:

- Bronchospasm;
- Airway hyper-responsiveness to a wide range of common allergens;[17]
- Smooth muscle hypertrophy; and
- Excessive mucous secretion and airway oedema.

The exact cause of these airway changes is not completely understood. However, the interaction between genetic and environmental factors is thought to play a central role. The physiological and clinical features of asthma derive from an interaction among the resident and infiltrating inflammatory cells in the airway surface epithelium, inflammatory mediators, and cytokines. The cells thought to play an important part in the inflammatory response are mast cells, eosinophils, lymphocytes, airway epithelial cells, neutrophils, macrophages,[18,] etc. Each of the major cell types can contribute mediators and cytokines to irritate and amplify both acute inflammation and long-term pathologic changes.

The mediators released produce an intense immediate inflammatory response producing the aforementioned reactions. There is a production of thick, tenacious mucous plugs containing fibrin and eosinophils, which may obstruct the airways due to impaired mucociliary transport.[19]

7.5 Physiological Response

The resultant effects of the above mechanisms in an acute setting include:

- An increase in airway expiratory resistance;
- An increase in expiratory time and high volumes of functional residual capacity (FRC);
- Increased total lung capacity (TLC) and residual volume (RV);
- Decreased FEV_1 (forced expiratory volume in 1 second) and peak expiratory flow.

Dynamic hyperinflation also occurs as a result of gas trapped in the lungs. In very severe asthma, FEV_1 may be reduced to about 33% of its predicted value and the RV increased to about 400% of normal. These physiological changes result in breathing becoming more laboured.

7.6 Evolution of Acute Severe Asthma

There are two different pathogenic scenarios involved in the asthma attack progression.[20] When airway inflammation is predominant, the patient shows a progressive (over many hours, days, or even weeks) clinical and functional deterioration (Type 1/slow-onset acute asthma) (see Table 1). Upper respiratory tract infections (URTIs) are frequent triggers and these patients exhibit a slow therapeutic response. In addition, they may have allergic inflammation with eosinophils in the airway.

In the less common asthma progression scenario, bronchospasm is predominant and patients with a sudden-onset asthma attack (Type 2 or asphyxic or hyperacute asthma), characterized by rapid development of airway obstruction (<3–6 h after the onset of the attack). Respiratory allergens, exercise, and psychosocial stress are the most frequent triggers.

Surprisingly, these patients show more rapid and complete response to treatment. Finally, they have a predominance of neutrophils in their airways.

Table 19: Evolution of acute severe asthma.

TYPE 1: SLOW PROGRESSION	TYPEE 2: SUDDEN PROGRESSION
• Slow onset acute asthma • Progressive deterioration >6hrs (usually days to weeks) • 80-90% of asthmatic patients presenting to the emergency room (ER) • F>M • More likely to be triggered by Upper respiratory tract infection. • Less severe obstruction at presentation • Slow response to treatment and higher hospital admission • Airway inflammation mechanism	• Sudden-onset, asphyxic, brittle hyper acute asthma • Rapid deterioration <5hrs • 10-20% of patients presenting to the ER • M>F • More likely to be triggered by respiratory allergens, exercise or psychosocial stress • More severe obstruction at presentation • Rapid response to treatment and lower hospital admission • Bronchospasm mechanism of obstruction

Rodrigo et al. Chest 2004; 125; 1081–102.

7.7 Management of Acute Severe Asthma

7.7.1 Initial Assessment

The essential goals are to determine the degree of airflow obstruction, to identify possible exacerbating factors and possible life-threatening complications.

The clinical assessment includes a brief history. This will include assessing the following:

- Determining the time of onset and severity of symptoms (especially compared with previous exacerbations),
- All current medications,
- Prior hospitalizations, and
- Emergency department admission.

Attempts should be made to uncover the cause of the recent exacerbations.

Common causes include exposure to extrinsic antigens, severe viral respiratory infections,[21] inadequate or incorrect medications, exercise, emotions, drugs (such as aspirin, NSAIDS, beta-blockers), seasonal variations, etc. Early warning signs may include nocturnal symptoms of

cough, wheeze, and dyspnoea, which are progressive and poorly responsive to bronchodilators. As the severity increases the patient may manifest a variety of clinical features. These include difficulty with breathing, tachypnea, inability to complete sentences, tachycardia, and audible wheeze, exercise limitation and disturbing sleep.

Physical examination: Look for signs of exacerbation or severity including level of consciousness, temperature, pulse rate, respiratory rate, blood pressure, ability to complete sentences, use of accessory muscles, etc.

Check for signs of complicating factors (e.g. anaphylaxis, pneumonia, atelectasis, pneumothorax or pneumomediastinum).

7.7.2 Physiological Assessment

This is essential in all patients with asthma, particularly during an episode of acute attack. The peak expiratory flow rate (PEF) using a peak-flow meter is a simple and useful test for monitoring the patient's progress.[22] The Peak Expiratory Flow Meter is inexpensive portable and safe.[23,24] The importance of an objective assessment cannot be over emphasised. It has been shown that poor perception of the severity of asthma on the part of the patient and the physicians is a major factor causing delay in treatment, which may result in increased asthma-related morbidity and mortality.[11] Approximately 55% of patients presenting with acute severe asthma will have values 40% of normal of the PEF and one-fifth will range between 40% and 60% of normal. Generally however, FEV_1 of less than 1L or PEF of less than 120 L/min is indicative of severe obstruction.[25]

7.7.3 Radiological Assessment

A Chest radiograph should be obtained to exclude the possibility of life-threatening complications such as pneumothorax, the presence of which may make the attack unyielding to treatment. It could also show evidence of chest infection, which could have been the precipitant of the acute attack.

7.7.4 Other Investigations

During an episode of acute severe asthma, hypoxaemia and hypocapnia are usually the rule. The onset of normocapnia signifies a worsening state and the presence of hypercapnia indicates respiratory failure which portends a worse prognosis. Pulse oximetry is necessary to measure the oxygen saturation (SPO2) in all patients with acute severe asthma to exclude hypoxaemia; this also allows monitoring of SPO2 during treatment which should be maintained at $\geqslant$ 92%. Arterial blood gases measurement should also form part of the assessment of the patient with acute severe asthma,[26] although this may not be readily available in many resource-limited settings.

Serum electrolytes, particularly potassium, should be measured. Low potassium may be the result of hyperventilation or treatment with bronchodilators. Hypokalaemia can cause diaphragmatic muscle weakness and thus worsen the patient's condition.

Electrocardiogram (ECG) changes are usually non-specific but may include sinus tachycardia, ventricular strain pattern, and right axis deviation. A reversible P-pulmonale may occasionally be seen due to increase in pulmonary artery pressure caused by severe hypoxaemia.

Sputum test is not routinely recommended. This may show evidence of bipyramidal crystals (Charcot - Laden crystals) which are composed of eosinophils lysophospholipase, clump of slough epithelial (Creola bodies) and condensed twist of mucus called Curschmann's spirals. Sputum eosinophil count can be done.[27]

Table 20: Clinical assessments/acute severe asthma

Symptoms	Signs	Investigations
▪ Increase nontunal awaking with cough, wheeze and chest tightness ▪ Recent increase in the use of relieve inhalers ▪ Decrease exercise tolerance ▪ May be preceded by upper respiratory tract ▪ Infection or exposure to allergen or other triggers ▪ Difficulty in breathing ▪ Increase in rate of breathing ▪ Anxious, agitated, nervous and irritable ▪ Audible wheezes	▪ Talks in monisyllable ▪ Dyspheic with the use of accessory muscles of respiration ▪ Intercostal, supraclavicular muscle recession ▪ Diaphoretic ▪ RR≥25 cycle/min ▪ RV≥119 beat/min ▪ Loud polyphonic wheeze ▪ ± Pulsus paradoxus	▪ PEF between 50% and 33% of patient's best or predicted ▪ Absolute valued 120 1/min ▪ FEV_1 < 50% of patients or predicted ▪ FEV_1 < 1L ▪ Oxygen saturated d 92% ▪ Hypoxeamia ▪ Hypocapnia ▪ Respiratory Alkalosis ▪ Chest X-ray to rule out pneumothrorax and chest infections

7.8 Summary of Assessments

Table 21: Physiological/biochemical assessment

TESTS	COMMENTS
Lung function measurement	PEF or FEV_1 should be recorded before treatment is initiated, although spirometry may not be possible especially in children. (GINA)PEF provides objective airway assessment. FEV_1 maneuver in can provoke cough. Infants and children do not have necessary cognitive skill to perform spirometry. Only 65% can perform spirometry during acute exacerbation. (EPR-3) PEF is more convenient in the acute situation. Where possible, the same or similar type of peak flow meter should be used. (BTS)
Oxygen saturation	Use Pulse oximeter. Saturation levels <90% signal the need for aggressive therapy (GINA). The aim of oxygen therapy is to maintain SpO2 93–95% (94–98% for children 6–11 years (GINA); 94-98% for all (BTS). Pulse oximetry should be repeated within 30minutes-1hr of initiation of therapy.
Arterial blood gases	1. Blood gases are the goal standard for assessing very severe airway obstruction. However, in less severe exacerbation, it is unnecessary if other objective measurements have been monitored. 2. Considered for patients with a PEF or FEV_1 <50% predicted, or for those who do not respond to initial treatment or are deteriorating. A PaO2<60 mmHg (8 kPa) and normal or increased PaCO2 (especially >45 mmHg, 6 kPa) indicate respiratory failure. Supplemental controlled oxygen should be continued while blood gases are obtained. 3. In acute severe asthma, findings are hypoxaemia because of mismatch and hypocapnia and respiratory alkalosis because of hyperventilation. PaO2 <50mmHg is associated with FEV_1<15% predicted. The degree of hypoxaemia correlates with severity of obstruction. Because of mismatch and ease of correcting hypoxaemia with oxygen therapy, the PaCO2 is the more sensitive indicator of ventilatory abnormalities in acute asthma. With prolonged or chronic airway obstruction, hypercapnia and respiratory acidosis are prominent.

7.9 Treatment

7.9.1 Initial Therapy

The goals for treating acute severe asthma include:

Correction of significant hypoxemia by administering supplemental oxygen, using a face mask, Venturi mask or nasal cannulae to maintain SpO2 of 94-98%. [28] (Evidence C)

Rapid reversal of airflow obstruction. This is best achieved by: - **Repetitive or continuous administration of a Short-Acting bronchodilator (SABA)** [29-31] (EVIDENCE A)

AND

- Early in the course of treatment, **systemic corticosteroids should be administered** to patients who have moderate or severe exacerbations or to patients who fail to respond promptly and completely to SABA treatment. [31,33] **(Evidence A)**

For reduction of the likelihood of relapse of the exacerbation or future recurrence of severe airflow obstruction and in order to intensify therapy), often, a short course of systemic corticosteroids is useful. **(Evidence A)**

7.9.2 Reassessment after Initial Therapy

The patient should be reassessed every 15 minutes after the initial treatment. These should include symptoms assessment and objective measurement with the Peak Flow Meter and pulse oximeter. Improvement will be indicated by reduction in the respiratory rate, ability of the patient to speak in complete sentences, reduction in wheezes and a rising value for the Peak Flow meter measurement and oxygen saturation level. Failure to improve will require use of adjunctive therapy as indicated below.

7.9.3 Adjunctive Therapy

Nebulized Ipratopium Bromide: The use of SABA and ipratropium, a short-acting anticholinergic, was associated with fewer hospitalizations and greater improvement in PEF and FEV_1 compared with SABA alone.[34]

Intravenous Aminophylline (5mg/kg loading dose over 20 mins then 0.5mg/kg/hour): This should not be used in the management of asthma exacerbations, in view of their poor efficacy and safety profile, and the greater effectiveness and relative safety of SABA.[35] Therapy with oral or intravenous methylxanthines does not improve lung function or other outcomes in hospitalized adults. [36] (EPR-3, BTS, GINA)

7.9.4 Other Treatments Continued

Intravenous Magnesium sulphate (1.2-2g infusion over 20 mins): It is not recommended for routine use in asthma exacerbations.[37] However, when administered as a single 2g infusion over 20 minutes, it reduces hospital admissions in some patients, including adults with FEV_1 <25–30% predicted at presentation; adults and children who fail to respond to initial treatment and have persistent hypoxemia; and children whose FEV_1 fails to reach 60% predicted after 1 hour of care (Evidence A).[37] The use should however be in addition to the administration of short-acting bronchodilator, oxygen and steroid and not as a single therapy.

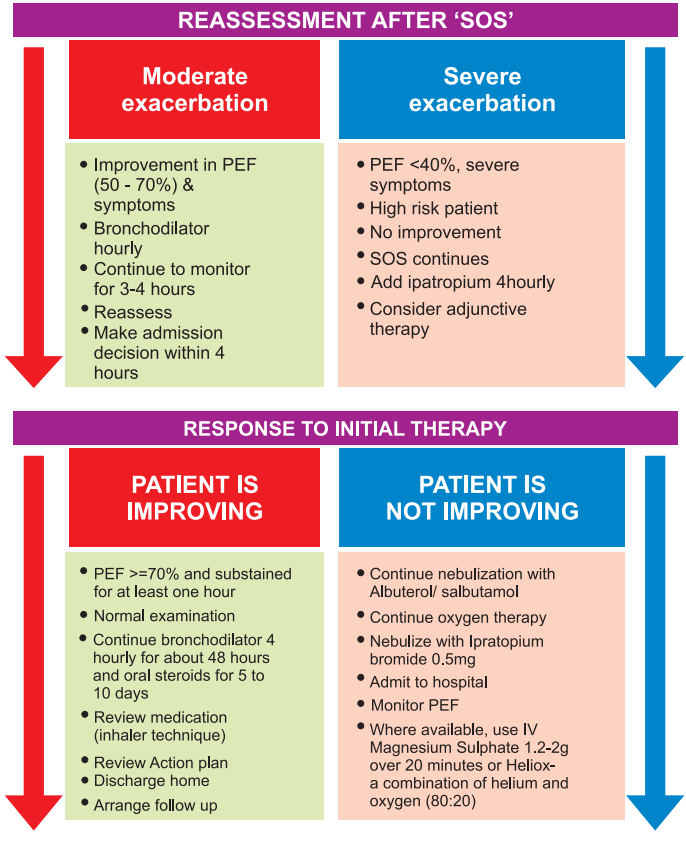
Heliox: Heliox is a combination of oxygen and Helium. Studies suggest there is no role for this intervention in routine care (Evidence B), but it may be considered for patients who do not respond to standard therapy. [38]

7.9.5 ANTIBIOTICS

Antibiotics are not usually indicated in management of acute severe asthma except as needed for comorbid conditions (Evidence B; EPR-3). [39] Bacterial, Chlamydia, or Mycoplasma infections infrequently contribute to exacerbations of asthma.

The use of antibiotics is not usually indicated unless there is strong evidence of infection (such as fever and purulent sputum and for patients who have evidence of pneumonia) (EPR–3).[39]

SUMMARY OF INITIAL THERAPY	
Treatment	**Comments**
Inhaled short-acting beta2-agonists (Salbutamol/Albuterol) Dose of 2.5-5mg	**Nebulized or via pMDI/Spacer delivery** (GINA, BTS, EPR-3). Repeat 15-30mins or continuous in lack of initial response. Reduced hospitalizations and better lung function with continuous compared with intermittent nebulization (1).
Oxygen	**40-60% continuously. This is usually given by nasal cannula or face mask** to achieve arterial oxygen saturation of 93–95% (94–98%) for children 6 – 11 years (GINA). Controlled low flow oxygen therapy is associated with better physiological outcomes than with high flow 100% oxygen therapy (2)
Systemic Steroids	**Speedy resolution of exacerbations and prevent relapse** (Evidence A). Should be administered within 1 hour of presentation(3). Given mainly in form of oral prednisolone (40-60mg). Intravenous hydrocortisone (200mg 4-6 hourly) may also be given especially. in moribund patients or patients that cannot tolerate orally.



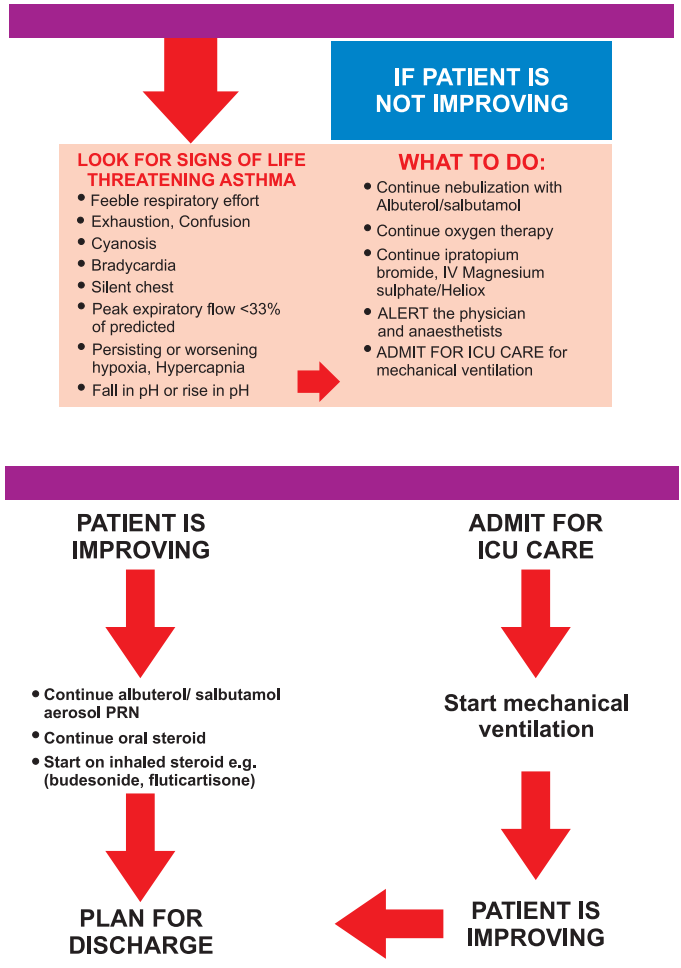


Figure 4: Algorithm for management of acute severe asthma

7.10 The Use of Pressurized Metered Dose Inhalers (MDIs) and Nebulizers (EPR-3)

Studies that compared nebulization with pressurized metered dose aerosols in acute asthma have not shown much difference.

In mild or moderate exacerbations, equivalent bronchodilation can be achieved either by high doses (4–12 puffs) of a SABA by MDI with a valved holding chamber (VHC) in infants, children, and adults under the supervision of trained personnel or by nebulizer therapy

Advantages of Nebulizers

- Nebulizer therapy is preferred for patients who are unable to cooperate effectively in using an MDI because of their age, agitation, or the severity of the exacerbation[2].
- Nebulization is the preferred option:
  - the acutely ill,
  - the elderly who do not have good hand coordination, and young children.
- Since it can be oxygen-driven it gives an extra advantage in the management of acute asthma.
- Ease of use by the patient
- Can be inhaled by tidal breathing either by face mask or nasal canula
- Moisture obtained from wet aerosol may be helpful in loosening the mucus in the airways.

Note: Oxygen-driven nebulizers are preferred for nebulizing β2 agonist bronchodilators because of the risk of oxygen desaturation while using air-driven compressors.

In severe asthma that is poorly responsive to an initial bolus dose of β2 agonist, consider continuous nebulization with an appropriate nebulizer. (BTS 2014)

7.11 Further Investigation and Monitoring

- Measure PEF every 15-30mins initially and at least 4 times daily while admitted
- Measure SPO2
- Measure arterial blood gas if SPO2 is <92%, patient deteriorates or has not improved in 4 hours
- Measure vital signs: heart rate, respiratory rate
- Assess the skin turgor and tongue for signs of dehydration
- Potassium and blood glucose
- Serum theophylline (10-20mg/L)
- Chest radiograph to exclude pneumonia and pneumothorax

PLEASE DO NOT GIVE SEDATIVE.

7.11.1 Signs of Deterioration

- Respiratory rate moves from tachypnea to bradypnea.
- Pulse rate moves from tachycardia to bradycardia.
- The blood pressure will be low and decreasing.
- Sensorium moves from drowsiness to stupor and to coma if not reversed.
- PFR less than 33% of expected or patient's best
- The blood gases move towards hypoxia with normocapnia or hypercapnia.

7.11.2 When to Discharge

- Absence of symptoms like dyspnoea, chest tightness, wheeze or cough
- Pulse rate falls to between 60 -100beats/min
- Respiratory rate 16 - 20 cycles/min
- Chest becomes clear with normal breath sounds
- Sputum becomes clear with thin secretions showing adequate airway clearance

- Absence or resolution of anxiety
- Afebrile
- Normal chest x-ray
- Normal Arterial blood gases/pulse oximetry
- Normal and improved peak flow and spirometry
- When the absolute lung function and peak flow is greater than 80% of patient's best or predicted
- When the variation between morning and evening peak flow reading is less than 25%

7.11.3 Discharge Criteria

- Patient should have been on discharge medication for 24h and have had inhaler technique checked and recorded
- FEV1 or PEF $\geqslant$ 70% or diurnal variability should be <25%
- Treatment with oral and inhaled steroids in addition to bronchodilators. Prescribe at least a 5–7 day course of oral corticosteroid OCS for adults (prednisolone or equivalent 1 mg/kg/day to a maximum of 50 mg/day) (GINA), 3-10day OCS course (EPR-3).
- Ensure that the patient is educated about his/her asthma.
- Teach them to study their asthma and avoid possible triggers.
- Make sure they possess a peak flow meter and teach how to use and calibrate it. (See previous chapters on Inhaler Devices and Techniques)
- Give a written self-management plan which should specify what to do in case of deterioration of symptom and where to seek help.
- Check and recheck their inhaler techniques.
- Link them up with asthma charity organizations.
- Link them up with a respiratory physician for continued care and management.
- Certain patients may need MEDIC ALERT bracelet (Brittle Asthmatics).

- Follow-up appointment in respiratory clinic within one week of discharge.
- Encourage regular clinic visit.

Before discharge, the patient should be well educated and a written management plan should be given.

7.12 Component of Patient's Education

1. Patients should know the inflammatory nature of asthma.
2. The attending physician and nurse should encourage partnership between the patient, care giver and asthma care groups.
3. They should emphasize the need for preventative therapy preferably inhaled steroids.
4. The patient should know the purpose and action of their medication.
5. The patient should be taught how to recognize asthma triggers and strategies to avoid them.
6. The patient should be taught proper inhaler techniques.
7. The patient should be taught how to perform the peak flow reading and use it to monitor their symptoms
8. There should be a written action plan and patients should be taught how to implement it.
9. The patient should be taught when, where and how to seek assistance when the need arises.
10. They need to encourage the patient to be compliant with therapy and clinic visit.

Alert level	Features	Recommended action
Green	Peak flow 80 - 100% of personal best. No symptoms, normal activities, sound sleep.	Continue maintenance therapy. B agonist as required ± regular inhaled steroids.
Yellow	Peak flow 50 - 80% of personal best; there may be coughing, wheezing and activities could be restricted; sleeps poorly.	Double the dose of inhaled steroids and continue other medications.
Red	Peak flow less than 50% of personal best. Coughing, short of breath, difficulty walking and talking.	Start course of oral steroids and institute management for severe asthma. Seek medical help.

Figure 5: The traffic light system of self-management plan

7.13 Complications of Acute Severe Asthma

1. Respiratory failure
2. Pneumothorax due to rupture of a bullae
3. Hypokalaemia as a result of hypoxia and as a complication of the B2 agonist
4. Severe bronchial obstruction due to mucous plugging (Asphyxia)
5. Dehydration
6. Other symptoms of the complications of drugs like palpitation, vomiting, headache, cardiac arrest, arrhythmias (aminophylline), tremor (salbutamol)
7. Hypoxic brain damage

7.14 Differential Diagnosis

- Acute pulmonary oedema
- Acute bronchiolitis in children
- Foreign body inhalation
- Acute exacerbation of COPD

- Upper airway obstruction
- Pulmonary thromboembolism
- Hyperventilation syndrome
- Vocal cord dysfunction.

7.15 Factors that Increase the Risk of Asthma Related Deaths

- A history of near-fatal asthma requiring intubation and mechanical ventilation
- Hospitalization or emergency care visit for asthma in the past year(s)
- Currently using or having recently stopped using oral corticosteroids (a marker of event severity)
- Not currently using inhaled corticosteroids
- Over-use of SABAs, especially use of more than one canister of salbutamol (or equivalent) monthly
- A history of psychiatric disease or psychosocial problems
- Poor adherence with asthma medications and/or poor adherence with (or lack of) a written asthma action plan
- Food allergy in a patient with asthma

Table 22: Summary table of drugs for acute severe asthma

DRUGS FOR ACUTE SEVERE ASTHMA				
Drugs	**Route of administration/Dosage**	**Main side effect**	**1st/2nd line**	**Nursing considerations**
B_2 agonists	• Inhaled route nebulizer e.g salbutamol (2.5mg 5mg) per dose • Metered dose inhaler 4-10puffs through a volumatic • · Intravenous route	• Muscle tremor • Tachyucardia • Hypocalcaemia • Restlessness • · Hypoxemia	**1st line**	• Check vital signs • Check inhalational technique • Monitor baseline and periodic pulmonary function • Monitor blood glucose level for diabetes patients.
Oxygen	Nasal cannula 40-60% 4-6 litres	• Fire accident • Pulmonary edema	**1st line**	• Oxygen therapy can be anxiety provoking • Provide sufficient explanations and allow patient to express their anxiety • Identify those at risk of oxygen toxicity. • Avoid facemask for claustrophobic patients • Check oxygen delivery system to ensure adequate functioning.

DRUGS FOR ACUTE SEVERE ASTHMA				
Drugs	**Route of administration/ Dosage**	**Main side effect**	**1st/2nd line**	**Nursing considerations**
Steroid	Oral e.g predisolone1mg/kg 40-60mg Intravenous e.g hydrocortisone.200mg iv 6hr	Rare in acute administration Weight gain Hypertension etc.	1st line	Check for symptoms for excess steroid use. Moon face Excessive fat pad Acne Edema
Amino-phylline	Parental 5mg-7.5mg/kg as a start dose 0.5mg/kg/hr as an infusion	GIT disturbance Headache Cardiac Arrhythmia	2nd line	Assess for toxicity Check serum theophylline level
Antichol-inergic	Nebulized	Dry mouth Bitter taste Glaucoma in the elderly	2nd line	Monitor closely elderly patients especially people with PBH Encourage enough fluid intake.

7.16 Summary of Key Recommendations in the Management of Acute Severe Asthma

- ✓ Assess patient to establish the diagnosis.
- ✓ Carry out an objective assessment using spirometry and/or Peak Expiratory Meter.
- ✓ Give patient short acting bronchodilator either in the form of nebulization or with spacer device. ***(EVIDENCE A)***
- ✓ Give intranasal oxygen –moderate to high dose (40-60%). (***EVIDENCE C)***
- ✓ Give oral steroid at 0.5-1mg/Kg body weight. ***(EVIDENCE A)***
- ✓ In patients who can are vomiting, very ill and cannot tolerate orally, Intravenous steroid in form of hydrocortisone may be administered.
- ✓ Assess patient clinically and objectively every 15 minutes for response.
- ✓ Add other medications like Ipratropium bromide***(EVIDENCE B)*** and intravenous aminophylline(***GOOD PRACTICE POINT***) if response is not adequate.
- ✓ Add IV Magnesium sulphate where available.***(EVIDENCE B)***
- ✓ Heliox may also be administered if available. ***(EVIDENCE B)(USE IS MAINLY IN CLINICAL TRIALS)***
- ✓ Prepare patient for mechanical ventilation if there is no adequate response to all of the above. ***(EVIDENCE C)***
- ✓ Ensure patient fulfil discharge criteria before discharge.

Schedule a follow-up visit within the next two weeks.

7.17 Asthma Phenotypes and Endotypes

Phenotype is defined as the characteristic of an organism resulting from the interaction of its genetic make-up and environment. It is any observable characteristic or trait of a disease, such as morphology, development, biochemical or physiological properties, or behaviour, without any implication of a mechanism.[40]

The goal of the asthma phenotype task force, which was a collaboration among the National Heart, Lung, and Blood Institute (NHLBI), National Institute of Allergy and Infectious Diseases (NIAID), American Academy

of Allergy, Asthma & Immunology (AAAAI), American Thoracic Society (ATS) and European Respiratory Society (ERS), was to develop definitions of asthma phenotypes that will:

- enhance interpretation of studies, promote appropriate comparisons among studies; and
- facilitate genetics research in which phenotype is correlated with genotype.

The group defined 9 phenotypes in 3 general categories:[42]

7.17.1 Trigger-Induced Asthma

1) Allergic
2) Non-allergic
3) Aspirin-exacerbated respiratory disease (AERD)
4) Infection-induced
5) Exercise-induced

7.17.2 Clinical Presentation Of Asthma

1) Pre-asthma wheezing in infants
2) Episodic (viral) wheeze
3) Multi-trigger wheezing
4) Exacerbation-prone asthma
5) Asthma associated with apparent irreversible airflow limitation

7.17.3 Inflammatory Markers of Asthma

1. Eosinophilic; and
2. neutrophilic asthma

7.18 Asthma Endotypes

An endotype is a subtype of a condition, which is defined by a distinct functional or pathobiological mechanism.[41]

It is envisaged that patients with a specific endotype present themselves within phenotypic clusters of diseases.

Variability in clinical characteristics, inflammatory profiles and responses to treatment has made it increasingly clear that severe asthma is not a single disease.

Treating asthma based on phenotypes has been shown to be suboptimal. Although phenotyping refers to grouping individuals with similar observable characteristics, endophenotyping, or 'endotyping,' reefers to groups of individuals on the basis of underlying molecular mechanisms or treatment responses.[43]

In order to define possible endotypes, a group of experts selected 7 parameters, which include: [42]

1. Clinical Characteristics;
2. Biomarkers;
3. Lung Physiology;
4. Genetics;
5. Histopathology;
6. Epidemiology; and
7. Treatment Response.

It was proposed that each endotype should form a distinct entity based on these parameters.

The concept of endotype is still evolving and its clinical significance has not been fully established.

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DIFFICULT/SEVERE **ASTHMA**

8.1 Summary of Practice Points

1. We suggest that patients with difficult asthma should be systematically evaluated, including confirmation of the diagnosis of asthma, and asthma mimics excluded. (Evidence D)
2. We suggest that the assessment and treatment of coexisting comorbidities should be facilitated by a dedicated multidisciplinary team of specialists. (Evidence D)
3. We suggest that physicians should always consider poor adherence to maintenance therapy before escalating treatment in patients with severe asthma. (Evidence C)
4. We suggest the use of inhaled corticosteroids (ICS) and one or two controller agents as pharmacotherapy. (Evidence B)
5. We suggest that in patients with severe asthma and recurrent exacerbation, allergen testing to molds should be performed. A trial of simple avoidance strategies should be given consideration. (Evidence C)
6. We suggest four months trial of Itraconazole in adults with severe asthma and recurrent exacerbations of ABPA. (Evidence C)
7. We recommend bronchial thermoplasty in adults with severe asthma in highly selected patients with difficult asthma despite the use of recommended therapeutic regimens. (Evidence A)
8. We recommend that treatment is guided by clinical criteria and biomarkers if expertise is available (Evidence A). In children with severe asthma: we suggest treatment guided by clinical criteria alone rather than by clinical criteria and sputum. The use of FeNO to guide therapy in adults or children is not recommended because of the cost and lack of benefit.
9. We suggest that clinicians do not use immunotherapy, methotrexate, azathioprine, chloroquine, cyclosporine, gold and macrolide antibiotics in adults and children with severe asthma (Evidence GPP). This recommendation applies only to the treatment of asthma; it does not apply to the use of macrolide antibiotics for other indications, e.g. treatment of bacterial respiratory infections.

8.2 Definition of Severe Asthma

Most patients with asthma have a mild-to-moderate disease that can be well controlled with inhaled corticosteroids with or without add-on therapy.[1] There is a subset of patients apparently unresponsive to corticosteroids and in the literature, they have been given arrays of terminologies. These include difficult-to-treat asthma, therapy-resistant asthma, steroid-dependent asthma, brittle asthma, refractory asthma, severe asthma and difficult asthma.[2-6] In 1999, a European Respiratory Society Task Force adopted the term difficult asthma. In 2000, the American Thoracic Society (ATS) adopted refractory asthma while both societies and WHO adopted severe asthma in their reports in 2013 and 2000 respectively.[7-8]

According to ATS/ERS definition, severe asthma includes patients with refractory asthma and those in whom treatment of comorbidities such as severe sinus disease or obesity remains incomplete, the types of patients that are of greatest concern to the countries primarily served by the two societies. This position is understandable because most anti-asthma treatments are available and for the majority of patients are affordable.

The WHO Consultation on Severe Asthma in 2009 characterized severe asthma into three groups to facilitate epidemiologic research and comparisons across studies in different populations. The three groups of severe asthma include 1) Untreated severe asthma 2) Difficult-to-treat severe asthma and 3) Treatment-resistant severe asthma. In Nigeria, most patients with severe asthma will fall into the first category because of the unaffordability of asthma medication.

The decision-making steps for characterizing severe asthma by WHO, with correlating action steps for clinical management, are depicted in Figure 6.[8]

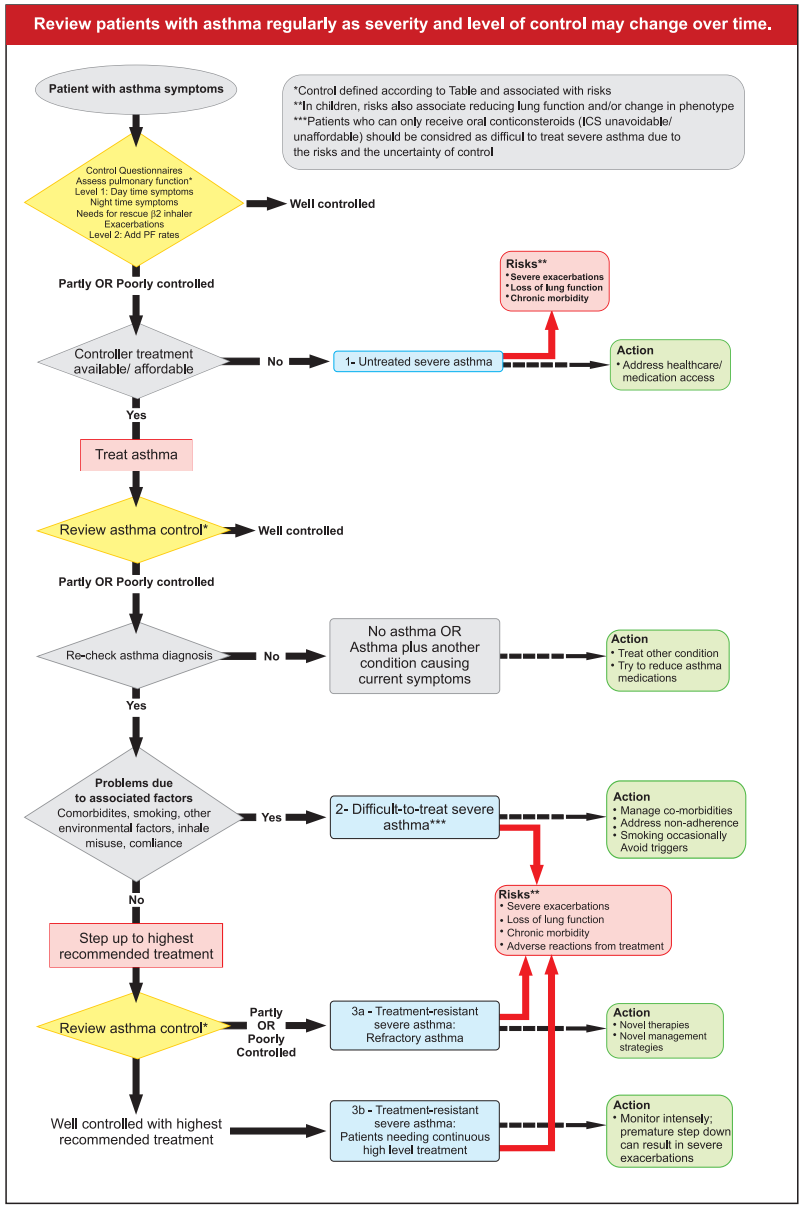

Figure 6: Decision-making steps for characterizing severe asthma, with correlating action steps for clinical management. PF: Pulmonary function.

8.3 Epidemiology

Approximately 5–10% of asthmatics are estimated to have the severe disease in western countries,[10] while in Nigeria 16.0 % of patients reported their asthma as severe.[11] Patients with difficult asthma account for up to 50% of the total health costs through hospital admissions, use of emergency services and unscheduled physician visit.[12] The risk factors for severe asthma are non-adherence to treatment and poor inhaler technique, persistent environmental exposures, incorrect diagnosis of asthma and psychosocial factors. Other factors may include allergen exposure, obesity, cigarette smoking, occupational irritants, obstructive sleep apnoea and medication like aspirin, non-steroidal anti-inflammatory drugs.[1,6-21]

8.4 Management of Severe Asthma

The first step in the management of severe asthma is to confirm the diagnosis of asthma and exclude asthma mimics (Table V in section on Diagnosis). The second step is to determine that the patient with asthma has "severe asthma" and the third step is to conduct an appropriate assessment of confounding factors and comorbidities (Table I).[22-32] Finally, determine the phenotypes and biomarkers which may be useful in optimising therapy and then instituting appropriate therapy (Table II).

Table 23: Factors Contributing to Difficult Asthma

Comorbidities and risk factors	Treatment	Evidence
1) Poor inhaler technique	a) Checking and correcting inhaler technique using a standardized checklist	A
2) Poor medication adherence		
3) Incorrect diagnosis 4) Rhinosinusitis/(adults) nasal polyps	and b) Individualised interventions [22-24] Adherence intervention[1,9,20]	GPP
5) Psychological factors: personality trait, symptom perception, anxiety, depression	Multidisciplinary approach[9]	D
	Nasal corticosteroid[1,9,20]	GPP
	Psychiatric intervention[25]	C
6) Vocal cord dysfunction	Speech therapy	GPP
7) Obesity	Weight reduction	B
8) Smoking/smoking related disease	Treatment of the condition	B
9) Obstructive sleep apnoea	Weight Reduction strategies[26]	GPP
10) Hormonal influences: premenstrual, menarche, menopause, thyroid disorders	Cessation therapy [27-29]	GPP
	Weight Reduction, CPAP/Surgery [26,30]	GPP
11) Gastro-oesophageal reflux disease (symptomatic)	Specialist referral	GPP
12) Drugs: aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), b-adrenergic blockers, angiotensin converting enzyme inhibitors	Proton-pump Inhibitor and anti-reflux [31] surgery	GPP
13) Persistent environmental exposures	Avoidance of the implicated drug [1,9,20]	A
14) to allergen chemical and irritants	Serum IgE and Consider trial of simple avoidance strategies [1,9,20,32]	C

Table 24: Phenotypes & Biomarkers Guiding Therapy

Inflammatory biomarkers	Recommendation	Evidence
Fractional exhaled nitric oxide (FENO)	Not recommended	E
Sputum differential eosinophil count	Recommended only for adult	A
Phenotypes		
Allergic	Recommended for children and adult	A
eosinophilic asthma	Recommended for children and adult	A
aspirin-exacerbated	Recommended for children and adult	B

8.5 Pharmacotherapy

8.5.1 Inhaled Corticosteroids (ICS)

The mainstay of pharmacotherapy for severe asthma is inhaled corticosteroids (ICS) because only very few patients are completely resistant to corticosteroids. ICS and one or two controller agents such as long-acting ß-agonists (LABA), leukotriene modifiers , oral theophylline

and more recently, tiotropium bromide can be combined together to achieve therapeutic effects[1,4,9,47-48](Evidence B). When the maximum dose of the conventional drug is attained and the patient is not responsive to treatment, a low dose (⩽ 7.5mg/day) oral steroid therapy is indicated in the management of patients [20, 49] (Evidence D). The risk of side effect is common in a patient taking OCS for three months and beyond. The patient should be educated on early recognition of osteoporosis and other side effects, also be monitored and then treated at each clinic visit if the need arises[1,9,20] (Evidence D). The pharmacotherapy for severe asthma is shown in Table 25.

8.5.2 Anti-Ige Monoclonal Antibody

Omalizumab is a humanised monoclonal antibody which binds to circulating IgE, reducing levels of free serum IgE in adults and children over 12 years of age.[1,50,51] It is indicated in patients with severe asthma caused by an allergy.

8.5.3 IL-5 Monoclonal Antibody

Mepolizumab and Reslizumab are humanized monoclonal antibodies to interleukin (IL)-5 that reduce the rate of exacerbations by approximately 50 percent compared with placebo[52-57]. It is specifically indicated for patients with severe asthma aged 18 years and older with an eosinophilic phenotype.

Given the clinical benefits of monoclonal antibodies in severe asthma, in Nigeria, the cost-effectiveness has to be considered. Hence, careful patient selection is paramount and physicians should explore all options before turning to these classes of medication.

8.5.4 Antifungal Agents

Sensitization to molds has been shown to be a risk factor for difficult/severe asthma. Systematic reviews of randomized controlled trials to determine the efficacy of azoles in the treatment of allergic bronchopulmonary aspergillosis concluded that Itraconazole causes over 25% or more decline in serum IgE and improves clinical outcome, at least over the period of 16 weeks.[58-59] Adrenal suppression with inhaled corticosteroids and Itraconazole was noted to be a potential concern.

8.5.5 Bronchial Thermoplasty

Bronchial thermoplasty is a bronchoscopic procedure where controlled radio frequency energy is delivered to the airways in order to reduce the airway smooth muscle mass and attenuate bronchoconstriction. It is indicated in highly-selected adult patients with severe asthma despite the use of recommended therapeutic regimens.[20]

8.5.6 Other Therapies

The use of immunotherapy, macrolides, and steroids sparing agents as single therapy are not recommended for the treatment of severe asthma in adults or children.[60-67]

8.6 Non-Pharmacological Therapy

The non-pharmacological therapy of difficult/ severe asthma includes patient education, development of an action plan, smoking cessation, and review of medication adherence and symptom triggers which were discussed previously in this document.[1,9,20]

Table 25: Treatment of Severe Asthma

Treatment of severe asthma	Evidence
Inhaled Corticosteroids + LABA	**B**
Oral Corticosteroids	**D**
Anti-IgE	**A**
Bronchial Thermoplasty	**A**
Interleukins-5 monoclonal Antibody	**B**
Antifungal agents for recurrent exacerbations of ABPA	**C**
Macrolides	**E**
Steroids sparing agents	**E**

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9

GUIDELINE FOR THE **MANAGEMENT OF ASTHMA** IN NIGERIAN CHILDREN

9.1 Childhood Asthma

9.1.1 Introduction

Asthma in children is a multifactorial, chronic inflammatory disease of the airways. It does not differ symptom-wise from what obtains in adults with asthma, but has a wider variation of possible mimics. Physicians who attend to children can have asthma presenting as flare-ups (exacerbations) or in stable state chronic asthma requiring long term management.

9.1.2 Acute Asthma Exacerbation in Children

A flare-up or exacerbations of asthma are episodes characterized by a progressive increase in symptoms of shortness of breath, cough, wheezing or chest tightness and progressive decrease in lung function that does not respond to the patient's usual bronchodilator therapy. They represent a change from the patient's usual status that is sufficient to require a change in treatment and usually necessitates a visit to a health care provider or treatment with systemic corticosteroids.

Early symptoms of exacerbations in young children may include:

- ✓ increased asthma symptoms
- ✓ increased nocturnal cough
- ✓ reduced exercise tolerance or lethargy
- ✓ impaired daily activities (including feeding)
- ✓ poor response to reliever medication

Exacerbations usually occur in response to exposure to an external agent (e.g. viral upper respiratory tract infection, pollen or pollution) and/or poor adherence with controller medication.

9.1.3 Classification of Acute Exacerbation

Acute asthma exacerbations can be classified into four (mild, moderate, severe, life threatening) and have identifiable parameters for making a bedside clinical diagnosis for the pediatric patient with acute asthma – see Table 1.

Table 26: Classifications for Acute Asthma in Children

Findings	Mild exacerbation	Moderate exacerbation	Severe exacerbation	Life threatening
Confused	No	No	Agitated	Confused or drowsy
Oximetry on presentation (SpO_2)	94%	<94% - 92%	Less than 92%	Less than 92%
Talks in	Sentences	Phrases	Words	Unable to speak
Heart rate (beats/min)	Less than 100	100 - 200	More than 200	Bradycardia, a pre-terminal event
Central cyanosis	Absent	Absent	Absent	Present
Wheeze intensity	Variable	Moderate to loud	Loud or soft	Silent chest
FEV_1/PEFR (best or predicted)	More than 60%	50% - 60%	33% - 50% or unable to perform PEFR measurements due to fatigue	Less than 33% or unable to perform PEFR measurements due to fatigue

9.1.4 Assessment of Acute Exacerbation

The goal of assessment is to properly classify the episode in the child in order to initiate the appropriate therapy.

The initial assessment pathway for acute asthma should follow this sequence:

- ✓ Stabilize the patient (ABC of resuscitation)
- ✓ Assess degree of respiratory distress and classify appropriately (Table 1, Table 2).
- ✓ Obtain relevant history - Presenting history of possible trigger and past asthma history, such as:

1. When diagnosed
2. Previous admissions including to ICU
3. Known triggers
4. Interval asthma symptoms
5. Smoking exposure (direct and indirect)
6. Current and past asthma treatments including compliance and devices used
7. Other atopic/allergic conditions including food allergies
8. Family history of atopic/allergic conditions

- ✓ Assess degree of respiratory distress to enable proper classification and appropriate intervention (Table 2). This includes:

1. Respiratory rate and heart rate and compare with age-appropriate normal ranges (Table 3)
2. Use of accessory muscles and recession
3. Oxygen saturation
4. Ability to talk in phrases, sentences or words
5. Ability to feed
6. Wheeze intensity
7. Presence of cyanosis
8. Assess the mental state (alertness and responsiveness)
9. Assess for any clinical signs of pneumothorax or lung collapse

Increasing tachycardia generally denotes worsening asthma, whereas a fall in heart rate in life-threatening asthma is a pre-terminal event. Although wheezing initially becomes more apparent as airway obstruction increases, severe airway obstruction decreases air flow, with wheezing becoming softer and then diminishing completely (silent chest). It is important to realize that clinical signs correlate poorly with the severity of airways obstruction.[4-8]

Table 27: Paediatric normal ranges

Age (years)	Respiratory rate at rest (breaths/minute)
<1	30-40
1-2	25-35
2-5	25-30
5-12	20-25
>12	15-20

Age (years)	Heart rate at rest (beats/minute)
<1	110-160
1-2	100-150
2-5	95-140
5-12	80-120
>12	60-100

9.2 Investigations

- ✓ **Pulse oximetry** – used to assess for oxygen saturation levels. Low arterial oxygen saturation in room air (SpO_2 <92%) after the initial bronchodilator therapy suggests a more severe group of patients and is an indication for admission.
- ✓ **Lung function measurements (PEFR/Spirometry)** – done to help properly classify patient and monitor response to therapy once treatment is commenced (Table 1)
- ✓ **Routine chest radiograph -** this is not generally required except if pneumothorax or major collapse/consolidation is considered with deterioration despite adequate treatment.
- ✓ **Arterial blood gases (ABG) -** consider this analysis if patient continues to deteriorate. The $PaCO_2$ is low in the early stages of acute asthma as a compensatory mechanism. A normal or raised $PaCO_2$ indicates worsening asthma and respiratory failure.

9.3 Management of Acute Asthma (Table 4, Figure 1)

9.3.1 Initial treatment

The initial treatment of an acute asthma attack consists of repeated doses of rapidly and short-acting inhaled β_2-agonists and systemic corticosteroids (CS). Additional treatment may include ipratropium bromide and oxygen if patient is hypoxic (**Evidence A**).

9.3.1.1 Short-acting inhaled β_2-agonists

These are the mainstay of therapy for acute asthma, and the first-line treatment **(Evidence A).** They stimulate β_2 receptors on airway smooth muscle, resulting in smooth muscle relaxation. The most commonly used agents are salbutamol.

Inhaled β_2-agonists are preferably delivered by pressurised metered dose inhaler (pMDI) with a spacer (2 - 10 puffs, each inhaled separately with five tidal breaths at 15 – 30 second intervals) or by oxygen-driven nebuliser **(Evidence A).** A pMDI and spacer with mouthpiece is recommended for older children, while a spacer with a mask is preferable in younger children

(3 years and less). Ensure that the mask fits closely onto the child's face. A pMDI plus spacer is the preferred drug-delivery device for the treatment of mild to moderate acute asthma, while oxygen-driven nebulisers are preferred for severe or life-threatening acute asthma **(Evidence A).** A locally fabricated spacer can be used if the standard spacer is not available.[9,10]

Frequent doses/multiple doses of β_2-agonists are safe for the treatment of acute asthma **(Evidence A).** Two to four puffs repeated every 20 – 30 minutes depending on age and clinical response should be given for mild attacks; up to 10 puffs may be needed for more severe asthma. When hourly bronchodilators are required for more than 4 - 6 hours, the pMDI-spacer combination should be changed to a nebuliser.

9.3.1.2 Steroids

Corticosteroids (CS) are standard first-line treatment for acute asthma, as they treat the underlying cause of asthma which is inflammation **(Evidence A).** They increase β_2 receptor sensitivity by upregulating β_2 expression on airway smooth muscle. The earlier they are administered in the acute attack, the better the outcome **(Evidence A).** The recommended dose of oral prednisone or prednisolone is 1 mg/kg/d, i.e. 20 mg in children aged 2 - 5 years and 30 - 40 mg in those above 5 years. Oral steroids are as effective as intravenous therapy, and preferable because of their ease of administration, cost-effectiveness and fewer side-effects.

9.3.1.3 Ipratropium bromide (IB)

This is an anticholinergic agent that produces bronchodilation within 20 - 30 minutes. Nebulised IB (250 μg/dose mixed with the nebulised β_2-agonist solution) should be added if the child does not respond to three doses (nebulisation or multidosing via pMDI-spacer combination) of β_2-agonists, or if the symptoms are severe **(Evidence A).** Frequent doses of IB can be used every 20 – 30 minutes, together with β_2-agonists, for the first 2 hours of a severe asthma attack.

The dose frequency should be reduced to 4 - 6-hourly as clinical improvement occurs. Inhaled IB may be especially useful in patients who have been using high doses of β_2-agonists before seeking medical care. IB

alone is a less effective bronchodilator than a β_2-agonist alone, but the combination of nebulised IB with a nebulised β_2-agonist results in greater bronchodilation than a β_2-agonist on its own.[11,12]

9.3.1.4 Oxygen

Children with life-threatening asthma, severe asthma or oxygen saturations less than 95% should receive oxygen via a high-flow face mask or nasal cannulas to maintain normal saturations **(Evidence A)** and be admitted **(Evidence B).** In hospitals, nebulisers should preferably be oxygen-driven.

9.3.2 Additional Therapy for Acute Asthma

When acute severe asthma is not responding to the initial standard therapy additional medications may be required. These include:

- ✓ Magnesium sulphate
- ✓ Intravenous salbutamol
- ✓ Aminophylline
- ✓ Intravenous fluid

9.3.2.1 Magnesium sulphate

A single dose of intravenous magnesium sulphate 25 - 75 mg/kg (recommended dose 50 mg/kg, maximum dose 2 g) given over 20 minutes has been shown to be safe and effective in children with acute severe asthma, who have had a poor response to initial therapy. The response to magnesium appears to be best in patients who present with very severe illness **(Evidence C).** Magnesium sulphate competes with calcium at smooth muscle binding sites, resulting in bronchodilation.

9.3.2.2 Intravenous salbutamol

The use of IV low-dose salbutamol (15 μg/kg as a once-off bolus dose), added to standard therapy in the early management of acute severe asthma in children presenting to the paediatric emergency department may reduce the duration of the exacerbation and hasten the children's discharge from

hospital **(Evidence B).** In the paediatric intensive care unit, a high IV loading dose of salbutamol (5 - 10 μg/kg/min of 1 mg/ml solution infused at 0.3 - 0.6 ml/kg/h for 1 hour) followed by continuous infusion (1 - 5 μg/kg/min at 0.06 - 0.3 ml/kg/h) may be effective, and is probably safer than aminophylline. Continuous intravenous infusion should be considered when there is uncertainty about reliable inhalation of β_2-agonists or for severe refractory asthma. Electrolytes should be monitored regularly **(Evidence C).** Nebulised bronchodilator therapy should be continued while the patient is receiving IV salbutamol.

9.3.2.3 Aminophylline

Aminophylline is the water-soluble salt of theophylline. Both are methylxanthines. Neither theophylline nor aminophylline is indicated in patients with mild to moderate acute asthma **(Evidence A),** but may be used in cases of near-fatal or life-threatening asthma in the ICU **(Evidence C).**

They are less recommended due to their narrow therapeutic index and potentially severe side-effects, such as cardiac arrhythmias or convulsions. A 5 mg/kg loading dose should be given over 20 minutes under continuous ECG monitoring, followed by a continuous infusion at 0.9 to 1 mg/kg/h. The loading dose should be omitted in children receiving maintenance oral theophylline. **(Evidence B)**

9.3.2.4 Inhaled steroids

Insufficient evidence exists to recommend the use of ICS as alternative or additional therapy in acute asthma.

9.3.2.5 Intravenous Fluid

Patients with prolonged severe asthma may become dehydrated as a result of poor intake or vomiting. It is, however, inadvisable to overhydrate patients with acute asthma as they are prone to transcapillary fluid migration and alveolar flooding.

9.3.3 Indications for Hospital Admission

The following are the indications for admission of a case of acute asthma into a hospital:

- ✓ Bronchodilator requirement more frequently than 3 hourly
- ✓ Children who have not improved after receiving up to 10 puffs of short-acting β_2-agonist
- ✓ Oxygen requirement
- ✓ Any sign of related life-threatening asthma, which are:

1. Silent chest
2. Cyanosis
3. Poor respiratory effort
4. Hypotension, bradycardia
5. Exhaustion
6. Confusion or drowsiness

- ✓ Any sign of severe asthma, which include:

1. Unable to complete sentences in one breath; too breathless to talk or feed
2. Agitation
3. Accessory muscle use
4. Heart rate >160 beats/min in children aged <1 year; >140 beats/min in children 1 - 5 2
5. Respiratory rate >50 breaths/min in children aged <1 year; >40 breaths/min in children 1 - 5 years; >30 breaths/min in children >5 years
6. Room air SpO_2 <90% ***at admission***
7. Room air SpO_2 <92% despite bronchodilator therapy
8. PEFR <50% predicted

- ✓ Moderately severe asthma not responding to β_2-agonist therapy
- ✓ Home circumstances which do not allow safe or reliable treatment

9.3.4 Indications for Admission to an Intensive Care Unit

- ✓ Cyanosis or hypoxaemia [PaO_2 <8 kPa (60 mmHg); SpO_2 <90%] unrelieved by oxygen
- ✓ $PaCO_2$ >4.5 kPa (34 mmHg)
- ✓ Minimal chest movement, 'silent' chest
- ✓ Severe chest retractions
- ✓ Deteriorating mental status, lethargy or agitation
- ✓ Cardiorespiratory arrest

9.4 Management of Acute Asthma in Very Young Children

9.4.1 Acute Asthma in Very Young Children

The assessment of acute asthma in early childhood can be difficult as intermittent wheezing attacks are usually due to viral infection and the response to asthma medication is inconsistent. Prematurity and low birth weight, are also risk factors for recurrent wheezing. Various differential diagnoses ought to be considered in this age group. These include aspiration pneumonitis from gastroesophageal reflux disease (GERD), acute bronchiolitis, acute pneumonia, tracheomalacia, and complications of underlying conditions such as congenital anomalies. Treatment in this age group does not differ much from that in the older child (Table 28).

9.4.2 Treatment of Acute Asthma in Children Aged < 2 Years

9.4.2.1 Bronchodilators

A trial of inhaled β_2-agonist bronchodilator therapy should be instituted, in the same doses as for the older child. If there is a poor response to this treatment, the diagnosis of asthma should be reviewed. Oral β_2 agonists are not recommended for acute asthma in infants. For mild to moderate acute asthma attacks, use a pMDI with a spacer and mask for optimal drug delivery. Consider inhaled ipratropium bromide in combination with an inhaled β_2 agonist for more severe symptoms.

Table 28: Management of Acute Exacerbation of Asthma in Children

Severity	Signs of Severity	Management
Mild	Normal mental state, Subtle or no increased work of breathing, Accessory muscle use/recession. Able to talk normally	Salbutamol by MDI/spacer - give once and review after every 20 mins. (×3) – with pre & post vital signs. Salbutamol dose: 6 puffs if < 6 years old, 10 puffs if >6 years old. Ensure device/technique is appropriate. If good response - discharge on β_2-agonist as needed. Given hourly for the next 4 hours, then 4 hourly for the next 2 days. If poor response - treat as moderate asthma. Start oral prednisolone within 1 hour of admission 1 - 2 mg/kg (max. 40 mg) initially, only continuing with 1 mg/kg daily for further 2 days. Provide written Asthma Action Plan on what to do if symptoms worsen. Consider overall asthma control and family's knowledge. Arrange follow-up 2 days to 2 weeks of discharge. Discharge on low dose ICS only or LTRA medication (especially in children <2years) (GINA step 2)
Moderate	Normal mental state Some increased work of breathing Accessory muscle use/recession Tachycardia Some limitation of ability to talk Heart rate ⩽140/min in children aged 2–5 years ⩽125/min in children >5 years Respiratory rate ⩽40/min in children aged 2–5 years; ⩽30/min in children >5 years	**Oxygen** if SpO_2 is < 94%. Need for Oxygen should be reassessed. Salbutamol by MDI/spacer - 1 dose every 20 minutes for 1 hour; review 10-20 min after 3rd dose to decide on timing of next dose. If good improvement manage as mild (above) If no improvement with salbutamol only, consider early add on of nebulized ipratropium bromide Start oral prednisolone within 1 hour of admission 1 – 2 mg/kg/day (max 40 mg) initially, only continuing with 1 mg/kg daily for further 2 days given in the morning. May be discharged same day if still stable, (with appropriate instructions as above)

Severe	Agitated/distressed Moderate-marked increased work of breathing Accessory muscle use/recession. Tachycardia Marked limitation of ability to talk Note: wheeze is a poor predictor of severity. Heart rate >140/min in children aged 2–5 years; >125/min in children aged >5 years Respiratory rate >30/min in children aged >5 years	**Oxygen** as above **Salbutamol** by nebulizer - 1 dose every 20 minutes for 1 hour; review ongoing requirements 10-20 min after 3rd dose. If improving, reduce frequency. If no change, continue every 20 minutes. If deteriorating at any stage, treat as critical requiring ICU admission. **Ipratropium** by nebulizer - 1 dose (dose below) every 20 minutes for 1 hour- 2 hours only. Start at commencement of salbutamol nebulization. Nebulized Salbutamol 2.5 or 5 mg depending on age </> 5 years Nebulized Ipratropium 250 or 500 µg depending on age </> 5 years **Magnesium sulphate 50% (500 mg/mL)** 50 mg/kg over 20 mins. Useful as a one off dose in acute severe asthma not responding/deteriorating after salbutamol use as above Dilute to 200 mg/mL (by adding 1.5mls of 0.9% saline to each 1ml of Mg Sulphate) for intravenous administration If going to ICU, this may be continued with 30 mg/kg/hour by infusion **Aminophylline** use only if deteriorating or child is very sick. Loading dose: 5 mg/kg i.v. (maximum dose 500 mg) over 20 mins. Unless markedly improved following loading dose, give continuous infusion (usually in ICU), or 6 hourly dosing (usually in ward). **Oral prednisolone** (2 mg/kg); if vomiting give **intravenous methylprednisolone** (1 mg/kg) or IV hydrocortisone sodium succinate (5 mg/kg) Arrange admission into the ward or ICU after initial assessment.

Critical/Life threatening	Confused/drowsy Maximal work of breathing Accessory muscle use/recession Exhaustion Marked tachycardia Unable to talk SILENT CHEST, wheeze may be absent if there is poor air entry. SpO_2 <90%	**Oxygen** **Continuous nebulised salbutamol** (use 2 x 5mg/2.5L nebules)* **Nebulised ipratropium** 250 µg 3 times in 1st hr only, (Every 20 minutes, added to salbutamol). **Methylprednisolone** 1 mg/kg i.v. 6-hourly. OR **IV hydrocortisone** 4-6 mg/kg 6 hourly till able to take orally **Magnesium sulphate (dose** as above). This may need to be started immediately (as soon as life threatening asthma is diagnosed) Aim to keep serum Mg between 1.5 and 2.5 mmol/L **Aminophylline** (as above) – to be considered at 4-6 hours after admission and no improvement on already listed medications including MgSO4 May also consider **i.v. salbutamol where available**. 5 µg/kg/min for one hour as a load, followed by 1-2 µg/kg/min.

* The following can occur with salbutamol toxicity: tachycardia, tachypnoea, metabolic acidosis. If these are noticed, consider stopping/reducing salbutamol as a trial if you think this may be the problem.

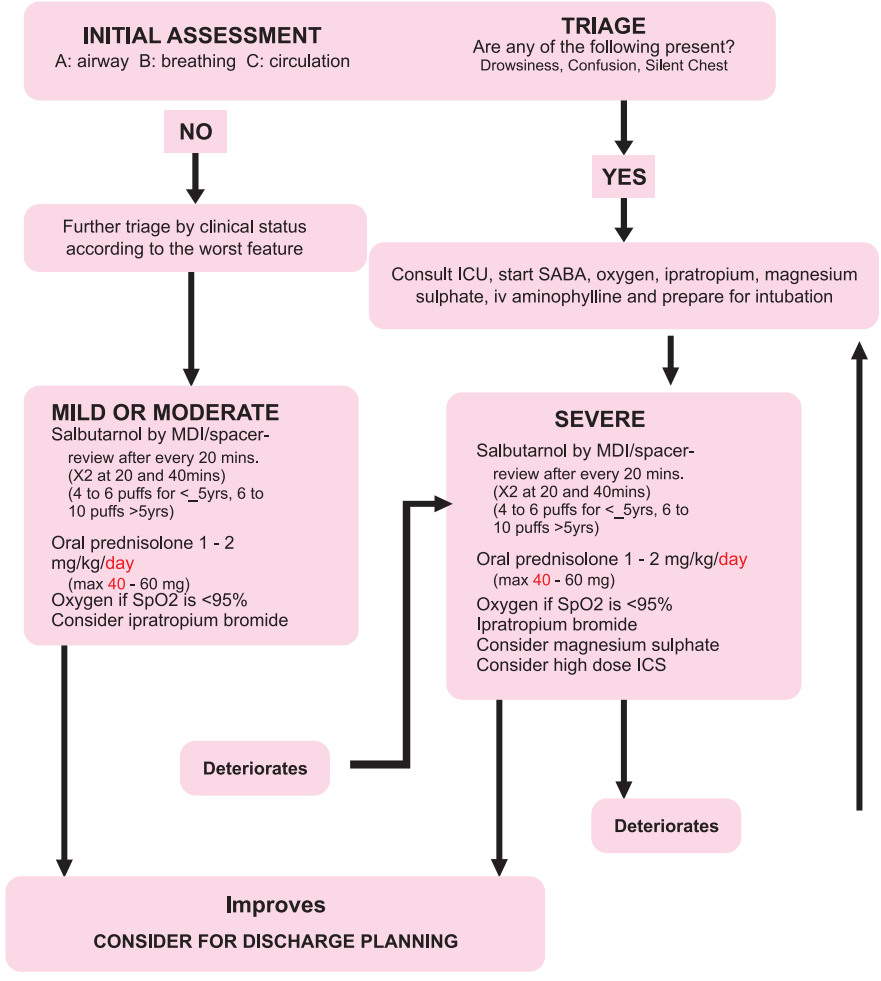

Figure 7: Algorithm for the Management of Acute Exacerbation of Asthma in Children

9.4.2.2 Ipratropium bromide

If there is a poor response to inhaled β_2-agonist therapy (after 3 treatments) or if the symptoms are more severe, add IB in the same dose as for older children.

9.4.2.3 Steroid

In infants, consider steroid tablets early in the management of severe asthma attacks in the hospital. For children with frequent episodes of wheeze associated with viruses, caution should be taken in prescribing multiple courses of oral steroids.

9.4.2.4 Oxygen

Oxygen via close-fitting mask or nasal prongs must be administered to attain $SpO_2 \geqslant 94\%$ **(Evidence A).**

9.5 Indications for Discharge

- ✓ Assess patient for clinical improvement 1 hour following initial therapy and discharge if clinically well. If necessary, reassess again after 30 minutes
- ✓ Adequate oxygenation
- ✓ Adequate oral intake
- ✓ Adequate parental education and ability to administer salbutamol via spacer

9.6 Before You Discharge

- ✓ Each child should have a written action plan.
- ✓ Observe pMDI inhaler technique before discharge.
- ✓ Advise parents to seek further medical attention should the patient's condition deteriorate or if there is no significant improvement within 48 hours.
- ✓ At discharge, all patients should have an outpatient appointment –

2 days to one week after discharge

- ✓ Prescribe first line therapy for asthma control to commence on 3rd day after, at end of oral steroids:[1]i.e. low dose inhaled corticosteroids or leukotriene inhibitors (montelukast).
- ✓ For children with intermittent asthma who commenced ICS following an exacerbation episode, ICS use may be reviewed for discontinuation after 2 weeks.
- ✓ In children less than 2 years, the use of oral LTRA can serve as alternative discharge medication.[1]

9.7 Long-Term Therapy of Asthma in Patients Ages 5 Years to < 18 Years

After a successful management of an acute exacerbation of bronchial asthma, long-term therapy is instituted to prevent acute exacerbations. The goals for therapy are as follows:

- Control asthma by reducing impairment through prevention of chronic and troublesome symptoms (e.g. coughing or breathlessness in the daytime, in the night, or after exertion).
- Reduce the need for a short-acting β_2-agonist (SABA) for quick relief of symptoms (not including prevention of exercise-induced bronchospasm).
- Maintain near-normal pulmonary function.
- Maintain normal activity levels (including exercise and other physical activity and attendance at work or school).
- Satisfy patients' and families' expectations for asthma care.

There are four components of long-term therapy:[13]

- Assessment and monitoring
- Education
- Control of environmental factors and comorbid conditions
- Pharmacologic treatment

Table 29: Classification of Asthma Severity for Initiating Therapy

Components of SEVERITY		Age (Years)	Intermittent	Persistent		
				Mild	Moderate	Severe
IMPAIREMENT	Symptoms	All	⩽2 days/week	>2 days/wk but not daily	Daily	Throughout the day
	Night time awakenings	⩾5	⩽2x/month	3 – 4x/month	> 1x/week but not nightly	Often 7x/week
	SABA use for symptom control	All	⩽2 days/week	>2 days/wk but not daily	Daily	Several times a day
	Interference with normal activity	All	None	Minor limitation	Some limitation	Extremely limited
	Lung function:					
	FEV_1 or PEF (predicted or personal best)	⩾5	Normal FEV_1 between exacerbations >80%	>80%	60 – 80%	<60%
	FEV_1/FVC	5 -11	> 85%	> 80%	75 – 80%	< 60%
		⩾12	Normal	Normal	Reduced 5%	Reduced > 5%
RISK	Exacerbations requiring oral corticosteroids	5 – 11	⩽1 x/year	⩾2 x in 6 months or ⩾ 4 wheezing episodes/year lasting > 1 day AND risk factors for persistent asthma		
		⩾12		⩾ 2 x/year Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. Relative annual risk of exacerbations may be related to FEV_1.		
Recommended step for starting treatment		5 -11	Step 1	Step 2	Step 3	Step 3 or 4
		⩾12				Step 4 or 5
		All			Consider short course of oral corticosteroids	
		All	In 2 – 6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.			

FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; PEF, peak expiratory flow;
SABA, short –acting $beta_2$- agonist.

*Provide guided self-management education (self-monitoring + written action plan + regular review)
* Treat modifiable risk factors and comorbidities e.g. smoking, obesity, anxiety
*Advise about non-pharmacological therapies and strategies e.g. physical activity, weight loss, avoidance of sensitizers where appropriate
* Consider stepping up if… uncontrolled symptoms, exacerbations or risks, but check diagnosis, inhaler technique and adherence first
*Consider stepping down if …symptoms controlled for 3 months + low risk for exacerbations. Ceasing ICS is not advised.

9.8 Assessment and Monitoring

9.8.1 Classify Asthma Severity

Asthma severity is measured in a patient who is not receiving long-term control therapy. Assessment of asthma severity is based on two domains: measures of current impairment and future risk. The concept of impairment includes frequency and intensity of symptoms, and current or recent functional limitations experienced by the patient. The concept of risk includes the likelihood of either asthma exacerbations, progressive decline in lung function, reduced lung growth, or risk of adverse effects from medication. The information gathered is used to characterize the patient's asthma in order to guide decisions for initiating therapy (Table 29). The therapy is deployed as indicated in Figure 8, which is taken together with GINA cycle of asthma care (Figure 9).

"Assess" includes not only symptom control (e.g. with tools such as Asthma Control Test[14] or Asthma Control Questionnaire[15]), but also risk factors, inhaler technique, adherence and patient preference, to ensure that treatment can be tailored to the individual. "Adjust treatment" (up or down) includes not only medications but also non-pharmacological strategies and treatment of modifiable risk factors. "Review response", including side-effects and patient satisfaction, is essential to avoid over- or under-treatment.

Once treatment is started, the focus shifts to how well the patient is able to control his or her asthma using measures of impairment and risk to monitor asthma control rather than severity. Assessment of impairment focuses on the frequency and intensity of symptoms and the functional limitations associated with these symptoms. Risk assessment focuses on the likelihood

of asthma exacerbations, adverse effects from medications, and the likelihood of the progression of lung function decline; spirometry should be measured every 1-2 years, or more frequently for uncontrolled asthma. Because asthma varies over time, follow-up every 2-6 weeks is initially necessary (when gaining control of the disease) and then every 1-6 months thereafter.

The asthma control is determined using the same measures of two domains like asthma severity: 1) current impairment, and 2) future risk (Table 6). Monitoring the level of asthma control is used to adjust medication as needed. Asthma control is defined as "the degree to which the manifestations of asthma are minimized by therapeutic intervention and the goals of therapy are met."[13] Asthma control can be classified as well controlled, not well controlled, or very poorly controlled; classification criteria vary by patient age (Table 30).

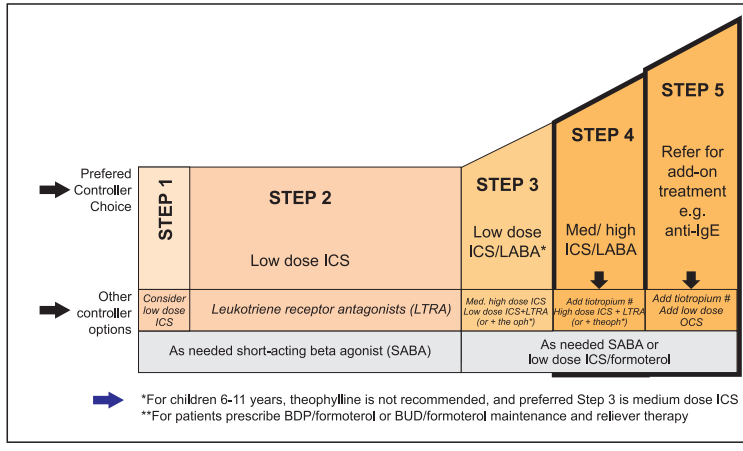

Figure 8. Stepwise Approach to Asthma Medications ©GINA, 2016

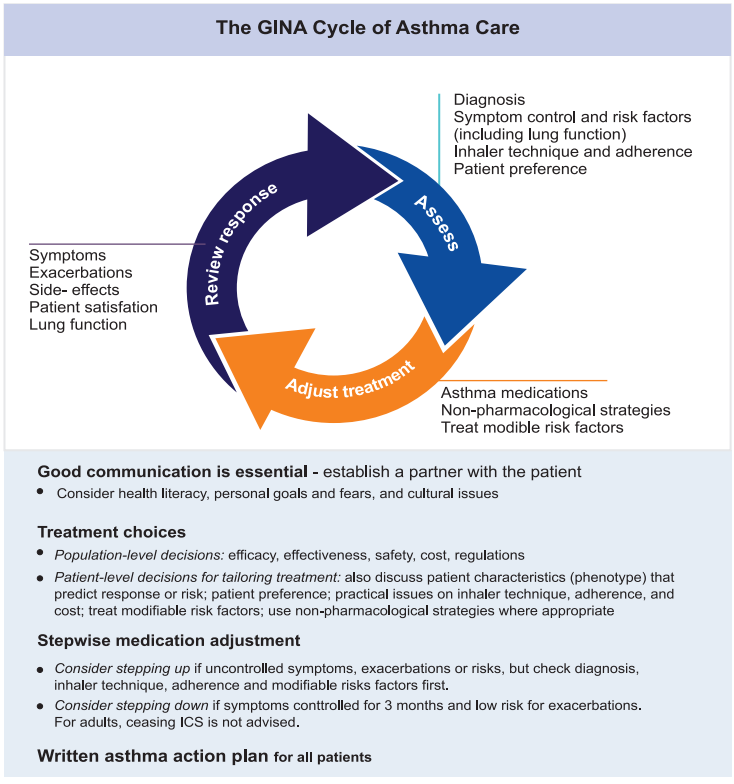

Figure 9: The GINA Cycle of Asthma Care

9.8.2 Education

Adolescent patients and parents or caregivers of younger patients are taught the importance of recognizing the level of control and signs of progressively worsening asthma symptoms.

Both peak flow monitoring and symptom monitoring have been shown to be equally effective; however, peak flow monitoring may be more helpful in cases in which patients have a history of difficulty in perceiving symptoms, a history of severe exacerbations, or moderate-to-severe asthma.

Education on environmental control and avoidance strategies and medication use and adherence (e.g. correct inhaler techniques and use of other devices) is also important.

Table 30: Classification of Asthma Control

Components of Severity		Classification of Asthma Control (5-11 Years of Age)		
		Well Controlled	**Not Well Controlled**	**Very Poorly Controlled**
IMPAIRMENT	Symptoms	⩽ 2 days/ week but not more than once on each day	>2 days/ week or multiple times on ⩽2 days/week	Throughout the day
	Night-time awakenings	⩽1x/ month	>2x/ month	⩾2x/ week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short acting beta2-agonist use for symptom control**	⩽ 2 days/ week	>2 days/ week	Several times per day
	▪ FEV_1 or peak flow	>80% predicted/ personal best	60-80% predicted/ personal best	<60% predicted/ personal best
	▪ FEV_1/ FVC	>80%	75-80%	<75% predicted
RISK	Exacerbations requiring oral systemic corticosteroids	**0.1 per year**	⩾ 2 per year	
		Consider severity and interval since last exacerbation		
	Reaction in lung growth	Evaluation requires long-term follow-up care.		
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		
Recommended Action for Treatment		• Maintain current step • Regular follow-up every 1-6 months • Consider step down if well controlled for at least 3 months	• Step up 1 step and re-evaluate in 2-6 weeks • For side effects, consider alternative treatment options.	• Consider short course of oral systemic corticosteroids • Step up 1-2 steps and re-evaluate in 2 weeks • For side effects consider alternative treatment options.

Adapted from the 2007 NAEPP Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma.
To access the complete report, go to: www.nhlbi.nih.gov/guidelines/asthma/asthgdin.pdf.

Components of Severity		Classification of Asthma Control (12 Years of Age and Older)		
		Well Controlled	**Not Well Controlled**	**Very Poorly Controlled**
IMPAIRMENT	Symptoms	⩽ 2 days/ week	>2 days/ week	Throughout the day
	Night-time awakenings	⩽2x/ month	1-3x/ month	⩾4x/ week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short acting beta2-agonist use for symptom control**	⩽ 2 days/ week	>2 days/ week	Several times per day
	▪ FEV_1 or peak flow	>80% predicted/ personal best	60-80% predicted/ personal best	<60% predicted/ personal best
	Validated questionnaires			
	▪ ATAQ*	0	1.2	3 –4
	▪ ACQ**	⩽0.75	⩾1.5	N/A
	▪ ACT***	⩾20	16 - 19	⩽15
RISK	Exacerbations requiring oral systemic corticosteroids	**0.1 per year**	⩾ 2 per year	
		Consider severity and interval since last exacerbation		
	Reaction in lung growth	Evaluation requires long-term follow-up care.		
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		
Recommended Action for Treatment		• Maintain current step • Regular follow-up every 1-6 months • Consider step down if well controlled for at least 3 months	• Step up 1 step and re-evaluate in 2-6 weeks • For side effects, consider alternative treatment options.	• Consider short course of oral systemic corticosteroids • Step up 1-2 steps and re-evaluate in 2 weeks • For side effects consider alternative treatment options.

Adapted from the 2007 NAEPP Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma.
To access the complete report, go to: www.nhlbi.nih.gov/guidelines/asthma/asthgdin.pdf.

Written asthma action plans is provided in partnership with the patient emphasizing the differences between long-term control and quick-relief medications.

9.8.3 Control of Environmental Factors and Comorbid Conditions

Symptom exacerbations may be due to environmental exposures and irritants. Hence, in patients with persistent asthma, the use of skin testing or *in vitro* testing to assess sensitivity to perennial indoor allergens is important. Once the offending allergens are identified, counsel patients on avoidance from these exposures. In addition, education to avoid tobacco smoke (both first-hand and second-hand exposure) is important for patients with asthma.

Lastly, comorbid conditions that may affect asthma must be diagnosed and appropriately managed. These include the following:

- Bronchopulmonary aspergillosis
- Gastroesophageal reflux disease (GERD)
- Obesity
- Obstructive sleep apnea
- Rhinitis
- Sinusitis
- Depression
- Stress
- Low vitamin D levels

Based upon reports of an inverse correlation between low vitamin D levels and asthma control, vitamin D supplementation in children might enhance corticosteroid responses, control atopy, and improve asthma control.[16]

9.8.4 Pharmacologic Treatment

Pharmacologic management includes the use of agents for control and agents for relief. Control agents include inhaled corticosteroids, long-acting bronchodilators, theophylline, and leukotriene modifiers. More recent strategies include the use of anti-immunoglobulin E (IgE) antibodies (omalizumab), which is not available in Nigeria. Relief medications include short-acting bronchodilators, systemic corticosteroids, and ipratropium.

A stepwise approach to pharmacologic therapy is recommended to gain and maintain control of asthma in both the impairment and risk domains.

The type, amount, and scheduling of medication is dictated by asthma severity (for initiating therapy) and the level of asthma control (for adjusting therapy). Step-down therapy is essential to identify the minimum medication necessary to maintain control (Figure 2).

When children are well controlled (Table 6), it is reasonable to try to reduce their therapy. Whether on relatively high-dose inhaled steroids, or a combination of steroid/long-acting β_2-agonist, it is best to try to continue to control them on a lower dose, or on less medication. Reducing inhaled steroids and/or eliminating the long-acting β_2-agonist could result in a deterioration in asthma control. When such steps are taken, it is critical to see those children frequently, monitoring their history, physical examination and spirometry.[17]

The most effective treatment to prevent exacerbations in children with mild persistent asthma is daily inhaled corticosteroids.[18] Results of the long-term use of inhaled steroids (budesonide) in children suggest no sustained adverse effect on growth.[19,20]

A review by Rodrigo et al looked at 8 studies of omalizumab in children with moderate to severe asthma and elevated IgE levels.[21] Children treated with omalizumab were more significantly able to reduce their use of rescue inhalers and their inhaled and/or oral steroid dose than patients in the placebo group. Although no significant differences in pulmonary function were observed, patients receiving omalizumab had fewer exacerbations than the children receiving placebo. These studies lasted a year or less and did not reveal any significant adverse effects of the omalizumab.

Another study, by Deschildre et al, indicated that adding omalizumab to maintenance therapy can improve asthma control in children with severe, uncontrolled allergic asthma.[22,23]

9.9 Delivery Devices and Best Route of Administration

In paediatric asthma, inhaled treatment is the cornerstone of asthma management. Inhaler devices currently used to deliver inhaled corticosteroids (ICSs) fall into the following 4 categories:

- Pressurized metered dose inhaler (pMDI) - Propellant used to dispense steroid when canister is pressed manually
- Dry powder inhaler (DPI) - Does not require hand-breath

coordination to operate

- Breath-actuated pMDI - Propellant used to dispense steroid when patient inhales
- Nebulized solution devices

In paediatric patients, the inhaler device must be chosen on the basis of age, cost, safety, convenience, and efficacy of drug delivery.[24]

Based on current research, the preferred device for children younger than 4 years is a pMDI with a valved holding chamber and age-appropriate mask. Children aged 4-6 years should use a pMDI plus a valved holding chamber. Lastly, children older than 6 years can use either a pMDI, a DPI, or a breath-actuated pMDI. For all 3 groups, a nebulizer with a valved holding chamber (and mask in children younger than 4 years) is recommended as alternate therapy.[24] Nebulizers are the only viable alternative delivery systems in children. These are reserved for the minority of children who cannot be taught effective use of a spacer device. If a nebulizer is used for delivery of ICS, it should be used with a mouthpiece to avoid the medication reaching the eyes.[24]

Valved holding chambers are important. The addition of a valved holding chamber can increase the amount of drug reaching the lungs to 20%. The use of a valved holding chamber helps reduce the amount of drug particles deposited in the oropharynx, thereby helping to reduce systemic and local effects from oral and gastrointestinal absorption.

A Cochrane review on the use of valved holding chambers versus nebulizers for inhaled steroids found no evidence that nebulizers are better than valved holding chamber.[25] Nebulizers are expensive, inconvenient to use; they require longer time for administration, require maintenance, and have been shown to have imprecise dosing.

Newer devices are showing greater efficacy. For MDIs, chlorofluorocarbon (CFC) propellants (implicated in ozone depletion) have been phased out in favour of the hydrofluoroalkane-134a (HFA) propellant. Surprisingly, the HFA component is more environmentally friendly and has proven to be more effective, due to its smaller aerosol particle size, which results in better drug delivery. MDIs with HFA propellant have better deposition of drug in the small airways and greater efficacy at equivalent doses compared with CFC-MDIs.

9.10 Long-Term Monitoring

Regular follow-up visits are essential to ensure control and appropriate therapeutic adjustments. In general, patients should be assessed every 1-6 months. At every visit, adherence, environmental control, and comorbid conditions should be checked.

If patients have good control of their asthma for at least 3 months, treatment can be stepped down. However, the patient should be reassessed in 2-4 weeks to make sure that control is maintained with the new regimen.

Outpatient visits should include the following:

- Interval history of asthmatic complaints, including history of acute episodes (e.g., severity, measures and treatment taken, response to therapy)
- History of nocturnal symptoms
- History of symptoms with exercise, and exercise tolerance
- Review of medications, including use of rescue medications
- Review of home-monitoring data (e.g., symptom diary, peak flow meter readings, daily treatments)

Patient evaluation should include the following:

- Assessment for signs of bronchospasm and complications
- Evaluation of associated conditions (e.g., allergic rhinitis)
- Pulmonary function testing (in appropriate age group)

Address issues of treatment adherence and avoidance of environmental triggers and irritants.

Long-term asthma care pathways that incorporate the aforementioned factors can serve as roadmaps for ambulatory asthma care and help streamline outpatient care by different providers.

9.11 Long-Term Management of Asthma in Children Ages 5 Years and Younger

Recurrent wheezing occurs in a large proportion of children who are 5 years and younger, typically with viral upper respiratory tract infections. Deciding when this is the initial presentation of asthma is difficult.

Previous classifications of wheezing phenotypes (episodic wheeze and multiple-trigger wheeze; or transient wheeze, persistent wheeze and late-onset wheeze) do not appear to identify stable phenotypes, and their clinical usefulness is uncertain.

A clinical diagnosis of asthma in young children with a history of wheezing is more likely if they have:

- Wheezing or coughing that occurs with exercise, laughing or crying in the absence of an apparent respiratory infection;
- A history of other allergic diseases (eczema or allergic rhinitis) or asthma in first-degree relatives; and
- Clinical improvement during 2–3 months of controller treatment, and worsening after cessation.

9.12 Tests to Assist in Diagnosis

There are no tests to diagnose asthma with certainty in children 5 years and younger. The following are useful adjuncts.

9.12.1 Therapeutic Trial

A trial of treatment for at least 2–3 months with as-needed short-acting β_2-agonist (SABA) and regular low dose inhaled corticosteroids (ICS) may provide some guidance about the diagnosis of asthma (Evidence D). Response should be evaluated by symptom control (daytime and night-time), and the frequency of wheezing episodes and exacerbations. Marked clinical improvement during treatment and deterioration when treatment is stopped support a diagnosis of asthma. Due to the variable nature of asthma in young children, a therapeutic trial may need to be repeated in order to be certain of the diagnosis.

9.12.2 Other Tests

These are tests for atopy, chest X-ray film radiography, lung function test, exhaled nitric oxide and risk profiles.

9.12.2.1 Tests for Atopy

Sensitization to allergens can be assessed using either skin prick testing or allergen-specific immunoglobulin E. Skin prick testing is less reliable for confirming atopy in infants. Atopy is present in the majority of children with asthma once they are over 3 years of age; however, absence of atopy does not rule out a diagnosis of asthma.

9.12.2.2 Chest Radiograph

A plain chest radiograph may help to exclude structural abnormalities (e.g. congenital lobar emphysema, vascular ring) chronic infections such as tuberculosis, an inhaled foreign body, or other diagnoses. Other imaging investigations may be appropriate, depending on the condition being considered.

9.12.2.3 Lung Function Testing

Most children 5 years and younger are unable to perform reproducible expiratory manoeuvres, therefore lung function testing, bronchial provocation testing, and other physiological tests are not helpful. However, by 4–5 years of age, if coached by an experienced technician with visual incentives, performing reproducible spirometry may be possible.

9.12.2.4 Exhaled Nitric Oxide

Elevated fractional concentration of exhaled nitric oxide (FENO), recorded >4 weeks from any URTI in pre-school children with recurrent coughing and wheezing, may predict physician-diagnosed asthma. However, FENO testing is not widely available.

9.12.2.5 Risk Profiles

A number of risk profile tools to identify wheezing children aged 5 years and younger who are at high risk of developing persistent asthma symptoms have been evaluated for use in clinical practice. The applicability and validation of this tool in Nigeria and other African countries have not been substantiated.

9.13 Differential Diagnosis

A definite diagnosis of asthma in this young age group is challenging but has important clinical consequences. It is particularly important in this age group to consider and exclude alternative causes that can lead to symptoms of wheeze, cough, and breathlessness before confirming an asthma diagnosis.

Any of the following features suggest an alternative diagnosis and indicate the need for further investigations (Table 31):

- Failure to thrive
- Neonatal or very early onset of symptoms (especially if associated with failure to thrive)
- Vomiting associated with respiratory symptoms
- Continuous wheezing
- Failure to respond to asthma controller medications
- No association of symptoms with typical triggers, such as viral URTI
- Focal lung or cardiovascular signs, or finger clubbing
- Hypoxaemia outside context of viral illness

Table 31: Common Differential Diagnoses of Asthma in Children 5 years and Younger

Condition	Typical feature
Recurrent viral respiratory tract infections	Mainly cough, runny congested nose for <10 days; wheeze usually mild; no symptoms between infections
Gastroesophageal reflux	Cough when feeding; recurrent chest infections; vomits easily especially after large feeds; poor response to asthma medications
Foreign body aspiration	Episode of abrupt, severe cough and/or stridor during eating or play; recurrent chest infections and cough; focal lung signs
Tracheomalacia	Noisy breathing when crying or eating, or during upper airway infections (noisy inspiration if extrathoracic or expiration if intrathoracic); harsh cough; inspiratory or expiratory retraction; symptoms often present since birth; poor response to asthma medications
Tuberculosis	Persistent noisy respirations and cough; fever unresponsive to usual antibiotics; enlarged lymph nodes; poor response to bronchodilators or inhaled corticosteroids; contact with someone who has tuberculosis
Congenital heart disease	Cardiac murmur; cyanosis when eating; failure to thrive; tachycardia; tachypnoea or hepatomegaly; poor response to asthma medications
Cystic fibrosis	Cough starting shortly after birth; recurrent chest infections; failure to thrive (malabsorption); loose greasy bulky stools
Primary ciliary dyskinesia	Cough and recurrent, mild chest infections; chronic ear infections and purulent nasal discharge; poor response to asthma medications; *situs inversus* occurs in about 50% of children with this condition
Vascular ring	Respirations often persistently noisy; poor response to asthma medications
Bronchopulmonary dysplasia	Infant born prematurely; very low birth weight; needed prolonged mechanical ventilation or supplemental oxygen; difficulty with breathing present from birth
Immune deficiency	Recurrent fever and infections (including non-respiratory); failure to thrive

ASSESSMENT AND MANAGEMENT IN CHILDREN

9.14 Goals of Asthma Management

As with other age groups, the goals of asthma management in young children are to achieve good control of symptoms and maintain normal activities, minimize risk of flare-ups, maintain lung functions, and minimize side effects from medications. The Global Initiative for Asthma (GINA) offered a stepwise approach to treatment that is customized to the individual child taking into account the effectiveness of available medications, their safety, and their cost to the payer or family.

9.15 Stepwise Treatment of Asthma in Children Ages 5 Years and Younger

According to the 2015 GINA guidelines, asthma treatment steps proposed for children 5 years and younger are as follows (Figure 10):

Step 1: As-needed inhaled short-acting β_2-agonist (SABA)

Step 2: Initial controller treatment, plus as-needed SABA. Regular daily low dose inhaled corticosteroid (ICS) is recommended as the preferred initial controller treatment. It should be given for at least 3 months to establish its effectiveness in achieving good asthma control. As an alternative, leukotriene receptor antagonist (LTRA) may be considered.

Step 3: Additional controller treatment plus as-needed SABA. For children whose symptoms are not controlled after 3 months of low dose ICS, doubling the initial dose is often the best option. Another option is adding LTRA to low-dose ICS. This step up should be preceded by considering other diagnoses and checking on inhaler techniques and adherence.

Step 4: Continue controller treatment and refer for expert assessment for further diagnosis and investigation. Addition of regular LTRA or

increasing the dose or frequency of ICS is another option to be considered.

Treatment adjustment is based on regular reviewing of the child's response (every 3-6 months). Asthma-like symptoms remit in a substantial proportion of children aged 5 years and younger, so stepping down treatment should be considered. In addition, marked seasonal variations may be seen in symptoms. For some children with only seasonal symptoms, daily long term controller therapy can be discontinued. In that case, a follow-up visits 3-6 weeks later to check whether symptoms have recurred, as therapy may need to be reinstituted.

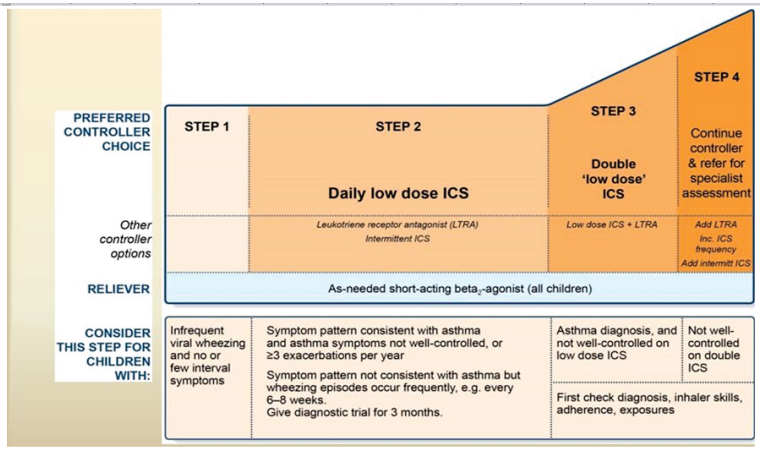

Figure 10: Stepwise Management of Asthma in Children ages 5 years and Younger

An asthma action plan should enable family members and care givers to recognize asthma worsening or flare-up, initiate treatment, and identify when urgent hospital care is necessary. Initial pharmacotherapy for mild-moderate exacerbations include higher or more frequent doses of SABA, ipratropium bromide for children who fail to respond to SABA, and a 3-5 days' treatment with oral corticosteroids (prednisolone or equivalent) may be considered.

Urgent transfer to hospital is indicated in case of any of the following 3 situations. First, if there is actual or impending respiratory arrest, inability

to speak or drink, central cyanosis, subcostal retractions, oxygen saturation < 92% in room air, or silent chest on auscultation. Second, if there is lack of response to initial bronchodilator therapy namely 6 puffs of inhaled SABA over 1-2 hours or persistent tachypnoea despite three administrations of inhaled SABA. The third indication is when the social environment impedes delivery of acute treatment at home.

Table 32: Low Daily Doses of Inhaled Corticosteroids for Children 5 years and Younger Low daily dose (mc)

Drug	Dose in µg
Beclomethasone dipropionate (HFA)	100
Budesonide pMDI + spacer	200
Budesonide nebulized	500
Fluticasone propionate (HFA)	100

HFA: hydrofluoralkane propellant; pMDI: pressurized metered dose inhaler

This is not a table of clinical equivalence. A low daily dose is defined as the dose that has not been associated with clinically adverse effects in trials that included measures of safety.

The goals of asthma management are achieved through a partnership between the parent/carer and the health professional team, with a cycle of:

- *Assess* (diagnosis, symptom control, risk factors, inhaler technique, adherence, parent preference)
- *Adjust treatment* (medications, non-pharmacological strategies, and treatment of modifiable risk factors)
- *Review response* including medication effectiveness and side-effects. This is carried out in combination with:

– Education of parent/carer, and child (depending on the child's age)
– Skills training for effective use of inhaler devices and encouragement of good adherence
– Monitoring of symptoms by parent/carer
– A written asthma action plan.

9.16 Assessing Asthma Symptom Control

No objective measures to assess symptom control have been validated for children <4 years, although the Childhood Asthma Control Test has been developed for children aged 4–11 years.

Table 8 shows a working schema for assessing asthma control in children ⩽ 5 years, based on current expert opinion. It incorporates assessment of symptoms; the child's level of activity and their need for reliever/rescue treatment; and assessment of risk factors for adverse outcomes (Evidence D).

Table 33: Assessment of Asthma Control in Children 5 years and Younger

A. Level of asthma symptom control in young children In the past 4 weeks, has the child had;		**Well Uncontrolled**	**Partly Uncontrolled**	**Uncontrolled**
Daytimes symptoms for more than a few minutes, more than once a week	**Yes/No**	None of these	1-2 of these	3-4 of these
Any activity limitation due to asthma?(runs/plays less than other children, tires easily during walks/playing)	**Yes/No**			
*Reliever needed more than once a week?	**Yes/No**			
Any night waking or night coughing due to asthma?	**Yes/No**			

B. Risk factors for poor asthma outcomes in young children

Risk factors for flare-ups (exacerbations) in the next few months

- Uncontrolled asthma symptoms
- One or more severe exacerbations in the previous year
- The start of the child's usual 'flare-up'
- Exposures: tobacco smoke; indoor or outdoor air pollution; indoor allergens; (house dust mite, cockroach, pets, mold), especially in combination with viral infection
- Major psychological or socio-economic problems for the child or family

- Poor adherence with controller medication, or poor inhaler technique

Risk factors for fixed airflow limitation

- Severe asthma with several hospitalizations
- History of bronchiolitis

Risk factors for medication side-effects

- Systemic: frequent courses of OCS; high-dose and/or potent ICS
- Local: moderate /high-dose or potent dose of ICS; incorrect inhaler technique; failure to protect skin or eyes when using ICS by nebulizer or spacer with face mask

*** Excludes reliever taken before exercise**

9.17 Choice of Inhaler Device

This has been discussed earlier. In addition, the optimal number of breaths required to empty the spacer depends on the child's tidal volume, and the dead space and volume of the spacer. Generally, 5–10 breaths will be sufficient per actuation. The way a spacer is used can markedly affect the amount of drug delivered:

- Spacer size may affect the amount of drug available for inhalation in a complex way depending on the drug prescribed and the pMDI used. Young children can use spacers of all sizes, but theoretically a lower volume spacer (<350 mL) is advantageous in very young children.
- A single pMDI actuation should be delivered at a time, with the inhaler shaken in between. Multiple actuations into the spacer before inhalation may markedly reduce the amount of drug inhaled.
- Delay between actuating the pMDI into the spacer and inhalation may reduce the amount of drug available. This varies between

spacers, but to maximize drug delivery, inhalation should start as soon as possible after actuation.

- If a health care provider or a carer is giving the medication to the child, they should actuate the pMDI only when the child is ready and the spacer is in the child's mouth.
- If a face mask is used it must be fitted tightly around the child's mouth and nose, to avoid loss of drug.
- Ensure that the valve is moving while the child is breathing through the spacer.
- Static charge may accumulate on some plastic spacers, attracting drug particles and reducing lung delivery. This charge can be reduced by washing the spacer with detergent (without rinsing) and allowing it to air dry, but it may re-accumulate over time. Spacers made of anti-static materials or metals are less subject to this problem. If a patient or health care provider carries a new plastic spacer for emergency use, it should be regularly washed with detergent (e.g. monthly) to reduce static charge.

Nebulizers, the only viable alternative delivery systems in children, are reserved for the minority of children who cannot be taught effective use of a spacer device. If a nebulizer is used for delivery of ICS, it should be used with a mouthpiece to avoid the medication reaching the eyes.

9.18 Asthma Self-Management Education for Carers of Young Children

Asthma self-management education should be provided to family members and carers of wheezy children 5 years and younger when wheeze is suspected to be caused by asthma. An educational programme should contain:

- A basic explanation about asthma and the factors that influence it;
- Training about correct inhalation technique;
- Information on the importance of the child's adherence to the prescribed medication regimen; and
- A written asthma action plan.

Crucial to a successful asthma education programme are a partnership between patient/carer and health care providers, with a high level of agreement regarding the goals of treatment for the child, and intensive follow-up (Evidence D).

9.19 Written Asthma Action Plans

Asthma action plans should be provided for the family/carers of all children with asthma, including those aged 5 years and younger (Evidence D). Action plans, developed through collaboration between an asthma educator, the health care provider and the family, have been shown to be of value in older children, although they have not been extensively studied in children of 5 years and younger. A written asthma action plan includes:

- A description of how the parent or carer can recognize when symptom control is deteriorating
- The medications to administer

9.20 Primary Prevention of Asthma

The development and persistence of asthma are driven by gene–environment interactions. For children, a 'window of opportunity' exists *in utero* and in early life, but intervention studies are limited.

- For intervention strategies that include allergen avoidance:
  1. Strategies directed at a single allergen have not been effective
  2. Multifaceted strategies may be effective, but the essential components have not been identified.

- Current recommendations, based on high quality evidence or consensus, include:
  1. Avoid exposure to environmental tobacco smoke during pregnancy and the first year of life
  2. Encourage vaginal delivery

3. Advise breast-feeding for its general health benefits (not necessarily for asthma prevention)
4. Where possible, avoid use of paracetamol (acetaminophen) and broad-spectrum antibiotics during the first year of life.

9.21 Resources

- South Australian Child Health Clinical Network
- British guideline on the management of asthma
- South Africa Guideline for the management of acute asthma in children:2013 update
- Global Strategy for Asthma Management and Prevention (updated 2015)
- Pocket Guide for asthma management and prevention for adults and children older than 5 years (updated 2015)
- Pocket guide for asthma management and prevention in children 5 years and younger (updated 2015)
- Canadian Thoracic Society 2012 guideline: Diagnosis and management of asthma in pre-schoolers, children and adults.

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10

ASTHMA IN **PREGNANCY**

10.1 Summary of Practice Points

1. We suggest that the drug therapy for acute asthma including systemic steroids and magnesium sulphate should be as for non-pregnant patients. (Evidence C)
2. We suggest counselling of women with asthma regarding the importance and safety of continuing their asthma medications during pregnancy to ensure good asthma control. (Evidence B)
3. We suggest that acute severe asthma in pregnancy is an emergency and should be treated vigorously in the hospital with high flow oxygen to maintain saturation 94–98% (Evidence D).
4. We suggest continuous foetal monitoring for acute severe asthma (Evidence GPP).
5. Encourage women with asthma to breastfeed (Evidence C).

It is generally accepted that one-third of asthma patients experience an improvement, one-third a worsening and one-third remain unchanged in their condition during pregnancy. [1-2] Generally, asthma exacerbation is least likely in the last month of pregnancy whereas it is most likely in the 2nd and 3rd trimester with the peak in the 6th month.[3] The overall pregnancy outcome for women and perinatal prognosis for children born to women with well-controlled asthma in pregnancy are similar .[4]

Uncontrolled asthma is associated with several maternal and fetal complications including hyperemesis, hypertension pre-eclampsia, vaginal haemorrhage, difficult labour, respiratory failure, fetal growth retardation, preterm birth, increased perinatal mortality and neonatal hypoxia.[3]

The followings are likely to experience worsening of asthma in pregnancy:

- Poorly controlled symptoms before pregnancy
- Poor medication adherence
- A first pregnancy marked by worsening asthma may predict worsening asthma in later pregnancies
- Female fetus
- Atopic women with allergen exposures during pregnancy
- Obesity

- lower socioeconomic status
- younger age
- unmarried status
- Smoking

Poor patient adherence during pregnancy is one of the key reasons for asthma exacerbation. This is often due to fear of side effects of drugs in pregnancy.

Pregnant women should, therefore, be well counseled and educated on the importance and safety of continuing their asthma medications to ensure good control .[3]

Management of Acute Asthma in Pregnancy

Up to 45% of pregnant women with asthma have moderate- severe exacerbation requiring medical intervention during pregnancy. The management of acute severe asthma in pregnancy is essentially the same as in the nonpregnant state

Measures

1. Give drug therapy for acute asthma as for the non-pregnant patient including systemic steroids and magnesium sulphate.
2. Deliver high flow oxygen immediately to maintain saturation between 94% - 98%. Monitor with pulse oximetry.
3. In the hospital, continuous foetal monitoring is to be ensured.
4. The threshold of intubation should be low to prevent or limit hypoxia to the foetus. Intubated and mechanically ventilate patients who are in or near respiratory arrest and patients who do not respond to treatment as shown by the following:
   - ✓ Hypoxemia despite supplemental oxygen
   - ✓ Increasing CO_2 retention
   - ✓ Persistent/ worsening level of consciousness

- ✓ Haemodynamic instability

5. Chest physicians and obstetricians should be involved in the joint care of pregnant women with poorly controlled asthma. Early involvement of critical care physicians is necessary for acute severe asthma.

10.2 Drug Therapy in Pregnancy

Generally, drug treatment for asthma in pregnancy is safe. In a study among obstetricians in Nigeria, the majority of them considered the use of theophylline, short-acting β2 agonists (SABA) and inhaled LABA safe in a pregnant woman in all the three trimesters. About 52% of them considered the use of ICSs safe and as a controller medication in the first trimester.[4] The risk of harm to the foetus from severe or chronically under-treated asthma outweighs any small risk from drugs used for asthma control.[5]

1. β_2 agonists and Inhaled Steroids are safe in pregnancy[6-8] (Evidence C).
2. Other asthma medications like Theophylline, Oral Steroids, Leukotriene receptor antagonists (LTRA), and Magnesium sulphate are safe in pregnancy [6-8] (Evidence C). Theophylline may be used as an alternative rapid-acting bronchodilator.
3. Epinephrine should be avoided in pregnancy because it can lead to possible congenital malformations, foetal tachycardia, and vasoconstriction of the uteroplacental circulation.
4. Immunomodulation therapy
5. There is currently no clinical data on the use of Omalizumab for moderate/severe allergic asthma in pregnancy.

10.3 Management during Labour

Acute attacks of asthma are quite rare in labour due to endogenous steroid production. In pregnant patients receiving oral steroid, there is a theoretical risk of maternal hypothalamic-pituitary-adrenal axis suppression.

Prostaglandin F2α used for the treatment of postpartum haemorrhage due to uterine atony may cause bronchospasm. Either avoid or use with extreme caution.

1. Advise women that acute asthma is rare in labour
2. Women should continue their usual asthma medications in labour.
3. In the absence of acute severe asthma, caesarian section should be reserved for the usual obstetric indications.
4. Regional blockade is safer than general anaesthesia should an asthmatic need surgery.
5. Women receiving steroid tablets at a dose exceeding 7.5mg daily for more than 2 weeks prior to the onset of labour should receive parenteral hydrocortisone 100mg 6 – 8 hourly during labour.
6. F2α should be used with extreme caution in asthmatic patients for postpartum haemorrhage control because of the risk of inducing bronchoconstriction.

10.4 Drug Therapy in Breastfeeding Mothers

Asthma medications, including oral steroid, are safe in nursing mothers. There is less experience with newer drugs. Breastfeeding should be encouraged in women with asthma.

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11

OCCUPATIONAL **ASTHMA**

11.1 Summary of Practice Points

1. We recommend a detailed and systematic work history and exposure is, therefore, essential in all patients with adult-onset asthma (Evidence A).
2. We suggest that the diagnosis of occupational asthma should be made using serial peak flow measurements, with at least four readings per day (Evidence D).
3. We suggest the use of skin prick testing or tests for specific IgE in the investigation of occupational asthma (Evidence D).
4. We suggest sensitized patients should be removed from further exposure as soon as the diagnosis is confirmed (Evidence D).
5. Early diagnosis is essential as persistent exposure is associated with poor outcome.[1] A thorough and systematic work history and exposure are therefore essential in all patients with adult-onset asthma (Evidence A). It is often essential to confirm the diagnosis of occupational asthma objectively as it may have serious socio-economic and legal implications to the patient. This usually requires keeping a peak expiratory flow (PEEF) diary over prolonged periods including weekends and holidays with at least four readings per day [4](Evidence D).

11.2 Introduction

Occupational asthma (OA) presents a major health challenge with significant potential for acute morbidity, long-term disability, and adverse social and economic impacts.[1] Currently, agents that cause OA encompass more than 300 distinct natural and synthetic chemicals. Isocynates are widely used in many industries and are commonly responsible for most forms of OA. [2] An estimated 5-20% of new cases of adult-onset asthma can be attributed occupational exposure.[3] Asthma in the work workplace is more commonly aggravated, and sometimes induced, by exposure to allergens and other sensitizing agents. In Nigeria, adults are involved in many occupational activities that may trigger asthma attack, make control difficult or engineer onset of asthma.[4-9] These make guideline as this, for managing such patients, imperative.

11.3 Classification and Definition

Work-related asthma (WRA) is a broad term that refers to asthma that is exacerbated or induced by exposures in the workplace. [2, 10] It includes OA and work-exacerbated asthma. The term 'work-exacerbated asthma' refers to asthma triggered by various work-related factors (e.g. aeroallergens, irritants, or exercise) in workers who are known to have pre-existing or concurrent asthma i.e. asthma that is occurring at the same time but is not caused by workplace exposures.[11,12]

The term OA refers to 'de novo' asthma or the recurrence of previously quiescent asthma, i.e. asthma as a child or in the distant past that has been in remission induced by a specific substance at work.[13] It is important to realise that WEA and OA are not mutually exclusive. Aguwa et al reported a prevalence of 6.5% among woodworkers in South-East Nigeria.[14] [2] There are generally two distinct forms of OA. This is based on whether there is a prolonged interval of time between exposure and appearance of symptoms, called latency period (see Table 34).[11,12,15]

Table 34: Types of Occupational Asthma

Characteristic	Asthma With Latency	Asthma Without Latency
A. Clinical		
1. Interv al between onset of exposure and symptoms	Longer	Within hours
2. Pattern of asthmatic reaction on inhalation testing	Immediate & Dual/biphasic	
B. Epidemiologic	5-10%	
1. Prevalence in exposed Population	Genetics, smoking, Atopy, sex	Not known
2. Host predisposition		Not known
3. Pathologic		
1. Eosinophil change	+++	+++
2. Lymphocyte change	+++	+
3. Subepithelial fibrosis	+	+++
4. Thickened basement membrane	++	+++
5. Desquamation of epithelium	+	+++

11.4 Risk factors for OA

Various factors have been identified as risk factors for the development of OA.

The most important of this is exposure.[2] In a review of studies on OA with latency, it was observed that there was a direct correlation between the degree of exposure to an occupational agent and the risk of asthma.[2,15]This concept was supported again by Frew, who stated that, in general, the higher the level of exposure, the more likely the sensitised person is to develop asthma.[16]

Other risk factors include: atopy, rhinoconjunctivitis symptoms, having a measurable PC20, and cigarette smoking. Atopy and smoking are important determinants as regard agents that induce asthma through an IgE dependent mechanism.[17,18] Others include gender and genetics.

Genetics predisposition might be both a confounder and an effect modifier. Implicated are HLA type II and glutathione S-transferase (GST), a family that is critical for protecting cells from oxidative stress products.

11.5 Natural History and Long-Term Consequences

The risk of OA is highest soon after the first exposure, since most subjects develop asthma within 1 to 2 years of exposure. Nevertheless, the latency period can vary from months to years.[19] The rate of acquiring both sensitization and asthmatic symptoms may differ according to the nature of the agent and the intensity of exposure.

11.6 Diagnosis [2,15]

Diagnosis of OA should be confirmed by objective testing for asthma and then demonstrating the relation between asthma and work.[20,21] The possibility of OA should be considered in all adults with asthma. A detailed occupational history that covers the past and present including activities carried out is an important step in the initial evaluation of the patient. The diagnosis should be confirmed as soon as possible to prevent worsening of symptoms. The assessment should include a detailed history of specific job duties and work processes for both the patient and co-workers. The number and intensity exposure to peak concentrations of potential agents should be

assessed. Safety-data sheets for chemicals in the workplace, industrial-hygiene data, and employee health records may be obtained. A walk-through visit to the workplace may help the physician to understand the work situation better. In general, patients with OA have similar clinical presentations as asthma of non-occupational origin. They present with mild, moderate-to-severe bronchospasm with dyspnea and wheezing, cough, chest tightness, and even nocturnal symptoms. There may be other extrapulmonary symptoms such as conjunctivitis, rhinitis, and other forms of atopic manifestations. However, they experience some relief when away from work especially in the early stages. Hence, a history of improvement of symptoms when the patient is away from work – for example during weekends and holidays – and a worsening on return to work suggests OA. However, history is not enough for the diagnosis. It should, therefore, be confirmed by objective methods.

11.6.1 Peak Flow Meter

Serial peak expiratory flow (PEF) measure is an important investigation when occupational asthma is suspected and have a considerable evidence base.[22,23] With appropriate training and explanation, it is possible to achieve high-quality recordings in workers suspected of asthma. While they are subject to potential falsification and inaccurate transcription, they offer the best and easiest first-line approach to assessing the physiological response to inhaled agents in the workplace. The patient is asked to record PEFR every 2 hours when at work and away from work for about 2–4 weeks. A computer-assisted system [Occupational Asthma System (OASYS)] has been used to provide a simple and validated method for interpretation of serial measurements of peak expiratory flow (see Figure 11).

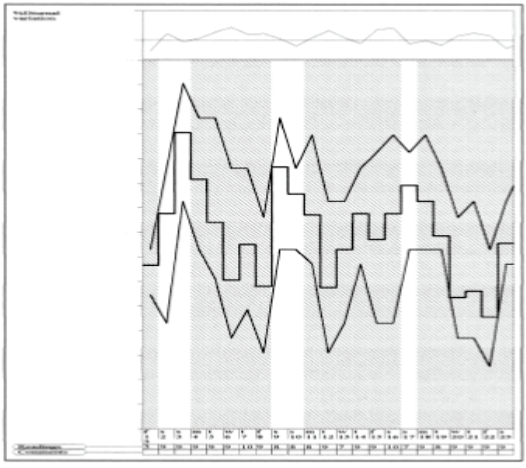

Figure 11: *The Oasys plot of a carpenter. The upper panel shows the daily diurnal variation. The middle panel shows the daily maximum (top line), mean (middle line) and minimum (bottom line) PEF. Days at work have a shaded background, days away from work a clear background. There is recovery during each period off work, with variable deterioration on workdays which is likely to reflect variable daily exposures to wood dust. Oasys-2 generates a score of between 1 and 4 for the probability of workdays being worse than rest days. Scores over 2.5 have a 92% specificity for occupational asthma and a sensitivity of 70%. The score here is 3.93 confirming occupational asthma. The bottom panel shows the date and the number of readings made each workday. Courtesy Prof. P.S. Burge*

11.6.2 Immunologic Tests [2,15]

Immunologic tests are useful for demonstrating IgE antibodies to a high-molecular-weight agent, with high values of sensitivity and specificity.

11.6.3 Inhalation Challenge Tests [2,15]

There are specific and non-specific challenge tests. Non-specific tests demonstrate airways hyper responsiveness by measuring PC20 and specific inhalation challenge tests with occupational agents. This seems the gold standard. These should be carried out only in specialised centres as the test require the expertise of physicians to monitor the response of a patient in the laboratory and of engineers and occupational hygienists to generate and monitor exposure levels of the causal agent. [24]

A positive test identifies the cause of occupational asthma, provided exposures received are equivalent to those in the workplace. Negative tests do not necessarily exclude occupational asthma as the challenge may not adequately reproduce the full extent of the exposures in the workplace.

11.6.4 Lung Function

All suspected cases of OA should have FEV_1 and FVC measured according to agreed criteria. Comparison must be made with a predicted value and the worker's previous lung function, if available.

The use of significant bronchodilator response (15% improvement in FEV_1 and at least 200 ml) to help make a diagnosis of asthma should be consistent with any of the existing asthma guidance. Such measures may help to distinguish between asthma and chronic obstructive pulmonary disease (COPD), although clearly workers with smoking-related COPD may also develop occupational asthma. Pre- and post-shift measures of FEV_1 are not generally helpful to either confirm or refute a diagnosis of occupational asthma. [25]

11.6.5 Analysis of Induced-sputum

This is a valid and reproducible method for studying airway inflammation.[26] The finding of neutrophil inflammation, documented by an increase of neutrophils in induced sputum, after exposure to low-molecular-weight agents, is less common.[27,24]

Several studies have documented increased eosinophil count in OA caused by both high- and low-molecular-weight agents.[25,26]

11.7 Management

Management strategies for OA is summarised in Table 35.

Management of occupational asthma involves early identification from history and allergy test and removal of sensitizing agents.[27,28] Sensitized patients should also be removed from further exposure as soon as the diagnosis is confirmed (Evidence D). Routine pharmacologic management is applied appropriately for acute exacerbations and chronic symptoms.[29]

Table 35: Management strategies for OA[2]

Treatment Strategies	Comments
1. Avoidance	The ideal treatment for patients with occupational asthma with a latency period is removal from exposure. Transfer to another unit in the work place. Other steps like substituting the work process with a non toxic material, enclosure of industrial process are equally important steps.
2. Standard asthma therapy	The treatment of occupational asthma does not differ significantly from the management of asthma that is not work related. Patients diagnosed with OA should have medical treatment following published asthma guidelines. Patients should be placed on treatment commensurate with their severity of asthma symptoms. Because of the airway inflammation in OA, steroid still occupies a main place in treatment.
3. Long term management and monitoring of disease	Proper assessment of impairment and proper man agement of patients with OA and with work-aggravated asthma are important. The assessment for temporary disability should be performed immediately after the diagnosis of OA is made, and long-term assessment of impairment should be performed for 2 years after cessa tion of exposure, since the maximum rate of improvement occurs in the first 2 years after cessation of exposure. Clinicians should also support the patient in the pursuit of appropriate compensation. In many countries, compensation systems for OA are unsatisfactory because they largely underestimate the social and occupational
4. Prevention and surveillance *Primary prevention*	Workers should be diagnosed in an early phase of the disease and appropriate management of the disease should be offered. Involves a comprehensive risk assessment of the workplace, allowing reduction in exposure to asthmagens and thorough an appropriate health surveillance programme. The goal is also to identify workers at risk.
Secondary prevention	Continuous health surveillance programme. Main step is removal from exposure which may lead to regression of symptoms, preventing progression to established and disabling disease.
Tertiary prevention	Tertiary prevention is largely concerned with reducing the disability associated with occupational asthma in workers already diagnosed with this condition. The standard advice given to such workers is that further exposure to allergens known to cause their asthma is unadvisable.

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