

Ministry of Public Health and Sanitation

Guidelines for Asthma Management in Kenya

JANUARY 2011

© 2011 Division of Leprosy, Tuberculosis and Lung Disease

Division of Leprosy, Tuberculosis and Lung Disease New NASCOP Building – Kenyatta National Hospital P.O. Box 20781 NAIROBI Tel (254) 020-713198/721890 Fax (254) 020-713198 Email info@nltp.co.ke Website: www.nltp.co.ke

Developed by the Division of Leprosy Tuberculosis and Lung disease, Ministry of Public Health and Sanitation (DLTLD) and Kenya Association for the Prevention of Tuberculosis and Lung Diseases (KAPTLD)

Supported By: GlaxoSmithkline Astra Zeneca Lords Health Care

Contents

Prefaceiv
Forewordvi
Acknowledgementviii
Chapter 1: Asthma Definition, Disease Burden and Risk Factors
Chapter 2: Asthma Pathogenesis and Pathophysiology7
Chapter 3: The Diagnosis of Asthma10
Chapter 4: Medications used in asthma20
Chapter 5: Management of Asthma
Chapter 6: Organization and delivery of Asthma Care Services
Chapter 7: Monitoring and Evaluation of Asthma Care Programmes

Preface

Asthma is the commonest chronic lung disease in the world. Numerous reports suggest that the burden of Asthma may be increasing. In many parts of the world, asthma remains under-diagnosed and under-treated, leading to poor quality of life, and enormous social, family and economic costs. In many low income countries such as Kenya, there are no public supported asthma-care programmes designed to optimize care for patients with asthma which greatly compounds the diagnosis and treatment problems.

In 2006, the Kenya Association for the Prevention of Tuberculosis and Lung Disease (KAPTLD) in partnership with the Ministry of Health and the pharmaceutical industry developed a 'consensus statement' on the management of asthma in Kenya. The decision to call this document a 'consensus statement' rather than 'guidelines' was based on the recognition that local scientific data or data from settings similar to Kenya, was lacking. However, a commitment was made to make the 'consensus statement' a living document that would be updated regularly to incorporate new information to influence policy and practice.

The second edition of the 'consensus statement' has been renamed the 'Kenya national asthma guidelines' to reflect the purpose for which it has been developed. The primary purpose of this new document is to provide clinicians, researchers, policy makers, health programme developers and managers with a road map to guide the care of individual patients with asthma in Kenya. Secondary objectives are to highlight the need to develop public health care programmes that improve access to asthma care interventions known to positively influence patients' quality of life and to highlight major gaps in knowledge about asthma in Kenya that research groups can use to develop suitable research studies. Thus, even though local scientific data for the rigorous process of formulating evidence based guidelines is still lacking, the guideline development committee felt that this should not preclude calling this document the 'national asthma guidelines'.

The development of these guidelines was based on the synthesis of international guidelines that are regularly updated such as the Global Initiative for Asthma (GINA) guidelines and the International Union Against Tuberculosis and Lung Disease guidelines for management of asthma in low and middle income countries. These guidelines were extensively reviewed and an attempt made to adopt and adapt them to the Kenyan context. Relevant scientific literature in areas such as asthma and HIV infection, which are of public health concern in Kenya, but have not received adequate attention in international guidelines, was reviewed and included in the local guidelines. The revised document also includes completely new sections on the practical approach to lung health and asthma monitoring and evaluation.

The development of these guidelines was based on a consultative process involving KAPTLD, the Division of Leprosy, Tuberculosis and Lung Disease (DLTLD) of the Ministry of Public Health and Sanitation, the Ministry of Medical Services, the nursing

fraternity, patients with asthma and the pharmaceutical industry. A guidelines development committee was then constituted. Individual members of this committee revised and wrote relevant chapters which were then discussed in several consultative forums and later merged into a single document. Two members of the guidelines development committee served as the final editors of the document. The guideline development process was made possible through an unrestricted grant from GlaxoSmithKline. It is hoped that these guidelines will be accepted and used widely in Kenya to positively influence practice related to asthma care. By improving access and quality of asthma care services provided by health care providers both in public and private health care settings, it is hoped that ultimately, the lives of patients with asthma will be changed.

5127

Dr. S. K. Sharif, MBS, MBChB, M. Med., DLSHTM, MSc Director of Public Health and Sanitation January 2011

Foreword

Kenya, like many other developing nations, is at a cross road. While infectious diseases remain the greater cause of morbidity and mortality for the Kenyan population, non infectious diseases are increasingly becoming a major cause of ill health and death. The list of common non infectious diseases includes asthma, chronic obstructive airways disease, diabetes mellitus, hypertension, lipid disorders and various malignancies. The common thread that runs through most of these diseases is their chronicity, which implies long term health consequences for the sick, greater health resource utilization and a heavy economic burden to the country as a whole. Although a large proportion of these diseases are preventable through adoption of appropriate healthy lifestyles, there are no proven ways to prevent diseases such as asthma. The public health focus for such diseases relies on early case detection and placement of affected individuals on appropriate and largely lifelong treatment to control the disease. Under these circumstances, the development of standardized, well defined care programmes, operating on cost effective care practices is critical. It has been documented that patients suffering any disease who are managed according to set guidelines fair better than those managed otherwise.

Asthma is one of the commonest chronic diseases in the world. The prevalence of this disease appears to be increasing in most parts of the world including developing countries. In Kenya the few epidemiological studies that have been carried out suggest that the disease is common and may affect up to 10% of the population. The disease appears to be more common in urban areas compared to rural areas. The major drivers of the burden of asthma in Kenya, as in other parts of the world, are largely unknown even though it is appreciated that complex and poorly understood genetic factors interact with environmental factors to lead to the manifestation of the disease. As previously indicated, as the drivers of disease burden are largely unknown, the public health push is to rapidly identify persons who suffer asthma and to provide effective treatment to such persons in order to reduce asthma morbidity and prevent asthma mortality.

Kenya is making efforts to improve the health of its population through strengthening of the primary health care system. Strengthening of community structures to support the delivery of essential health interventions is an integral part of primary health care. If properly executed, primary health care will ensure that the majority of the Kenyan population have access to an essential package of care that includes care for chronic diseases such as asthma. It is therefore gratifying that the current national asthma guidelines include a chapter on the Practical Approach to Lung Health (PAL), the strategy that defines the management protocols to be used for the care of patients presenting to primary health care facilities with respiratory symptoms. The natural extension to the PAL strategy will be the development of appropriate communication and social mobilization approaches around asthma that will ensure that local communities fully understand this disease and are able to develop appropriate local strategies to cope with it.

These guidelines have been developed through a partnership among various stakeholders, including the Ministry of Public Health and Sanitation through the Division of Leprosy, Tuberculosis and Lung Diseases, the Ministry of Medical Services , the pharmaceutical industry and professional associations, primarily the Kenya Association for the Prevention of Tuberculosis and Lung Diseases. This is a demonstration of the power of partnerships. Kenya is likely to gain its public health goals faster if partnerships such as the one that has evolved around asthma are developed and nurtured.

These guidelines represent a major milestone in the development of asthma care services in Kenya. It is hoped that these guidelines will be widely disseminated and used by all cadres of health care providers in Kenya to promote asthma care practices that ensure the best possible outcomes for individuals who suffer this disease. It will be the duty of the Ministries of Health in Kenya to ensure that the essential products needed to provide basic but quality care to patients who suffer asthma, as outlined in these guidelines, are provided at all levels of the health care system. This is a commitment and a challenge that the Government of Kenya is willing to undertake.

Ruhano

Hon. Beth Mugo Minister for Public Health and Sanitation



Acknowledgement

The year 2010 was the international Year of the Lung. In partnership with the Division of leprosy, Tuberculosis and Lung Disease of the Ministry of Public Health Sanitation and the pharmaceutical industry, the Kenya Association for Prevention of Tuberculosis and Lung Disease (KAPTLD) undertook to review and revise the national asthma guidelines initially published in 2005 as part of the activities of theYear of the Lung. This activity was carried out to respond to the large public health burden of asthma in Kenya so as to enhance access and quality of asthma care services in Kenya. The process of revising the national asthma guidelines was led by the executive committee of the KAPTLD board comprising Dr. Joseph A. Aluoch (Specialist chest physician & the patron of KAPTLD) who created the momentum for these guidelines to be revised, Dr. Mohan Lumba, (Chair KAPTLD & Specialist chest pediatrician), Dr. Henderson Irimu, (Secretary KAPTLD), Dr. Christopher J Mureithi, (Treasurer KAPTLD , Chair of the KAPTLD Asthma task force & Specialist chest physician) who chaired the guidelines development committee and Dr. Muhwa J. Chakaya (Specialist chest physician, chief research officer, Centre for Respiratory Diseases Research, KEMRI & member KAPTLD) who was the chief editor for this version of the guidelines.

The following persons contributed to the development of the new asthma guidelines; Dr. Joseph Sitienei (Public health specialist & Head of the Division of Leprosy, TB and Lung Disease at the Ministry of Public Health Sanitation) who created and sustained an enabling environment for the development of these guidelines, Dr. Eric Mugambi (Specialist physician & member KAPTLD), who was the assistant editor for this version of the guidelines, Dr. Evans Amukoye (Specialist chest pediatrician ,director, centre for respiratory diseases research, KEMRI & member KAPTLD), Dr. Adil Waris (Specialist chest pediatrician & member KAPTLD), Dr. Jared Mecha (Specialist chest physician & lecture at the department f of internal medicine, school of medicine, University of Nairobi), Dr. Elizabeth Obimbo (Specialist chest pediatrician & lecture at the department f of child health, school of medicine, University of Nairobi), Dr. Francis Ogaro(Specialist chest pediatrician) Dr. Herman Weyenga (Public health specialist at the Division of Leprosy, TB and Lung Disease at the Ministry of Public Health Sanitation) who provided general guidance in the development of these guidelines, contributed chapters to these guidelines and provided continuous inputs as the document progressed.

The following people worked tirelessly towards making these guidelines a reality;

Dr. Bernard Langat (DLTLD), Dr. Chris Masila (DLTLD), Dr. Grace Karanja-Gitonga (KAPTLD), Hillary Kipruto (DLTLD/WHO), Dr. Warurua Mugo (KAPTLD), Alice Tebes (DLTLD), Emily Nyagaki (KAPTLD), Evelyn Njoroge (AKUH/KAPTLD), Peter Nguhiu (KAPTLD), Dr. Izaaq Odongo (KAPTLD), Sammy Arithi (KAPTLD), Dr. Timothy Panga (KAPTLD), Phanice Aloni (KAPTLD), Wesley Tomno (DLTLD), Bridget Wachira (GSK), Judy Mboya (GSK), Simon Mbaya (GSK), Maureen Ogada (GSK), Samuel Ngetich (DLTLD), Paul Malusi (DLTLD)

The development of these guidelines was supported by an unrestricted grant from GlaxoSmithKline (GSK) while the launch of these guidelines was jointly supported by the Division of Leprosy, Tuberculosis and Lung Disease, Ministry of Public Health and Sanitation, KAPTLD, GSK, Astra Zeneca and Lords Health Care .It is anticipated that these organizations, together with the Ministry of Medical Services and other partners, will spearhead the dissemination and promotion of use of these guidelines.

Mahen Hunto

Dr. Mohan Lumba Chair, KAPTLD.



Asthma Definition, Disease Burden and Risk Factors

Chapter Objectives

This chapter is intended to highlight the burden of disease and its risk factors so as to impress on policy makers the importance of asthma as a public health problem in Kenya. Recognition of asthma as a major public health problem in Kenya is expected to stimulate the development of nationwide public health care programmes designed to cope with this disease. Additionally this chapter highlights gaps in knowledge about the burden of asthma and its associated risk factors which hopefully will stimulate further epidemiologic studies.

The primary audience for this chapter includes policy makers, health care programme financiers, health care programme developers and researchers.

Asthma: Definition

The Global Initiative for Asthma (GINA) defines asthma as a chronic inflammatory disease of the airways in which many cells and cellular elements play a role. The chronic airway inflammation is associated with airway hyper responsiveness (AHR) that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing particularly at night or in the early morning. These episodes are usually associated with widespread but variable airways obstruction within the lung that is often reversible either spontaneously or with treatment.

The key components of this definition include:

- The presence of airway inflammation in all asthmatics.
- Airway hyper responsiveness which implies that the airways will narrow easily and too much in response to various stimuli.
- Recurrent episodes of symptoms of wheezing, breathlessness, chest tightness and coughing.
- Reversible airways obstruction that is demonstrable by changes in lung function (Forced Expiratory Volume in 1 second and Peak Expiratory Flow) in response to a bronchodilating agent such as salbutamol.

Asthma: Burden of disease.

Asthma is a global disease that affects persons of all ages and either sex. It is estimated that 300 million people suffer asthma globally but the prevalence varies widely from place to place which may reflect measurement issues in view of the lack of a uniform

definition of asthma used in epidemiologic studies, varying environmental exposures and possibly variations in genetic susceptibility. In the last decade or so, attempts have been made to standardize the measurement of asthma in epidemiologic studies in order to enable comparisons of prevalence to be made among countries and various populations. The most notable of these efforts have been the series of worldwide studies called the International Study of Asthma and Allergic Disease in Childhood (ISAAC). The prevalence of asthma from the ISAAC studies has varied from 1-18%. Kenya participated in ISAAC phase 1 and 3 studies at two sites, Nairobi and Eldoret. The prevalence of wheeze in the past 12 months (written questionnaire) among 13-14 year old children in the ISAAC phase 1 study carried out in 1995 was 17.1% and 10.4 % in Nairobi and Eldoret respectively. In the ISAAC phase 3 study of 2000, this prevalence had increased to 18% and 13.8 % in Nairobi and Eldoret respectively. An earlier study on the prevalence of asthma in children aged 10-14 years, revealed a higher prevalence of asthma in Nairobi compared with rural Murang'a. However the prevalence of asthma in children around the pineapple farms of Thika was very close to that seen among similar age children in Nairobi. The key conclusions (summarized in text box number 1), from these few population based epidemiological studies is that asthma is a very common disease in Kenya and its prevalence may be rising, at least among older children. There are no population based studies that have examined the prevalence of asthma among children below the age of 10 years and in adults above the age of 15 years. Based on the results of the ISAAC studies it is estimated that about 10% of the Kenyan population, or nearly 4 million people, have asthma.

Text Box 1: Prevalence of Asthma in Kenya

- It is estimated that about 10% of the Kenyan population, or 4 million people, have asthma
- The prevalence of asthma in older children between the ages of 12-14 years may be increasing
- Asthma is more prevalent in urban as opposed to rural areas
- There are no population based studies on asthma prevalence in children below 10 years or in adults over the age of 15.
- While clinical experience indicates that asthma is a common reason for health resource utilization there is no data on the burden of asthma that is routinely managed in the health care system

Asthma has important individual health consequences. Uncontrolled asthma results in recurrent or persistent symptoms that impair quality of life, reduce self esteem, reduce social interaction, increase psychosocial trauma and occasionally lead to fatal outcomes. The economic costs of uncontrolled asthma may be enormous and include direct costs from health resource utilization (medical consultations, drug and hospitalization costs), indirect costs from work absenteeism or premature deaths and intangible costs of persistent illness. Studies of the costs of uncontrolled asthma are urgently needed in Kenya.

Asthma: Risk Factors.

A distinction needs to be made between factors that increase the risk of developing asthma and those factors that increase the risk of an asthmatic attack or exacerbation in persons who have developed asthma.

Asthma: Risk Factors for developing asthma.

Asthma tends to run in families. Monozygotic twins have a higher concordance rate for asthma than dizygotic twins, suggesting that genetic factors are important in the development of asthma. However, asthma is not a simple single gene inherited disease. It is likely that multiple genes interact in complex ways to influence the expression of asthma. Although a number of genes have been identified to be associated with asthma, there are no asthma specific genes identified yet and thus no gene directed therapies are available.

Individuals who are atopic, i.e. have positive skin prick tests to common allergens, have an increased risk of asthma just like individuals with demonstrable airway hyper responsiveness (need a small dose of a bronchoconstrictor agent to narrow the airways (FEV₁) by 20%). Both atopy and airway hyper-responsiveness (AHR) may be genetically determined. It is important to note however that not all individuals with atopy or AHR develop asthma.

Early on in life, asthma is more common in boys than girls, especially among first born boys. In adult life, asthma appears to be more common in females than males.

Although there is some uncertainty it appears that children breastfed for longer than six months may be somewhat protected from developing asthma.

Dietary factors may also be important in the development of asthma. In general it appears that a high salt diet and a diet that is low in anti oxidant vitamins such as vitamin C or calorie intake from cereals may be associated with the development of asthma.

Obesity appears to be a risk factor for the development of asthma, an observation that has been seen in a number studies including among South African children.

Exposure to tobacco smoke may also be associated with the development of asthma. A large number of substances encountered in the occupational settings may also increase the risk of development of asthma in susceptible individuals. Though controversial, it is likely that air pollution may have no effect on the development of asthma.

Although the data remains inconclusive, many studies suggest that infestation with

intestinal helminthes is negatively correlated with asthma. Some viral infections encountered early in life may be protective while others such as RSV may increase the risk of asthma but the data is inconsistent. The hygiene hypothesis postulates that exposure to infections in early life may be protective against allergic illness.

There are appears to be an inverse relationship between infection with *Mycobacterium tuberculosis and* allergic disease including asthma.

It appears that untreated HIV infection and disease is not a risk factor for asthma, however, asthma- like symptoms may appear as HIV infected individuals (children in particular) are treated with anti- retroviral treatment and immune system recovery occurs.

A summary of some of the risk factors associated with the development of asthma is provided in text box 2.

Thus the development of asthma appears to be influenced by the interaction of multiple factors. While further epidemiologic studies are needed to further elucidate risk factors for asthma it appears reasonable to recommend that Kenyans breastfeed longer and adopt diets with high anti oxidant content while avoiding obesity and smoking.

Text Box 2: Risk Factors for Development of Asthma

Non Modifiable Factors

- Gender: early M>F; Later F>M
- Atopy
- AHR

Modifiable Factors

- Allergen Exposure
- Infections and Infestations
- Breastfeeding
- Air pollution
- HIV infection
- Occupational Exposures
- Tobacco smoking including environmental tobacco smoke(passive smoking)

Note: Explanations in the text

Asthma: Risk Factors for Asthma Attacks/Exacerbations

Asthma patients may suffer increasing symptoms or attacks when exposed to allergens, respiratory tract infections especially viral, tobacco smoke, strong smells, excessive

exercise, air pollution, and other environmental conditions such as thunderstorms. Intense emotional reactions, and drugs such as beta blockers and non steroidal antiinflammatory drugs (NSAIDS) may trigger attacks. In female patients, asthma symptoms may coincide with menses. A summary of the known risk factors for asthma exacerbations is provided in text box 3.

Text Box 3: Trigger Factors for Asthma attacks/Exacerbations

- Allergens
- Viral RTIs
- Tobacco Smoke
- Strong smells
- Air pollution (exposure to dust, fog, smoke etc)
- Other environmental conditions such as thunderstorms
- Emotional reactions
- Drugs such as beta blockers and NSAIDS.
- Menses

Suggested further reading

- 1. Global Strategy for asthma management and prevention 2009(update). Accessed from WWW.ginasthma.org on December 21, 2010.
- 2. Ait-Khaled N, Odhiambo J, Pearce N, et al Prevalence of symptoms of asthma, rhinitis and eczema in 13- to 14-year-old children in Africa: the International Study of Asthma and Allergies in Childhood Phase III. Allergy. 2007 Mar;62(3):247-58.
- Ng'ang'a LW, Odhiambo JA, Mungai MW, Gicheha CM, Nderitu P, Maingi B, Macklem PT, Becklake MR. Prevalence of exercise induced bronchospasm in Kenyan school children: an urban-rural comparison. Thorax. 1998 Nov;53(11):919-26.
- Odhiambo JA, Ng'ang'a LW, Mungai MW, Gicheha CM, Nyamwaya JK, Karimi F, Macklem PT, Becklake MR. Urban-rural differences in questionnaire-derived markers of asthma in Kenyan school children. Eur Respir J. 1998 Nov;12(5):1105-12.
- Ng'ang'a LW, Odhiambo JA, Omwega MJ, Gicheha CM, Becklake MR, Menzies R, Mohammed N, Macklem PT. Exercise-induced bronchospasm: a pilot survey in Nairobi school children. East Afr Med J. 1997 Nov;74(11):694-8.

- Esamai F, Ayaya S, Nyandiko W. Prevalence of asthma, allergic rhinitis and dermatitis in primary school children in Uasian Gishu district, Kenya. East Afr Med J. 2002 Oct;79(10):514-8.
- 7. Esamai F, Anabwani GM. Prevalence of asthma, allergic rhinitis and dermatitis in primary school children in Uasian Gishu district, Kenya. East Afr Med J. 1996 Jul;73(7):474-8.
- 8. Mohamed N, Ng'ang'a L, Odhiambo J, Nyamwaya J, Menzies R. Home environment and asthma in Kenyan schoolchildren: a case-control study. Thorax. 1995 Jan;50(1):74-8.
- Mitchell HS. Bronchial asthma in Kenya. East Afr Med J. 1970 Mar;47(3):142-5.
- 10. Wasunna AE. Asthma as seen at the casualty department, Kenyatta National Hospital, Nairobi. East Afr Med J. 1968 Nov;45(11):701-5.
- 11. Rees PH, Gitoho F, Mitchell HS, Rees C. Some aspects of the aetiology of asthma in Nairobi with special reference to parasites and the house dust mite. East Afr Med J. 1974 Oct;51(10):729-33.

Asthma Pathogenesis and Pathophysiology



Chapter objectives

This chapter is intended to highlight the pathogenetic mechanisms in asthma so as to allow prescribers and users of asthma therapies to understand and appreciate the scientific rationale of the various therapies currently recommended in asthma. The emphasis on airway inflammation is intended to promote the widespread and persistent use of anti-inflammatory therapies, especially inhaled corticosteroids for the control of asthma.

The primary audience for this chapter includes clinicians, health programme planners and managers, health programme financiers, asthma patients and their families.

Asthma: Pathology

The basic pathology of asthma is chronic inflammation of the airways. The airway inflammation is present even when patients are symptom free and is widespread across the entire airway system, including the upper airways. However, the pathophysiologic consequence of this airway inflammation is most pronounced in the medium sized airways. There is no consistent correlation between the severity of airway inflammation and severity of the clinical disease. The airway inflammation is associated, in complex ways, with airway hyper -responsiveness and asthma symptoms. No differences in the pattern of inflammation have been observed in different clinical forms of asthma, such as allergic and non allergic asthma and in different age groups.

A wide array of inflammatory cells are involved in the asthmatic inflammation including mast cells, eosinophils, T lymphocyets, dendritic cells, macrophages and to a smaller extent neutrophils. Additionally structural cells of the airways also appear to participate in the inflammatory process in the airways. These cells include airway epithelial cells, airway smooth muscle cells, endothelial cells, fibroblasts and myofibroblasts and airway nerves. It appears that everybody is invited to the inflammatory party.

The wide arrays of cells involved in airway inflammation produce a variety of chemical mediators. Over 100 such chemical mediators have been described. These chemical mediators include chemokines such as eotaxin , Thymus and Activation Regulated Chemokines (TARC) and Macrophage Derived Chemokines (MDC); Cysteinyl Leukotrienes; Cytokines such as IL1-_ , TNF-_, IL -5, IL -4 and IL -13; mast cell derived histamine; Nitric Oxide and Prostglandin D2. The sum effect of these chemical mediators (the mediator soup) is damage to the airways leading to structural changes.



The major pathologic changes observed in the airways as a result of the airway inflammation include epithelial necrosis, basement membrane thickening, airway smooth muscle hyperplasia and hypertrophy, and an increase in mucus producing elements such as goblet cells and sub mucosal glands.

Asthma: Pathophysiology

The characteristic pathophysiologic effect of the airway inflammation is airway hyper-responsiveness and airway narrowing from airway smooth muscle contraction, overproduction of airway mucus, airway edema and the airway remodeling from deposition of collagen in the basement membrane. The pathological and pathophysiologic changes in asthma are summarized in text box 4.

Text Box 4: Summary of Airway Pathophysiologic Processes in Asthma

- Airways Inflammation with increased number of activated inflammatory cells
- Production of various chemical mediators (mediator soup)
- Airway structural changes resulting from the airway inflammatory process
- Airway functional changes (Airway Hyperresponsiveness) from the inflammatory process and structural changes
- Airway Narrowing from airway smooth muscle contraction, airway thickening from collagen deposition, airway edema and excessive airway mucus

References: DIAGNOSIS OF ASTHMA

Suggested further reading

- 1. Global Strategy for asthma management and prevention 2009(update). Accessed from www.ginasthma.org on December 21, 2010.
- Murphy DM, O'Byrne PM. Recent advances in the pathophysiology of asthma. Chest. 2010 Jun; 137(6):1417-26.
- Holgate ST. A look at the pathogenesis of asthma: the need for a change in direction. Discov Med. 2010 May; 9(48):439-47.
- Holgate ST. A look at the pathogenesis of asthma: the need for a change in direction. Discov Med. 2010 May; 9(48):439-47.

8

- Lemanske RF Jr, Busse WW. Asthma: clinical expression and molecular mechanisms. J Allergy Clin Immunol. 2010 Feb;125(2 Suppl 2):S95-102.
- Finkelman FD, Boyce JA, Vercelli D, Rothenberg ME. Key advances in mechanisms of asthma, allergy, and immunology in 2009. J Allergy Clin Immunol. 2010 Feb;125(2):312-8.
- Arshad HS, Roberts GC, Howarth PH, Thurner P, Davies DE. A new look at the pathogenesis of asthma. Clin Sci (Lond). 2009 Dec 23;118(7):439-50.



Chapter objectives

This chapter highlights the key diagnostic steps in the evaluation of patients suspected to have asthma. If these steps are followed it should be possible to make an accurate diagnosis of asthma in most patients with this disease.

The primary audience for this chapter includes clinicians, patients and their families, health programme developers and managers and health programme financiers who need to put in place the basic health infrastructure necessary to facilitate the diagnosis of asthma. Clinical researchers will also find this chapter useful, especially in the development and evaluation of clinical algorithms for asthma.

Asthma: General diagnostic principles

An accurate diagnosis of asthma is essential to enable the provision of appropriate treatment. The clinical history is the most important element in the diagnostic process for asthma. A diagnosis of asthma should be considered in all patients who present with episodic or persistent wheeze, shortness of breath, chest tightness and cough. While the presence of wheeze on chest auscultation may enhance the clinical confidence with which the diagnosis of asthma is made, the absence of wheeze on chest auscultation should not be used to exclude asthma. It is recommended that all adult patients suspected or known to have asthma have a spirometric lung function test. Efforts will be made to make spirometric lung function testing widely available in Kenya. The measurement of lung function testing with spirometry or peak expiratory flow measurement may enhance the diagnosis of asthma, provide an indicator of disease severity and help distinguish this disease from chronic obstructive pulmonary disease or other diseases that may present with cough, wheeze and shortness of breath. If the clinical suspicion of asthma remains high but lung function testing is normal, it is recommended that airway hyperresponsiveness be measured. Despite what may appear as a complex process the measurement of airway hyperresponsiveness is simple and should be become readily available with the improved availability of spirometry. It should be highlighted that asthma may be particularly difficult to diagnose in children below the age of 5 years, in those with mild and intermittent disease, in the elderly who often have a poor perception of asthma symptoms and in the occupational setting.

Asthma: DIAGNOSIS OF ASTHMA IN CHILDREN

The general principles for the diagnosis of asthma apply to children. However the diagnosis of asthma may be particularly difficult in children under 5 years. Since lung function testing is difficult in young children, the diagnosis has to rely on clinical

Text Box 5: Asthma Diagnosis: General Principles

- Listen to the patient the clinical history is the most important element in the diagnosis of asthma.
 - $\circ~$ Is there recurrent or episodic wheeze, cough, chest tightness or shortness of breath?
 - Are the symptoms particularly troublesome at night or early morning?
 - Are the symptoms triggered by factors such as dust, cold exposure, strong smells or exercise?
 - Is there a consistent response to asthma specific treatment?
- Obtain a lung function Test (measure FVC, FEV1 and PEF)
 - Is there airflow limitation (FEV1/FVC% less than 70?)
 - Is there a bronchodilator response (FEV1 or PEF improved by greater that 12% or 15%, 30 minutes after inhalation of a short acting bronchodilator)?
 - Measure PEF variability (wide swings in the PEF between morning and evening or when at work and off work)
- Measure airway hyperresponsiveness.
 - o Does the FEV1 drop below 20% with only small doses of an inhaled bronchoconstrictor such as methacholine, histamine or with exercise?

suspicion, physical examination and a trial of asthma treatment. Asthma is highly suggested in the presence of frequent episodes (more than once a month) of wheeze, activity induced cough or wheeze and cough with or without wheeze in the absence of a viral respiratory tract infection. A strong family history of asthma or allergic disease is also supportive of the diagnosis of asthma in very young children. The clinical features to note when evaluating children for asthma are shown in text box 6.

Text Box 6: Factors that increase the likelihood of asthma in children

- Frequent episodes of wheeze, cough, chest tightness, breathlessness particularly experienced at night, early morning, or in response to exercise, common allergens, emotions, laughter or occur in the absence of 'common cold'
- o Personal history of atopy
- o Family history of atopy and or asthma

- o Widespread wheeze on chest auscultation
- o History of improvement in symptoms or lung function in response to asthma specific therapy

Factors that decrease the likelihood of asthma

- o Symptoms with 'colds' only with no interval symptoms
- o Isolated cough especially when 'moist'
- o Repeatedly normal chest auscultatory findings when symptomatic
- o Normal peak expiratory flow especially when symptomatic
- o No response to trial of asthma therapy
- o Clinical features pointing to an alternative diagnosis e.g. failure to thrive, malnutrition, finger clubbing, sternal anomalies, edema, heart murmurs.

Children can be classified into three groups based on the clinical probability that they have asthma: high, intermediate and low. Recommended action for the three groups is summarized in table 1.

Probability of asthma	Recommended Action		
High	Start trial of therapyReview and assess responseFurther testing for non responders		
	Compatible Spirometry	• Therapeutic trial	
Intermediate	Normal Spirometry (spirometry possible over age 5 years but interpretable results are best obtained with children over age 9 years)	• Specialist referral for atopic testing, bronchodilator reversibility, bronchial hyper- responsiveness challenge	
	Spirometry not feasible	• Therapeutic trial	
Low	• Specialist referral for further evaluation		

Table 1: Recommended action based on clinical likelihood of asthma

Common alternative diagnoses for asthma in children (especially the very young) are highlighted in text box 7 and the approaches to identifying these clinical problems are summarized in table 2.

Text Box 7: Non asthma causes of cough and or wheeze in children

- o Chronic rhino- sinusitis
- o Recurrent viral respiratory tract infections
- o Gastro-esophageal reflux
- o Tuberculosis
- o Congenital heart disease
- o Foreign body aspiration
- o Cystic fibrosis
- o Bronchopulmonary dysplasia
- o Congenital malformations with narrowing of the airways
- o Primary ciliary dyskinesia syndrome
- o Immune deficiency

Table 2: Approaches to identifying asthma mimics in children

DIAGNOSIS	EVALUATION	
 Upper airway disease Adeno-tonsilar hypertrophy Rhino-sinusitis Post nasal drip 	Clinical ENT examination Post nasal space radiography CT scan of the paranasal sinuses ENT specialist referral	
Congenital Structural bronchial disease	Bronchoscopy CT scan Chest	
Cartilage ringsCystsWebs		
Bronchial/tracheal obstruction	Chest X-Ray (CXR)	
Vascular rings/ sling	CT scan chest	
• Enlarged cardiac chamber	Echocardiogram	
• Lymph node enlargement from TB or Lymphoma	Cardiac MRI scan Mediastinoscopy	

Endobronchial disease	CXR
Foreign Body	Bronchoscopy
• Tumor	
Esophageal/Swallowing problems	Barium swallow
 Reflux In-coordinate swallowing Laryngeal cleft 	Upper Gastro Intestinal Tract Endoscopy PH probe Milk scan
Tracheo -Esophageal Fistula Pulmonary suppuration	Sweat/ genetic testing
 Cystic fibrosis Primary Ciliary Dyskinesia Severe immunodeficiency syndromes Agammaglobulinemia 	Lung/Sinus biopsy/ molecular genetic testing Complete Blood Count Immunoglobulin levels Complement levels
 Misc Post viral wheeze Acute bronchiolitis Laryngo-tracheo-bronchitis 	Characteristic viral syndrome Antigen tests for RSV Viral cultures PCR on respiratory secretions

Asthma: Diagnosis in older children and adults.

The general principles outlined at the beginning of this chapter should be applied when evaluating older children and adult patients suspected to have asthma. The common differential diagnosis of patients presenting with asthma like symptoms in older children and adults are highlighted in text box 8 and the approaches to evaluating patients suspected to have the various asthma mimics is summarized in table 3.

Table 3: Approaches to identifying asthma mimics in older children and adults

Chronic obstructive pulmonary disease	• Spirometry	
Congestive heart failure	• Echocardiogram	
	• Serum Brain Natriuretic Peptide(BNP)	
Pulmonary embolism	• Perfusion/ventilation scans	
	• CT pulmonary Angiogram	

Tumors	CT scan chestBronchoscopy
Pulmonary eosinophilia	• Sputum and blood eosinophil counts
Angiotensin Converting Enzyme (ACE) Inhibitor induced cough	• Medication review and discontinuation of ACE-I
Vocal cord dysfunction	• Bronchoscopy
Laryngeal dysfunction	• Laryngoscopy

Text Box 8: Asthma mimics in adults and older children

- o Hyperventilation syndrome and panic attacks
- o Upper airways obstruction and inhaled foreign bodies
- o Vocal cord dysfunction
- o Other forms of airways obstruction especially Chronic Obstructive Pulmonary Disease (COPD)
- o Non pulmonary causes of symptoms especially left ventricular failure
- o Non obstructive forms of lung disease such as diffuse parenchymal lung disease

Asthma diagnosis: role of lung function tests

- Objective tests of lung function are recommended in patients suspected to have asthma or diagnosed with asthma over the age of 5 years. However local, unpublished experience suggests that obtaining interpretable spirometric lung function test is difficult in children below the age of 9 years. By demonstrating reversibility and variability of airflow limitation, these tests increase the diagnostic confidence for asthma. Lung function tests are also useful for estimating disease severity and help guide treatment decisions.
- Spirometry and peak expiratory flow measurements are widely used to support the diagnosis of asthma and monitor response to therapy. FEV₁ and FVC are the most commonly used spirometric indices. PEF is measured using the peak flow meter. Predicted values of FEV₁ and FVC based on age, sex and height have been obtained from population studies. Predicted values for PEF are also available but the range of normal values is very wide.

- Spirometry is the recommended method for measuring airflow limitation. Most currently available spirometric lung function test machines of good quality come with in built quality assessment of the test performed and also will have in built test result interpretation capability. However knowledge of recommendations for standardization of spirometry, quality assessment and interpretation of results offers an added advantage to the user of the spirometric lung function tests.
- An FEV₁/FVC ratio of less than 0.70 in adults and less than 0.9 in children is an indicator of airflow limitation or obstruction.
- An increase in FEV₁ of 12% or more (absolute volume increase of 200mls or more) of the pre-bronchodilator value is highly supportive of a diagnosis of asthma.
- Peak Expiratory Flow measurements vary widely. PEF measurements should be compared to the individual's own previous best measurements.
- An increase in PEF of 20% or more (60mls or more) of the pre-bronchodilator value, or a diurnal variation in PEF of more than 20% is highly suggestive of asthma.
- PEF variability can be measured as:
 - 1. Maximum minus minimum PEF value of the day expressed as a percentage of the mean daily PEF value and averaged over one to two weeks
 - 2. Minimum morning pre-bronchodilator PEF over one week expressed as a percentage of the recent best *(preferred method)*

At the time of writing of these guidelines, spirometry and PEF measurement is largely unavailable in most health facilities (including the private health sector) in Kenya. The guidelines development committee strongly recommends that this situation be urgently addressed to make lung function testing widely available in Kenya. It is proposed that lung function testing should be made available according to the schedule shown in Table 4.

Table 4: Recommended lung function testing at various levels of the health care system in Kenya

LEVEL	FACILITY	AVAILABLE TEST
1	Community units	High index of suspicion and referral to higher level facilities
2	Dispensary	
3	Health centre	Peak flow monitoring in all facilities and spirometric lung function testing at busy
4	Sub-district/District hospitals	health centers and all hospitals

5	Provincial General hospitals	At least spirometry lung function test in all and ability to measure lung volumes
6	National Referral hospitals	and capacities and gas transfer at some regional hospitals and all national referral hospitals

Asthma diagnosis: measures of Airway Responsiveness

Airway challenge with bronchoconstrictor stimuli to determine the presence of airway hyperresponsiveness is a useful tool in patients with suggestive symptoms but who have normal spirometry. The test involves the inhalation of increasing doses of a bronchoconstrictor, such as histamine, methacholine or adenosine and to determine the provocative dose that reduces the FEV_1 by more than a set value, usually 20%. A positive test has low specificity for asthma as airway hyper-responsiveness is present in other conditions such as COPD, cystic fibrosis, allergic rhinitis and bronchiectasis. A negative test, is however useful in excluding asthma in patients not on prolonged inhaled corticosteroids.

Asthma diagnosis: Role Markers of airway inflammation

Measurements of sputum eosinophilia and neutrophilia provide information on underlying inflammation. Asthmatic airways (patients not on corticosteroids) produce more Nitric Oxide (NO) and Carbon monoxide (CO) than non-asthmatic airways. Therefore measuring the fraction of expired NO (FENO) and CO (FECO) has been suggested as non-invasive markers in evaluating airway inflammation in asthma. Previous methods for measuring FENO used bulky machines and were cumbersome. Recently smaller hand held devices have become available and measurement of FENO is increasingly being used to monitor the adequacy of treatment. The clinical utility of these measures however is yet to be established in prospective randomized clinical trials.

Asthma Diagnosis: Role of Allergy Tests

Testing for allergic status is usually accomplished by performing skin testing or measuring specific IgE in serum. Measurement of specific IgE in serum is however expensive. A positive skin allergy test or specific serum IgE may suggest the specific allergen related to asthma symptoms in individual patients but the false positive rate is high. Thus a positive skin allergy test or specific serum IgE should be carefully correlated with the clinical circumstances. There is no role for measuring total IgE in serum in the diagnostic work up of asthma.

Suggested further reading

- 1. The Global Strategy for asthma management and prevention 2009 (update). Accessed from www.ginasthma.org on December 21, 2010.
- ERS Task Force. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence based approach Eur Respir Journal 2008; 32: 1096 -1110
- Nicole Beydon , Stephanie D. Davies, Enrico Lombardi et al on behalf of the ATS/ERS Working Group in Infant and Young Children Pulmonary Function Testing.

Am J Respir Crit Care Med 2007; 175: 1304 -1345

- M.R. Miller, R. Crapo, J. Hankinson, V. Brusasco et al on behalf of the ATS/ ERS Task Force: Standardization of lung function testing General considerations for lung function testing Eur Respir J 2005; 26: 153-161
- M.R Miller, J. Hanknison, V. Brusasco et al on behalf of the ATS/ERS Task Force: Standardization of lung function testing: standardization of spirometry Eur Respir J 2005; 26: 319-338
- Barnes PJ, Dweik RA, Gelb AF et al Exhaled nitric oxide in pulmonary diseases: A comprehensive review Chest 2010 Sep; 138 (3): 682-92
- 7. Anderson SD.

Indirect challenge tests: Airway hyperresponsiveness in asthma: its measurement and clinical significance.

Chest. 2010 Aug;138(2 Suppl):25S-30S.

8. Brannan JD.

Bronchial hyperresponsiveness in the assessment of asthma control: Airway hyperresponsiveness in asthma: its measurement and clinical significance.

Chest. 2010 Aug;138(2 Suppl):11S-17S.

9. Cockcroft DW

Direct challenge tests. Airway hyperresponsiveness in asthma: its measurement and clinical significance

Chest 2010; 138 (2 suppl): 18S -24S



10. Guibert TW.

Identifying and managing the infant and toddler at risk for asthma. J Allergy Clin Immunol. 2010 Aug;126(2):417-22. Epub 2010 Jul 10.

11. Peter SP.

Special considerations in adults for diagnoses that may coexist with or masquerade as asthma.

Ann Allergy Asthma Immunol. 2010 Jun;104(6):455-60; quiz 461-3, 484.

12. Galant SP, Nickerson B.

Lung function measurement in the assessment of childhood asthma: recent important developments.

Curr Opin Allergy Clin Immunol. 2010 Apr;10(2):149-54.

chapter 4 Medications used in asthma

Chapter objective

This chapter is intended to provide information on the medicines that are used in the treatment of asthma.

The primary audience for this chapter includes clinicians, health programme developers and managers, health financiers and patients and their families.

Asthma Medications

In general medicines (drugs) used to treat asthma can be classified in two broad groups: Relievers (bronchodilators) and controllers (anti-inflammatory drugs) which are also called preventers. Relievers are in general used on an 'as-needed' basis to quickly reverse broncho-constriction and relieve its symptoms. Controllers are medications taken on a daily basis to keep asthma under control through their anti – inflammatory effects.

Because asthma is a chronic persistent disease these medicines need to be used on a long term basis by the majority of asthma patients. The preferred route of administration of most of these medicines, except the leukotriene antagonists, is the inhaled route because it allows small doses (micrograms) to be used and delivers the drug directly to the airways thus achieving high local concentrations and limiting systemic adverse effects.

Various inhaler devices have been developed. These include pressurized Metered Dose Inhalers (pMDI), breath actuated Metered Dose Inhalers, Dry Powder Inhalers (DPIs), soft mist inhalers and nebulized or wet aerosols.

Text Box 9: Inhaler Devices

- Pressurized Metered Dose Inhalers (pMDIs)
- Breath Actuated MDIs
- Dry Powder Inhalers
- Soft Mist Inhalers
- Nebulizers or wet aerosols
- Volume Spacers with or without face masks to be used with pMDIs



In general pMDIs are cheaper than the dry powder devices but require greater training to achieve the requisite finger-breath coordination for delivery of the drug aerosols into the airways. Dry powder devices on the other hand require a certain minimum peak inspiratory flow (PIF) to enable inhalation of the dry powder into the lungs. Most pMDIs now come with Hydrofluoroalkanes (HFAs) as opposed to Chlorofluorocarbons (CFCs) as the propellant because CFCs are ozone depleting.

Table 5: Asthma medicines that are in Kenya's current essential medicine list

Drug	Formulation	How Supplied
Aminophylline	Injection 25 mg/ml	10 ml vials
Beclomethasone Dipropionate	PMDI at 50µg/puff	packs
Salbutamol	PMDI at 100µg/puff	packs
Salbutamol	2 mg tablets	1000 tablets containers
Salbutamol	4 mg tablets	1000 tablet containers
Salbutamol	Injection 0.5 mg/ml	ampoules
Salbutamol	Nebulizing solution 5mg/ml	Bottles
Salbutamol	Suspension 2 mg/ml	100 ml bottles
Ipratropium bromide	PMDI at 20µg/puff	Packs

The Relievers - Bronchodilators

The beta 2 agonists are the bronchodilators or relievers most available currently for the treatment of asthma. They may be rapid and short acting, rapid and long acting or slow and long acting.

The rapid and short acting beta 2 agonists include salbutamol, fenoterol, terbutaline, pirbuterol and procaterol. These medicines are used on 'as needed' basis to relieve asthma symptoms. A high frequency of reliever use is an indicator of poor asthma control and should prompt a review of the asthma management plan or the short use of a rescue course of oral corticosteroids. The preferred route of administration of these medicines is the inhaled route. The effect of these medicines peaks at about 2 hours and lasts about six hours.

While oral salbutamol is commonly used in Kenya, this is associated with more frequent and severer side effects such as palpitations and tremor. However the oral preparations are cheap and widely available. As such it is anticipated that they will continue to play a useful role in asthma treatment until short acting inhaled be_ta 2 agonists become more affordable and widely available.

Both Salmetrol and Formoterol are long acting $be_ta 2$ agonists with prolonged bronchodilator action that lasts up to 12 hours. These two drugs differ in the rapidity with which bronchodilator effect take place. While Salmetrol has a slow onset of action, formoterol is fast acting and thus it may be used on as needed basis, as a reliever medicine. The long acting beta agonists should not be used alone but should always be used in combination with an inhaled steroid.

Long acting oral beta 2 agonists including slow release formulations of salbutamol, terbutaline and bambuterol are generally not preferred because of the higher frequency of adverse events.

Other Bronchodilators

Theophyllines

Short acting theophyllines such as aminophylline may be used to relieve bronchospasm and asthma symptoms. However because of their narrow therapeutic window and the availability of the safer and more effective beta agonists, short acting theophyllines are not the preferred bronchodilators for the management of asthma exacerbations. They should be reserved for patients who fail repeated doses of inhaled beta 2 agonists.

Slow release formulations of theophylline should be considered as add on medicines in patients who are not adequately controlled on low dose inhaled corticosteroids. Under these circumstances the theophylline may be exerting a more anti –inflammatory than bronchodilator effect.

Anti-cholinergics

Ipratropium bromide is the anti-cholinergic most commonly used for the treatment of asthma especially in the acute care setting. When Ipratropium is used in the acute care setting, it is usually combined with a short acting inhaled _2 agonist (salbutamol). This combination may have additional benefit on lung function and reduce the risk of hospitalization in the acute care setting.

Oxitropium is used less often while tiotropium is not currently used for treatment of asthma. However a recent study has suggested that tiotropium may have long term beneficial effects in asthma and thus the expectation is that in the near future tiotropium will be included in the list of agents that may be used routinely to control asthma. Ipratropium bromide may also be used on a long term basis as the 'as needed' bronchodilator in patients unable to tolerate beta 2 agonists.

The anti-cholinergics are safe medicines associated with minor side effects such as a bitter taste and dryness of the mouth.



Text Box 10: Drugs with predominantly Bronchodilator action
Rapid onset and Short acting Beta 2 agonists Salbutamol Fenoterol Terbutaline
Rapid onset and Long Acting Beta 2 Agonists (LABA) Formoterol
Slow Onset and Long Acting Beta 2 Agonists (LABA) Salmeterol
Long acting oral Beta 2 Agonists Slow release formulations of salbutamol and terbutaline
Short acting Theophyllines Aminophylline
Anti-cholinergics Ipratropium bromide Oxitropium

Controller medications- anti-inflammatory agents.

Long Acting beta 2 agonists (LABA)

Despite lack of significant anti-inflammatory effect, these drugs are classified as controllers and are used in combination with inhaled corticosteroids for the long term control of asthma. In addition to bronchodilator properties, they also inhibit mast cell mediator release, plasma exudation and reduce sensory nerve activation. The LABAs may potentiate the molecular mechanism of corticosteroid actions, with increased nuclear localization of glucocorticoid receptors and thus have additive or sometimes synergistic suppression of inflammatory mediator release. Concurrent use of LABA with Inhaled corticosteroids also reduces the total steroid requirement thus mitigating side effects.

Formoterol is currently the only rapid onset long acting $_{-2}$ agonist available. This drug, combined with an inhaled corticosteroid (ICS), is currently recommended for use as both reliever and controller. When the LABA/ICS combination is used as a reliever and controller in the Kenyan situation, there may be significant cost implications. Therefore it may still be prudent to reserve Formoterol/ICS for control and to use short acting $_{-2}$ agonist as the reliever.

Salmeterol is a slow onset, long acting $_{-2}$ agonist used in combination with an inhaled corticosteroid. Previous research on salmeterol mono-therapy resulted in higher mortality among a subset of subjects. This may have been due to lack of concurrent anti-inflammatory therapy and thus worsening of underlying disease.

It must be emphasized that anti-inflammatory therapy (ICS) forms the backbone of asthma control. Hence LABAs should only be used in combination with ICS.

Inhaled Corticosteroids (ICS)

The pillar of asthma treatment is the use of anti-inflammatory medicines of which inhaled corticosteroids (ICS) are the most effective. **All asthma patients except those with very mild and intermittent symptoms should be on inhaled corticosteroids.** Although at equipotent doses the various inhaled steroids should have the same efficacy, differences in formulation and delivery systems can create variations in therapeutic efficacy. Also chemical properties of the various inhaled steroids may also affect safety profiles. For example both ciclesonide and beclomethasone dipropionate are pro drugs which greatly lowers their potential to cause local oro-pharyngeal side effects. Recently small particle inhaled steroids have been introduced. These new formulations carry the advantage of improved total lung deposition including ability to reach small airways which may confer better asthma control at lower doses, but this advantage may be offset by higher systemic bioavailability with a greater risk of adverse effects. It has been observed that higher doses of any of the inhaled steroids may result in adverse effects without additional benefit.

In patients who fail treatment with low doses of inhaled corticosteroids, it is recommended that a LABA (preferred), a leukotriene modifier (alternative) or slow release theophylline, be added.

Inhaled corticosteroids are generally safe. Local side effects such as, oro-pharyngeal candidiasis, and dysphonia can be minimized through good inhaler technique, mouth rinsing after drug inhalation or even better brushing teeth after inhalations and use of high volume spacers when corticosteroids are delivered via a pMDI.

Small amounts of Inhaled corticosteroids absorbed from the lung and possibly the gut may cause systemic adverse events. The risk of such adverse effects is dependent on the dose and potency of the inhaled corticosteroid, the delivery system used, systemic bioavailability, first pass metabolism and the half life of the systemically absorbed drug.

In general there are no significant systemic side effects when these drugs are used in doses of about $400\mu g$ beclomethasone dipropionate or equivalent. In high doses and particularly when administered through the oral route, steroids can cause adverse effects such as easy bruising, adrenal suppression, reduced bone mineral density, increased risk of fractures, peptic ulceration, cataracts, hyperglycemia, hypertension and glaucoma. There is no evidence that inhaled corticosteroids increase the risk of lung infections including tuberculosis and these drugs can be used in the presence of active tuberculosis.

The anti-retroviral drug, ritonavir, significantly increases plasma fluticasone propionate concentration, resulting in significantly decreased serum cortisol concentrations. Systemic corticosteroid effects including Cushing's syndrome and adrenal suppression have been reported during post-marketing use in patients receiving ritonavir and inhaled or intra-nasally administered fluticasone propionate. Therefore, co-administration of fluticasone propionate and ritonavir is not recommended unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side effects. It appears that low dose beclomethasone or budesonide are safer options when concurrent administration with ritonavir is indicated.

Drug	Low Dose (mcg)	Medium Dose (mcg)	High Dose (mcg)
Beclomethasone dipropionate	100-200	>200-400	>400
Budesonide	100-200	>200-400	>400
Ciclesonide	80-160	>160-320	>320
Fluticasone propionate	100-200	>200-500	>500

Table 6: Inhaled Corticosteroids commonly available in Kenya and their equipotent doses

Leukotriene Modifiers

The leukotriene modifiers include the 5 lipo-oxygenase inhibitor, zileuton and the cysteinyl leukotriene receptor 1 antagonists, montelukast, pranlukast and zafirlukast. Leukotriene modifiers may be used as add on therapy in patients who fail to achieve control with low dose inhaled corticosteroids or as alternatives to low dose inhaled corticosteroids in patients with mild asthma and aspirin induced asthma (AIA). However Leukotriene modifiers are inferior in potency to inhaled corticosteroids and a LABA. Leukotriene modifiers may be particularly useful in the presence of allergic rhinitis and asthma as they may relieve both nasal and chest symptoms

This group of medicines is generally well tolerated. However, liver toxicity may occur with zileuton and thus monitoring of liver function tests is recommended in patients using this drug.

Theophyllines

Theophyllines are bronchodilators with anti-inflammatory properties at low doses.

They are used as add on therapy in patients not controlled on low dose inhaled corticosteroids. Long acting beta agonists are superior to theophyllines as add on therapy. For long term use, slow release theophyllines are recommended.

Theophyllines have a narrow therapeutic window and may be associated with a number of adverse effects including gastro-intestinal symptoms, cardiac arrhythmias, seizures and deaths. These adverse effects are more likely to occur at doses above 10mg/kg/day.

Physiological states like pregnancy, diseases affecting the heart and liver, and drugs such as anti-tuberculous agents, cimetidine, quinolones and macrolides alter theophylline metabolism. This may result in reduced clinical efficacy or increased drug toxicity.

The Cromones

The cromones which include nedocromil sodium and sodium cromogylcate have very limited role in the long term treatment of asthma. They have been used for intermittent asthma and exercise-induced bronchospasm but have very weak anti-inflammatory effect and are less effective than low dose inhaled corticosteroids.

Anti -IgE (Omalizumab)

This treatment may benefit asthma patients with high IgE levels and who have severe allergic asthma that is poorly controlled on optimized usual treatment which includes oral steroids. Anti –IgE is given subcutaneously every 2-3 weekly and is extremely expensive. This treatment is currently not available in Kenya.

Systemic Corticosteroids

Short pulses of systemic corticosteroids are recommended for patients with moderate to severe acute exacerbations of asthma. The preferred route of administration is oral. In a small subset of patients, asthma may remain uncontrolled unless systemic corticosteroids are used. In these patients with steroid dependent asthma the lowest possible dose of corticosteroid should be used. Dosing strategies such as alternate day therapy help mitigate systemic side effects.

Other controller therapies

Patients who require high doses of systemic corticosteroids to control their asthma may benefit from other controller medicines that are designed to reduce the overall dose of the corticosteroid. Such patients should be referred to a chest specialist familiar with these therapies. These alternative therapies have significant adverse effects and the desired steroid sparing effect may be offset by such adverse events. These medicines include low dose methotrexate, cyclosporine, gold and troleandomycin

Allergen specific Immunotherapy

Because most asthmatics react adversely to a wide range of allergens, allergen specific immunotherapy has a limited role in asthma. However in the rare instance when an atopic individual happens to sensitive to one or two allergens and when optimized asthma treatment still results in inadequate control there may be a role for this therapy.

Complementary and alternative medicine

Alternative and complementary approaches, including yoga, acupuncture, dietary supplements, herbal preparations, and breathing techniques have not been subjected to rigorous scientific research and hence their use cannot be recommended at present.

Suggested further reading

- 1. The Global Strategy for asthma management and prevention 2009(update). Accessed from www.ginasthma.org on December 21, 2010.
- N. Ait Khaled, DA Enarson, C-Y Chiang, G. Marks, K. Bissel Management of asthma: a guide to the essentials of good clinical practice International Union Against Tuberculosis and Lung Disease, Paris, France, 2008.
- 3. Gentile DA, Skoner DP

New asthma drugs: small molecule inhaled corticosteroids Curr Opin Phrmacol 2010; 10(3): 260-5

- Baptist AP, Reddy RC Inhaled corticosteroids for asthma: are they all the same? J Clin Pharm Ther 2009; 34(1): 1-12
- Peters SP, Kunselman SJ, Icitovic N *et al* Tiotropium bromide step-up therapy for adults with uncontrolled asthma. N Eng J Med. 2010 Oct 28;363(18):1715-26.
- Foisy MM, Yakiwchuk EM, Chiu I, Singh AE Adrenal suppression and Cushing's syndrome secondary to an interaction between ritonavir and fluticasone: a review of the literature HIV Medicine 2008; 9(6): 389–396.
- Albert Martin Li Ritonavir and fluticasone: beware of this potentially fatal combination J. Paed. 2006; 148: 294-295



chapter 5 Management of Asthma

Chapter objectives

This chapter is intended to provide information on the day to day management of asthma to achieve asthma control and to return patients to productive lives.

The primary audience for this chapter includes clinicians, health care programme developers and managers, health financiers, patients and their families.

The goals of asthma care/management

The goals of asthma care/management include:

- Achieve and maintain control of symptoms
- Prevent asthma exacerbations
- Maintain lung function as close to normal as possible
- Maintain normal level of activity including exercise
- Avoid adverse effects of asthma medications
- Prevent development of irreversible airflow limitation
- Maintain normal growth velocity in children
- Prevent asthma mortality

These goals can be achieved in most patients with asthma using simple interventions. GINA has defined five elements in the care of patients that if properly implemented, should lead to the achievement of "controlled" status for most patients. The five key asthma management elements include:

- Development of a close partnership between the patient and the health care provider
- Identification and avoidance of triggers of asthma symptoms
- Assessment of asthma severity, institution of appropriate treatment based on asthma severity and monitoring of the response to treatment
- Management of asthma attacks or exacerbations
- Special considerations.

Element 1: The partnership between patient (and family) and the health care provider.

Asthma is largely a lifelong disease and as with other chronic health problems a close partnership needs to be built between the patient and his or her family and the health care provider for the best possible outcomes to accrue. This partnership needs to begin
with a clear communication of the diagnosis. When asthma is diagnosed it should be called asthma and not any other name. The patient and his or her family should be given as much information as possible about the disease, the goals of treatment, the identification and avoidance of symptom triggers, the drug treatment including the distinction between relievers and preventers, the potential side effects and how they may be prevented and the steps to be taken when an asthma exacerbation occurs (text box 11). Additionally the patient who has been placed on a specific inhaler device should be trained on the appropriate use of that device and only allowed to take the device home after it is certified that the appropriate inhaler technique has been learnt. It is better to write down the information on treatment (drug, number of puffs and frequency of inhalation) and the steps to be taken when an exacerbation occurs to allow patients some autonomy in the management of their disease. This is called guided self management and it has been shown reduce asthma morbidity in both adults and children.

Text Box 11: The Patient - Health Provider Partnership

- Joint goal setting
- Personalized Education
 - o About the Disease
 - o Medication including Relievers and Preventers
 - o Potential side effects of medicines
 - Inhalation technique
 - Recognition of worsening asthma and actions to be taken
- Self monitoring of asthma control
- Regular review to assess control and adjust treatment as may be necessary
- A written asthma management plan

Element 2: Identification and avoidance of symptom trigger factors.

There are no interventions that have been scientifically proven to prevent the development of asthma in individuals at high risk of the disease. However avoiding exposure to tobacco smoke during the fetal stage of life and after birth may be useful for the prevention of wheezing illnesses and allergic sensitization in children. Breastfed infant appear to have lower rates of childhood wheeze and thus breastfeeding should be widely promoted.

Individual patients with asthma should be advised and supported to identify and

whenever possible avoid factors that are associated with the development of asthma symptoms. In many patients the trigger factors for asthma symptoms are multiple and it may be difficult to completely identify and avoid all the relevant factors. Expensive methods for reduction or elimination of trigger factors for asthma are mostly not needed and are therefore not recommended. It is important to note that the tolerance levels for asthma symptom triggers are usually improved with the use of effective controller medications.

Control of Indoor triggers factors

The common asthma symptom trigger factors encountered in the indoor environment include domestic mites, furred animals, fungi, cockroaches and indoor air pollution. Although the combination of approaches to comprehensively deal with allergens and pollutants encountered in the home environment have not been adequately tested, it appears reasonable to recommend that the home environment of asthma patients should be clean, devoid of animals, dust free, dry and as smoke free as possible.

Control of outdoor trigger factors

Most triggers encountered in the outdoor environment may be difficult to avoid. Unlike in temperate climates where certain plant derived allergens peak at certain times of the year, in the tropics, pollen exposure may occur throughout the year. However certain farm related pollens may be occur only at certain times of the year and asthma patients who have identified the ill effects of pollens from specific farm crops should be advised to avoid undue exposures to these crops. The most common crops that appear to be relevant in this category include Maize and Napier grass.

Air pollution has been associated with asthma exacerbations and patients with asthma should be advised to avoid being in places that are obviously polluted. It is also useful to advise asthma patients to avoid environments that are excessively dusty, or to engage in very strenuous exercise in cold environments.

Occupational (see section on occupational asthma) and other triggers

If the individual with asthma is suspected to have occupational asthma, in which the asthma inducing agent was encountered in the occupational setting, as far as feasible, further exposure to the inducing agent should be avoided.

In children food allergens may be an important cause of asthma exacerbations. Such allergens should be identified through food oral challenges and advice given to avoid food implicated in triggering attacks.

Some food additives, such as sulfite, benzoate and monosodium glutamate used for food preservation and food coloring agents such as tartrazine may be associated with

asthma exacerbations. When a causal link between asthma exacerbations and a food additive is strongly suspected advice to avoid the food additive should be given.

Asthma exacerbations may be associated with exposure to drugs such beta blockers, aspirin and other non steroidal anti-inflammatory drugs. In general beta blockers should be avoided in patients with asthma except for cardio- selective beta blockers used in the management of acute coronary syndromes. Most patients with asthma can tolerate aspirin and other non steroidal anti-inflammatory drugs. However aspirin and other NSAIDs should be avoided in patients known to react adversely to these agents.

There is no local data on the usefulness of influenza vaccination in patients with asthma. A provisional recommendation to vaccinate asthma patients with severe and difficult to control asthma may be appropriate as local clinical experience accumulates and local studies to examine the role of the influenza viruses in asthma exacerbations are undertaken.

Asthma control may improve with weight reduction in obese patients. Thus patients with asthma should be advised to maintain ideal weights and to lose weight when obese.

If asthma exacerbations are related to emotional stress, appropriate psycho social support should be provided.

Other factors that may be associated with asthma exacerbations included uncontrolled rhinitis, gastro esophageal reflux disease and menses in females in the child bearing age. Appropriate interventions should be provided to patients whose asthma is worsened by these factors.

Element 3: Assess asthma severity, treat and monitor asthma control.

With appropriate treatment most patients with asthma can gain and maintain asthma control and thus lead normal productive lives. At each visit, including the first visit, the health provider should assess the severity of asthma or the level of control for diagnosed asthma on treatment, initiate treatment at the appropriate treatment step based on the asthma severity or level of control and arrange for a follow up visit to assess response to treatment. GINA identifies three levels of asthma control: Controlled, Partly Controlled and Uncontrolled as outlined in table 7 for adults and table 8 for children.

Patients should also be assessed for the presence of risk factors that increase the likelihood of a severe exacerbation in the future, which include high medication requirements, need for emergency care in the past on year, hospitalization, low FEV1 and exposure to tobacco smoke.

Text Box 12: Factors that increase the likelihood of a future severe asthma exacerbation

- High medication requirements
- Need for Emergency treatment in the last one year
- Exposure to tobacco smoke
- Hospitalization ever.
- Low FEV1

Table 7: Asthma - Levels of Control

Characteristic	Controlled	Partly controlled	Uncontrolled
Day time symptoms	Twice or less per week	More than twice per week	3 or more of the features of partly
Limitation of activities	None	any	controlled in any week
Nocturnal symptoms/ awakening	None	any	
Need for relievers/ rescue treatment	Twice or less per week	More than twice a week	
Lung function (PEF or FEV ₁)	Normal	< 80% of predicted or personal best	

Table 8: Level of Asthma Control for Children Five Years Old or Younger*

Characteristic	Controlled (all of the following)	Partly Controlled (Any measure present in any week)	Uncontrolled (3 or more of features of partly controlled asthma
			in any week)



	1			
Daytime symptoms: wheezing, cough, difficult breathing	None (less than twice/wk, typically for short periods on the order of minutes and rapidly relieved by use of a rapid-acting bronchodilator	More than twice/ wk (typically for short periods on the order of minutes, and rapidly relieved by use of a rapid-acting bronchodilator)	More than twice/ wk (typically last minutes or hours or recur, but partially or fully relieved with rapid-acting bronchodilator)	
Limitation of activities	None (child is fully active, plays and runs without limitation or symptoms)	Any (may cough, wheeze, or have difficulty breathing during exercise, vigorous play, or laughing)	Any (may cough, wheeze, or have difficulty breathing during exercise, vigorous play, or laughing)	
Nocturnal symptoms/ awakening	Non (including no nocturnal coughing during sleep)	Any (typically coughs during sleep or wakes with cough, wheezing and/or difficult breathing)	Any (typically coughs during sleep or wakes with cough, wheezing and/or difficult breathing)	
Need for reliever/rescue treatment	< 2 days/week	> 2 days/week	> 2 days/week	
*Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate. Although patients with current clinical control are less likely to experience exacerbations they are still at rick during viral upper respiratory tract infections and may still				

adequate. Although patients with current clinical control are less likely to experience exacerbations, they are still at risk during viral upper respiratory tract infections and may still have one or more exacerbations per year.

Several tools have been developed to assist patients and health care providers to assess the level of asthma control (see appendix number 1). These tools include the asthma control test, asthma control questionnaire, asthma control scoring system and asthma therapy assessment questionnaire. There is some limited experience with the use of the asthma control test and the asthma control questionnaire in Kenya and thus it is recommended that these two tools should be made widely available and used in Kenya.

The treatment step chosen when initiating treatment for the first time will depend on the severity and frequency of symptoms at the initial visit to the health provider. Some patients will present for the first time at the emergency department with severe symptoms and thus initiate treatment beginning with the acute severe asthma management algorithm. Others will present with mild disease and could start treatment at step 1 of the treatment steps. Initiating treatment for asthma should therefore be individualized and should be based on the severity and frequency of symptoms and lung function test (PEF or FEV1) at the initial presentation. Following initiation of treatment the response to treatment should be reviewed regularly and controller treatment stepped up if needed until control is achieved. Once control is achieved and the level of control has stabilized for at least three months controller treatment should gradually be reduced to the minimum level that maintains control.

Treatment Steps and Recommended Therapies.

Step 1: This step will be used for rare patients with very mild and intermittent symptoms. No controller medicine is used. The patient uses an inhaled short acting bronchodilator such as salbutamol, terbutaline or fenoterol, as needed to control their disease. The use of short acting theophyllines and oral short acting beta agonists for this step is discouraged on account of their slow onset of action and higher risk of adverse effects.

Step 2: Most patients with asthma will be sufficiently controlled on this step of treatment. Symptoms are relieved as needed using an inhaled short acting bronchodilator such as salbutamol, terbutaline or fenoterol while low dose beclomethasone dipropionate (Hydrofluoalkane (HFA) based) pressurized meter dose inhaler at 100 ug per puff or equivalent at a dose of a puff twice daily is used as the controller medicine.

Step 3: Patients who remain uncontrolled with step 2 treatment continue to relieve symptoms using as needed inhaled short acting bronchodilator such as salbutamol, terbutaline or fenoterol. The controller options, depending on setting (private or public) and thus drug availability, affordability and willingness to pay, include:

- a) Moderate doses of inhaled steroids such as HFA based beclomethasone 100ug per puff or equivalent at a dose of 2 -4 puffs twice daily.
- **b)** Low dose inhaled steroid combined with a long acting beta agonist (salmetrol or formoterol) preferably given via a combination inhaler device.
- c) Low dose inhaled steroid combined with a leukotriene modifier or a slow release theophylline instead of the long acting beta 2 agonist.

Step 4: This treatment step will apply to patients with severe disease. Patients continue to relieve symptoms using as needed inhaled short acting bronchodilator such as salbutamol, terbutaline or fenoterol. The controller options, depending on setting (private or public) and thus drug availability, affordability and willingness to pay, include:

a) Moderate to high doses inhaled steroids combined with long acting



beta agonist and a leukotriene modifier with or without a slow release theophylline.

Step 5: This step is defined by the need for regular systemic steroids. Only a minority of patients need to be placed on regular systemic steroids to achieve and sustain asthma control. If a patient appears to require step 4 or 5 treatment on a long term basis, consultation with an asthma expert is warranted. Systemic steroids are toxic when used on a frequent or long term basis. The lowest possible oral doses to maintain asthma control should be used. There is no apparent advantage for the use of parenteral depot steroid preparations for most patients and their use is strongly discouraged.

There is hardly any experience in Kenya with the use of anti-IgE and other therapies in patients who remain poorly controlled even with regular systemic steroids. Most of these patients will be managed at specialist centers, whose establishment is strongly recommended.

Monitoring Asthma control and treatment adjustment

Patients on treatment for asthma should be reviewed regularly and their treatment adjusted as may be necessary. The frequency of clinic visits should be individualized but in general, stable patients should be seen about once every three months. If in the intervening period, between clinic visits , the patient remains well at a particular treatment step for about 3 months, the treatment should be stepped down to a lower treatment step. If on the other hand the patient appears not to have sustained asthma control, treatment should be stepped up to a higher treatment step. Patients controlled on low doses of inhaled steroids with or without long acting beta agonists may be switched to single daily doses. There has been some concern about the safety of long term use of LABA and thus as soon as clinically feasible, patients should be switched to inhaled corticosteroids alone.

Asthma that is difficult to control

A small proportion of patients have asthma that is difficult to control, which is defined as inability to achieve asthma control despite regular use of step 4 treatment options. In such patients referral to an expert is recommended. The management approaches include:

- Confirm that the diagnosis remains asthma and exclude other diagnoses (Is it asthma?)
- Evaluate the treatment and establish that it is correct and that the appropriate inhaler devices have been prescribed
- Establish that the asthma medicines are being used (Is the patient adherent to treatment)

- Reconfirmation that the correct inhaler technique is being used
- Exclusion of exposures that may impede asthma control such as tobacco smoking, occupational agents and irritants and allergens
- Exclusion of co-morbidities that may impede asthma control such as chronic rhinitis, gastro- esophageal reflux disease, obesity and sleep disordered breathing and psychiatric disorders.

If asthma is re- confirmed and no additional modifiable factors are found, an honest discussion should be held with the patient to reset the asthma control goals and to accept the sub-optimal level of control. Even under these circumstances attempts should be made to achieve and sustain a reasonable degree of asthma control at the lowest possible doses of asthma medications.

Element 4: Management of asthma exacerbations (acute severe asthma)

Asthma exacerbations are progressive worsening of asthma symptoms. For most patients the progression is slow although in a few adults acute catastrophic worsening may occur. Patients usually present with respiratory distress. All asthma patients should be provided with a written plan outlining actions to be taken when an asthma exacerbation occurs. In patients known or suspected to be at risk of severe life threatening exacerbations, some of whom are known to have a poor perception of asthma symptoms, home PEF monitoring should be encouraged. The level of PEF at which specific actions need to be taken should clearly be spelled out in a written action plan. It is important to identify patients who are at risk of severe life threatening exacerbations. These include patients with

- Previous episode of near fatal asthma
- Emergency visit or hospitalization in the last year
- Current or recent use of systemic glucocorticoids
- Non use of controller/anti-inflammatory medicine
- Psychiatric or psychosocial illness
- Non adherence to controller treatment

Every exacerbation must be assessed to determine its severity. Simple assessment of breathing disturbance, speech, breathing rate, PEF, mental status and oxygenation status should be able to provide an indication of the severity of the exacerbation (text box 13).

The three critical elements of treating an asthma exacerbation include the rapid achievement of bronchodilation, the early administration of systemic steroids and oxygen supplementation.

36

In most patients with mild to moderately severe exacerbations bronchodilation can be achieved by administration of 5-10 puffs of a short acting beta agonist through the PMDI and a volume spacer. The administration of bronchodilators via a nebulizer should be reserved for patients with severe exacerbations especially those who appear exhausted, drowsy, confused or have a silent chest. When nebulized bronchodilators are deemed to be necessary oxygen should as far as feasible be used as the driving gas.

The response to the bronchodilator should be assessed in about 15 to 30 minutes depending on the severity of the exacerbation and drug administration repeated at intervals of 15 - 30 minutes until a response is obtained. The anticholinergic, Ipratropium bromide may be added if the response to inhaled salbutamol is not satisfactory.

Although widely used in Kenya, intravenous aminophyline should probably be reserved for patients who do not respond to repeated administration of a beta 2 agonist plus anticholinergics. Similarly the use of adrenaline should probably be reserved for patients who do not respond to inhaled bronchodilators and intravenous aminophylline. Whether aminophylline and adrenaline should continue to have a role in the management of asthma in a resource poor setting such as Kenya needs to be evaluated in appropriately designed clinical trials that determine efficacy, safety and health care costs.

Severely ill patients should be placed on oxygen to keep the SpO₂ close to 95%. Patients who have signs suggestive of a potential fatal outcome should be transferred to or admitted to a critical care unit and continued on bronchodilators. Those judged to require mechanical ventilation should initially be placed on a fraction of inspired oxygen (FIO) of 1, with low tidal volumes of between of 5-7 ml/Kg, a low positive end expiratory pressure (PEEP) of below 5 cm H₂0, a long expiratory time with a Inspiratory to Expiratory Ratio (I: E ratio) of more than 1:2 and a low breathing frequency of 8-10 per minute. The peak inspiratory pressure should be limited to below 40 cmH2O. Intravenous magnesium sulphate therapy should be considered adjuvant in situations where usual treatment appears not to be working.

All patients with exacerbations of asthma should be prescribed systemic steroids (0.5 -1 mg/Kg) prednisolone or equivalent which should preferably be given by the oral route. The systemic steroids should be continued for about 5 days or until about 2 days after the attack appears to have resolved.

In most situations chest x-rays are not useful in the evaluation of patients with asthma attacks. Chest physiotherapy, mucolytics and mucokinetic agents, cough mixtures and antihistamines are also not needed in the management of patients with asthma attacks and may in fact be dangerous.

Only a minority of patients have a bacterial infection associated causally with the asthma exacerbation, hence the use of antibiotics to treat an asthma exacerbation is often not indicated unless there is a strong evidence of bacterial infection.



An attempt should be made to identify modifiable factors that led to the exacerbation with a view to preventing future exacerbations. Text box 14 outlines some of the issues that need to be examined in every patient who experiences a severe exacerbation of asthma.

Text Box 14: Issues to be examined to prevent future asthma exacerbations

- What was the usual level of control?
- Was the patient on appropriate therapy?
- Was the patient adherent to therapy?
- Was the inhaler technique correct?
- Are there trigger factors that the patient may be going back to?
- Was the patient being monitored adequately?

Text Box 15: Assessing the severity of an asthma exacerbation

- How breathless is the patient?
 - o Respiratory rate
 - use of accessory muscles
 - o pulsus paradoxus

• Is the patient able to talk?

- o Full sentences
- o Danger sign: speaking in phrases or words only

• Is the patient alert?

- o Danger sign : drowsy of confused
- Is the wheeze audible?
 - Danger sign: silent chest
- What is the PEF or FEV1?
 - Danger sign: PEF <30% of predicted
- What is the patient's oxygenation status?
 - Expect a low PaO_2 , low $PaCO_2$
 - \circ Danger sign: Normal or high ${\rm PaCO}_2$ or oxygenation saturation of below 90%

Suggested Further reading

Special issues related to Asthma Management in Children

The management of asthma in young children is largely similar to that of older children and adults in terms of general principles. However there are important differences.

Inhaled asthma medications are the most important aspect of treatment. For children less than 5 years inhaled medicines should be delivered from a pressurized metered dose inhaler (pMDI) through *spacer devices* and *face masks* to ensure efficient delivery of the drug to the young child's lungs. This maximizes the therapeutic effects and minimizes drug absorption and side effects. The parent should be trained on the use of these devices.

Choice of Spacer Device

Most children under 5 years will require a pMDI with a *spacer* and a *face mask*. Some older children, age six years and above may be able to use the mouthpiece of the spacer device directly, without a face mask.

When in more severe res	piratory distress a	ı nebulizer may	be used with a face mask.

Asthma Management Approach Based on Control for Children 5 Years or				
	Younger			
Asthma education, environmental control, and as needed rapid-acting _2-agonists				
Controlled on as needed rapid-acting _2-agonists	Partly controlled on as needed rapid-acting _2- agonists	Uncontrolled or only partly controlled on low-dose inhaled glucocorticosteroid*		

V.	×	×			
Controller Options					
Continue as needed rapid-acting _2-agonists	Low-dose inhaled glucocorticosteroid	Double low-dose inhaled glucocorticosteroid			
	Leukotriene modifier	Low-dose inhaled glucocorticosteroid plus leukotriene modifier			

* Oral glucocorticosteroids should be used only for treatment of acute severe exacerbations of asthma. Shaded boxes represent preferred treatment options.

In selecting which inhaled glucocorticosteroid to use, the following table provides guideline on low daily dose for those commonly available. Wherever there is indication to give the child a higher dose, one can double the low dose indicated in the table below.

Table 9: Daily doses of inhaled Corticosteroids in children 5 years and younger

Low Daily Doses of Inhaled Glucocorticosteroids for Children 5 Years and Younger*				
Drug Amount per Dose (µg) and frequency Total Daily Dose (µg)				
Beclomethasone dipropionate	50 µg bid	100 µg		
Budesonide	100 µg bid	200 µg		
Fluticasone propionate	50 µg bid	100 µg		

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

Preparations such as ciclesonide, mometasone furoate and triamcinolone acetonide have not been fully evaluated for use in this age group.

Intermittent wheezers

Those children that are symptomatic only during particular seasons of the year, and are well in-between may be managed with reliever medication as needed, and may not require controller medication.

Managing acute asthma exacerbations in children

Definition

Acute severe asthma is defined as an acute exacerbation of wheezing, difficulties in breathing and cough that is unresponsive to usual effective therapy and necessitating care in an emergency room or hospital ward. It is characterized by airways narrowing and inflammation, hyperinflation, impairment of pulmonary function, alterations in alveolar ventilation and hypoxemia.

Classification of acute exacerbations of asthma

Acute severe asthma in children is classified into mild, moderate and severe according to the criteria shown in Table 10.



Criteria	Severity			
	Mild	Moderate	Severe	
Pulsus paradoxus (mmHg)	<10	10-20	>20-40	
Wheeze	expiratory	Expiratory and Inspiratory	Soft breath sounds	
Respiratory Rate (per min)	<40	>40	>40	
Additional Signs		Speaks normally	Unable to speak	
		May be alert	Confused	
		Difficulty with feeding	Possible cyanosis	
		Intercostal retraction	Use of accessory muscles	
Arterial O ₂ saturation (%)	>95	91-95	<91	
Peak Expiratory Flow Rate (% Predicted)	70-90	50-70	<50	
PaCO ₂ (mmHq)	<35	<40	>40	

Table 10: Severity classification of asthma attacks in children.

In children unable to use a peak expiratory flow meter, the respiratory rate is regarded as the single most important measurement. A respiratory rate above 40/min is indicative of respiratory distress.

Children who have not responded to two properly administered beta 2 agonists at home require further management in an emergency room. Children who have responded to beta 2 agonists should maintain their response for 1 hour before being classified as responders

The single greatest danger to children suffering an acute attack of asthma is hypoxemia and not carbon dioxide retention. Therefore 100% oxygen should be given to all children with an acute asthma attack by means of a face mask at 5 litres or nasal prongs at 2 litres (cut off) at 3-4 litres/min. This will supply about 40% oxygen. This will supply about 40% oxygen. Oxygen must be used when _2 against bronchodilators are given by nebulizer in the emergency room. It is not necessary to humidify the oxygen. Children who have arterial oxygen saturations of below 90% are regarded as hypoxaemic. When monitoring arterial oxygen saturation, aim to maintain the saturation as close to 95% as possible.

If more than 40% oxygen is required this can be given by means of a mask with a rebreather at 8-10litres per min. It is also dangerous to give too much oxygen and the saturation should not be pushed much higher than 95%.

Administration of Beta 2 agonist bronchodilators

Most children with an acute asthma attack can be treated with a salbutamol containing PMDI at 6 puffs using a spacer with a face mask. If nebulized salbutamol is needed the dose should be 0.15 mg/kg/dose at 20 minute intervals with a maximum dosage of 5 mg/dose. The available salbutamol nebulizer solution comes in the concentration of 5 mg/ml. In children less than five years, 2.5 mg of this solution should be used for nebulization.

In patients on intensive regular beta 2-agonist treatment it is important to monitor the serum potassium level because of the risk of hypokalaemia. Oral potassium chloride is effective for treatment of hypokalaemia in this situation.

Other Bronchodilators

Adrenaline

Where inhaled **bet**a 2 agonists are not available or where nebulization is difficult, or if the child is not cooperative, subcutaneous adrenaline (0.01 ml/kg) 1:1000 may be used. A maximum of 0.3 ml may be given subcutaneously and this may be repeated a maximum of 3 times after 20 minutes

Anticholinergics

Ipratropium bromide

Ipratropium bromide is usually given with a _2-agonist to augment and sustain bronchodilatation in acute asthmatics. It should be added to the regimen of all children who are classified initially as non-responders at the dose of 0.1 ml/kg 6-hourly.

Use of steroids:

Oral steroids should be given early in the attack. Prednisone or prednisolone at a dose of 1- 2 mg/kg/day should be given as a single daily dose for at least 5 days. Most children with acute severe asthma will respond to the oral steroids and need not be given parenteral steroids. Thus the administration of steroids through the intravenous route should be reserved for children who are vomiting or are unable to take oral medicines for other reasons. If methylprednisolone is given intravenously it should be administered in no more than 3 doses of 1-2 mg/kg. Alternatively dexamethasone 0.4 mg/kg may be given as a bolus dose.

Monitoring the child with acute asthma

It is important to regularly measure indices of severity to assist in the assessment of progress. Improvements in the PEFR or forced expiratory volume (FEV1) are the most objective indices of response in children over the age of 8 years (attempt can be made for children over 5 years).

The importance of monitoring of the respiratory rate cannot be overstressed, particularly in children under the age of 8 years. A respiratory rate of less than 40/min is desirable. Repeated monitoring of the respiratory rate is a simple measurement of progress in the patient's condition and should always be recorded by medical and nursing staff.

Chest radiographs are not generally indicated in the child with an acute attack. If there is concern about the possibility of a pneumothorax or other air leak, chest radiographs should be done. Occasionally chest radiography may be necessary to exclude the possibility of a foreign body.

Dangerous and unnecessary practices

Rectal theophylline is absolutely contraindicated.

Although commonly used intravenous aminophylline should ideally only be used in selected patients in an ICU setting where blood levels can be monitored. If children are on oral theophylline avoid bolus administration. As previously indicated there is a need to conduct appropriately designed studies to determine the efficacy, safety and health care costs of commonly used therapies such as aminophylline in the management of acute severe asthma in children in Kenya.

There is no place for physiotherapy, mist tents or lung lavage in the management of acute asthma attacks. The administration of antihistamines, cough mixtures and mucolytics to children with acute asthma has not been shown to be beneficial. Children with acute asthma attacks should not be sedated. Antibiotics are not indicated in the management of most children with acute asthma.

The child with very severe asthma attack

Children with a severe life threatening acute asthma attack should be given 100% oxygen and adrenaline 0.3 ml subcutaneously, followed by intravenous salbutamol if they are unable to use a nebulizer. They should be admitted immediately to a high-care facility or ICU for intensive care. Between 1% and 6% of all asthmatics will require admission to an ICU and less than one-third of all children with asthma admitted to an ICU will require ventilation. Signs of deterioration and impending respiratory failure include a rising PaCO₂ of 5-10 mm/ h or PaCO₂ >55 mmHg, increasing dyspnoea or fatigue or confusion, a pulsus paradoxus of more than 40 mmHg and respiratory *acidosis* with a pH <7.25.

Hospital discharge and Follow-up

Children admitted to hospital for an acute asthma attack should have been stable on discharge medicines for at least 24 hours before discharge. These children should be discharged with sufficient medication for at least 3 days and their home care giver/guardian should be provided with a telephone number of a contact person at the hospital to reach in case of worsening symptoms in the child. The child or the care giver/guardian should be properly and adequately instructed in the use of the prescribed inhaler device for home use. It is also important to advice home PEF measurements at least 3 times a day until 3 days of discharge to pick up PEF deterioration which may indicate recurrence or continuation of the asthma attack. A written action plan should be given to the child and or the home care giver/guardian. The factors that triggered the attack should be identified and advice given on how they could be avoided to prevent a future attack.

Element 5: SPECIAL CONSIDERATIONS

NOCTURNAL ASTHMA

Nocturnal asthma refers to exacerbation of cough, chest tightness and wheeze in asthmatic patients that occurs at night. Some studies have defined nocturnal asthma as a drop in FEV_1 by more than 15% between bedtime and awakening. Up to 75% of asthmatics report night time symptoms at least once a week, while about 40% have symptoms on a nightly basis. Circadian variations in airway tone, airway hyperresponsiveness, histamine levels, epinephrine, inflammatory cells, glucocorticoid /_ adreno-receptor function, hypothalamic – pituitary axis, and decreased body temperature may account for worsened symptoms at night. Melatonin has been implicated in nocturnal asthma.

Almost half of patients with nocturnal symptoms and snoring have obstructive sleep apnea. Treating concurrent gastro-esophageal reflux disease and obstructive sleep apnea improves symptom scores but not measures of lung function. The timing of medications to allow for optimum serum levels at night is the main treatment strategy. Long acting beta 2 agonists like Salmeterol (recommended for use only in combination with an inhaled steroid) and sustained release theophyllines are particularly useful.

ASTHMA IN PREGNANCY

Maternal asthma does not increase the risk of fetal malformations. Medications for asthma have been used for many years and have been shown to be safe in pregnancy. Asthma may worsen, remain unchanged or even improve during pregnancy. Total control of symptoms should be the goal of treatment. Severe attacks may lead to fetal hypoxia, especially, during the third trimester when the enlarged abdomen presses on the diaphragm. Close follow-up is required.

ASPIRIN INDUCED ASTHMA (ASA)

This distinct syndrome is characterized by rhino-sinusitis/nasal polyposis, aspirin sensitivity, and asthma. Aspirin induced asthma (also called aspirin triad, or samter's triad) occurs in about 21% of adults and 5% of children. ASA commonly begins in the third and fourth decade of life and is more common in women. 70% of patients have a polymorphism in the LTC4 synthase gene that results in overproduction of cystenyl leukotrienes. The syndrome is more common in patients with severe asthma. The disease usually starts as repeated episodes of rhinitis, and most patients develop nasal polyps. Asthma and aspirin sensitivity then appear.

Within minutes to hours of exposure to aspirin and most NSAIDs affected individuals develop severe asthmatic attack, red eyes, flushing of the face, and profuse rhinorrhea. In severe cases, hypotension and anaphylaxis occur with loss of consciousness and respiratory arrest. Lifelong avoidance of NSAIDs and Aspirin is required. Paracetamol is much less likely to induce symptoms but should be cautiously used starting with half the dose and monitoring the patient to up to two hours of ingestion. In patients requiring long term pain medication, COX 2 inhibitors have been shown to be well tolerated.

In the rare cases where aspirin must be used for management of other conditions, desensitization under expert vigilance is an option. The cornerstone of ASA treatment remains corticosteroids though intravenous epinephrine should be administered first in the event of anaphylaxis. Leukotriene modifiers have a useful role in modulating the underlying causative pathways. Confirmation of the diagnosis through aspirin challenge is risky and is not routinely recommended.

All patients with adult onset asthma and upper airway disease should be counseled to avoid Aspirin and NSAIDs. Successful treatment of rhino-sinusitis, especially with leukotriene inhibitors, anti-cholinergics and immunotherapy may improve asthma symptoms. Nasal polyps may recur after removal and long term topical corticosteroids are often required to control symptoms.

ASTHMA AND SURGERY

Persons with asthma have an increased risk of adverse outcomes during surgery. This risk is higher with:

- o general anaesthesia and endo-tracheal intubation
- thoracic and upper abdominal procedures
- o poorly controlled asthma

The anesthetist must be informed of the patient's diagnosis and control in good time .Elective cases should be deferred until asthma is controlled. Pre-operative assessment of asthmatic patients should include a lung function test assessment. In patients with FEV_1 less than 80% predicted, a one week course of oral corticosteroid therapy should be considered prior to surgery. Peri-operative hydrocortisone at 100mg three times a day should be given to all patients who have been on systemic corticosteroids in the previous six months. Rapid reduction of the dose within 24 hours after surgery should be done to enable adequate wound healing.

Whenever possible, local and regional anaesthesia should be used. Even in cases where general anaesthesia must be used, adjuvant local and regional anaesthesia techniques reduce the total amount of volatile gas required as well as post operative opioid requirement. Atracurium and morphine cause release of histamine and should be avoided. Pethidine is preferred for wheezy patients. Avoidance of Aspirin, NSAIDs and other allergens is vital.

During surgery airway manipulation should be kept to a minimum until the patient is under adequate anaesthesia. Humidified oxygen should be continued up to 72 hours after major thoracic and abdominal surgery and regular chest physiotherapy instituted. Nebulised salbutamol 2.5 to 5mg can be given with premedication. Benzodiazepines and opioids can cause respiratory depression and should be used with caution in patients with poor respiratory function. Anti-cholinergic drugs such as atropine help dry secretions and may be useful before ketamine or ether administration. The patient's usual dose of asthma medication should be resumed immediately after surgery.

EXERCISE INDUCED BRONCHOSPASM (EIB)

Between 80-90% of asthma patients also have EIB which is defined as transient airflow limitation manifesting with wheeze, dyspnea, and chest tightness within 5 to 15 minutes of exercise. Symptoms of EIB are most effectively prevented and relieved by 2-4 puffs of inhaled short acting beta 2 agonists such as salbutamol 100 μ g, or terbutaline 200 μ g, used 15 minutes prior to exercise and on an 'as needed basis'. Long acting beta 2 agonists (LABA) are effective but should not be used as mono-therapy in asthma as they do not have an effect on the underlying inflammation. These should be used as part of the patient's preventer regime (combined with ICS) if required based on the severity classification and level of control of asthma symptoms. Mast cell stabilizers such as cromolyn 2-4 puffs four times daily are moderately effective.

Patients with EIB should be advised to exercise in a warm humidified environment, cover their mouths and noses during exercise in cold weather, warm up for at least 10 minutes before actual exercise, gradually cool down before stopping exercise, and avoid aeroallergens and pollutants. Often EIB goes un-recognized resulting in exercise avoidance and poor fitness among persons with asthma.

COUGH PREDOMINANT ASTHMA (CPA)

A subset of patients with chronic cough but no wheeze or dyspnea as in classic asthma respond to treatment with bronchodilators and inhaled corticosteroids. Such patients

often have normal Spirometry. These patients were earlier said to have cough variant asthma. The term 'cough predominant asthma' is currently preferred reflecting the observation that most of these patients later go on to develop classic asthma. Recent clinical trials support the view that cough predominant asthma and classic asthma represent a continuum in severity, with classic asthma being defined by greater bronchial hyper-responsiveness (lower pc20 on methacholine challenge), steeper dose response curve and increased levels of vascular endothelial growth factor (VEGF).

Patients suspected to have cough predominant asthma should be provided with a one month trial of asthma medication (Inhaled corticosteroid alone or in combination with LABA). In specialist centers, broncho-provocation testing can be done to confirm the diagnosis.

GASTRO-ESOPHAGEAL REFLUX (GERD) AND ASTHMA

Asthma and GERD are common medical conditions. Asthma patients have a threefold risk of GERD when compared to the general population. Both asthma and GERD symptoms frequently worsen at night. Proposed mechanisms of GERD induced asthma include:

- o vagal mediated reflex
- o heightened bronchial reactivity
- o micro-aspiration
- o immune system modification

Asthma treatments like theophylline and oral beta 2 agonists relax the lower esophageal sphincter and may worsen pre-existing GERD. A recent Cochrane meta-analysis of 12 randomized controlled trials concluded there was no overall improvement in asthma in patients treated for GERD. In the asthmatic patient with GERD, care should be taken to avoid theophyllines and oral _2 adreno-receptor agonists.

If oral corticosteroids are needed in patients with GERD and asthma, they should be used for the shortest time possible and with concurrent proton pump inhibitor/ H_2 receptor antagonist medication. Patients should be advised on lifestyle measures that improve GERD such as: taking smaller meal portions, avoiding drinks late in the evening, eating supper at least 2-3 hours prior to going to bed, and elevating the head of the bed. Where GERD is severe, hiatus hernia should be excluded and a gastroenterologist consulted.

ANAPHYLAXIS AND ASTHMA

Anaphylaxis may present with flushing, urticaria, pruritus, angioedema, stridor, wheeze, dizziness, hypotension, syncope, and abdominal symptoms such as nausea, vomiting, cramping and diarrhea. In known asthmatics, anaphylaxis may mimic a severe asthmatic

attack and hence go unrecognized. A high index of suspicion is required especially in situations where an injectable drug or vaccine was administered prior to symptoms.

Drugs that induce anaphylaxis include Penicillins, NSAIDS, Aspirin and ACE inhibitors. Certain foods including sea foods, eggs, milk and nuts may cause anaphylaxis. Exercise induced anaphylaxis may also occur. Whenever a diagnosis of anaphylaxis is suspected, epinephrine remains the bronchodilator of choice. Prompt treatment with oxygen, I.M. epinephrine, parenteral antihistamine, intravenous hydrocortisone, oropharyngeal airway, and intravenous fluids is essential. On recovery, the patient should be counseled on allergen avoidance and taught how to use preloaded epinephrine syringes.

Occupational Asthma

Introduction

Occupational asthma is defined as variable airflow limitation or bronchial hyper reactivity caused by inhalation of materials specifically found in the workplace environment. It is estimated that up to 10% of all adult-onset asthma is due to occupational asthma.

Occupational asthma should be distinguished from "work-exacerbated" or "work-aggravated" asthma where an individual with pre-existing (or previous) asthma experiences worsening symptoms as a result of new exposures in the work-place.

More than 250 agents have been identified that cause sensitization and subsequent occupational asthma.

The most frequently noted include inorganic and organic dusts, grains, fur, fungi, wood, latex, metals, welding fume, coffee and tea dust, hair treatment chemicals and many others.

Mechanisms

The underlying pathogenesis of occupational asthma can either be due to hypersensitivity or direct toxicity.

- More than 90% of occupational asthma follows a period of exposure to low concentrations of a sensitizing agent. Often there is a period of latency that may last for weeks, months but often less than 2 years. After sensitization, on-going exposure to the sensitizing agent causes predictable asthma symptoms.
- When toxicity mechanisms are involved, there is initial exposure to high concentrations of irritant chemicals, fumes, smoke, dust or extreme temperatures, often as a consequence of an industrial accident or inadequate ventilation in confined work space. Symptoms of wheeze, cough and chest tightness begin within minutes or hours of exposure and may persist for months, years or indefinitely.



Diagnosis in Primary Care Settings

Early recognition that newly developed asthma is occupational in origin provides the only chance of full recovery particularly if exposure ceases within 6 to 12 months. Longer exposures are associated with incomplete recovery.

A diagnosis of occupational asthma is made by demonstrating a temporal relationship between asthma symptoms (wheeze, breathlessness, chest tightness and cough) as well as airflow limitation to a specific occupational exposure.

History

Does the patient have asthma?

- Wheeze, breathlessness, chest tightness and cough,
- Symptoms are episodic or if persistent, of varying severity
- Often worse at night
- Often there are triggers
- Quickly relieved by inhaled bronchodilators

Is the asthma occupational in origin?

- In "irritant induced asthma" there is an initiating episode of high level exposure to an irritant gas, fume or dust at work. Asthma symptoms begin at the time of exposure or during the recovery period.
- In asthma due to hypersensitivity; asthma symptoms begin following onset of a period of employment. There is often a latency period from first exposure to onset of symptoms. Symptoms are often more troublesome on work days and relieved on rest days. Symptoms may be related to a particular task. Fellow workers may have similar symptoms.
- Patterns of symptoms (in relation to work exposures):
 - Improvement occurs during vacations or days off (this may take a week or more).
 - Symptoms may be immediate (<1 hour), delayed (most commonly, 2–8 hours after exposure), or nocturnal.
- There are recognized sensitizers such as inorganic and organic dusts, grains, fur, fungi, wood, latex, metals, welding fume, coffee and tea dust, hair treatment chemicals

Documentation of work-relatedness of airflow limitation:

Peak Flow Measurement

• Serial charting for 2–3 weeks (2 weeks at work and up to 1 week off work, as needed to identify or exclude work-related changes in peak expiratory flow):

Symptom Diary

• The patient record when symptoms and exposures occur as well as bronchodilator use

Referral

A diagnosis of occupational asthma may have far-reaching personal, occupational and legal implications. The only hope for full recovery is cessation of further exposure; which may involve loss of employment; and the process for workman's compensation. Thus, once occupational asthma is suspected, the patient should be referred to a specialist experienced in assessment and management of occupational lung disease.

Other tests that may be required include

- Serial measurement and recording FEV1 every 2 hours while awake.
- Immunologic tests.
- Bronchial challenge tests

Management

Medication

• Counseling and conventional medication should be used according to the level of control of asthma

Work-aggravated asthma:

- Work with occupational health and safety professionals as well as onsite health care providers and management to develop behavioral, administrative and physical control procedures to limit exposure to sensitizing material
- Discuss avoidance, ventilation, respiratory protection, tobacco smoke-free environment.

Occupationally induced asthma

• The only chance of full recovery is complete cessation of exposure to the initiating agent.

Suggested further reading

- 1. The Global Strategy for asthma management and prevention 2009(update). Accessed from www.ginasthma.org on December 21, 2010.
- N. Ait Khaled, DA Enarson, C-Y Chiang, G. Marks, K. Bissel Management of asthma: a guide to the essentials of good clinical practice International Union Against Tuberculosis and Lung Disease, Paris, France, 2008.

3. Quon BS, Fitgerald JM, Lemier C, Shahidi N, Durcharme FM

Increased versus stable dose of inhaled steroids for exacerbations of chronic asthma in adults and children

Cochrane Database Syst Rev. 2010; 10: CD 007524

- Durcharme FM, NiChroinin M, Greenstone I, Lasserson TJ Addition of long acting beta 2 agonists to inhaled corticosteroids versus same dose inhaled corticosteroids in adults and children. Cochrane Database Syst Rev. 2010; 5: CD 005535
- Salpeter SR, Wall AJ, Buclkey NS Long acting beta agonists with and without inhaled corticosteroids and catastrophic asthma events. Am J Med. 2010; 123(4): 322-8
- Marcela Davalos Bichara, Ran D. Goldman . Magnesium for treatment of asthma in children. Canadian Family Medicine 2009; 55: 886-889
- Anthony D Holley and Robert J Boots. Review article: management of acute severe asthma and near fatal asthma. Emergency Medicine Australasia 2009; 21:259-268.
- 8. National Asthma Education and Prevention Program. Expert Panel Report 3: www.nhlbi.nih.gov/guidelines/asthma/asthsumm.pdf.
- Harding SM, Richter JE. The role of gastro esophageal reflux in chronic cough and asthma. Chest. 1997;111:1389-140
- 10. Update in anaesthesia, Issue 12 (2000) Article 12: Page 2 of 3. Available at http://www.nda.ox.ac.uk/wfsa/html/u12/u1212_02.htm
- Kawabori I, Pierson WE, Conquest LL, Bierman CW. Incidence of exercise-induced asthma in children. J Allergy Clin Immunol. 1976;58:447–55.
- Rupp NT, Guill MF, Brudno DS. Unrecognized exercise-induced bronchospasm in adolescent athletes. Am J Dis Child. 1992;146:941–4.
- Sinha T, David AK. Recognition and management of exercise-induced bronchospasm. Am Fam Physician. 2003 Feb 15;67(4):769-74, 675.





Organization and delivery of Asthma Care Services

Chapter Objectives

To highlight the steps that will need to be taken to improve access to and quality of asthma care in Kenya and to outline the desired organization of asthma care services at all levels of the health care system in Kenya in order to achieve universal access and the highest possible quality of care for asthma.

The target audience for this chapter includes health care planners and managers, health financiers, asthma advocates and those involved in training health care providers.

Organization and delivery of asthma care services: the role of the Practical Approach to Lung Health

Asthma patients will be found in the community, primary health care facilities (dispensaries and health centers) and in secondary and tertiary health care facilities. At all these levels it is desirable that patients with asthma are rapidly recognized and placed on appropriate treatment to achieve control at the minimum cost possible. The Practical Approach to Lung Health offers the opportunity to achieve this.

Rationale of the PAL

Cough and other respiratory symptoms are common reasons for seeking care in primary health care settings. It has been estimated that between 25-35% of persons seeking care in primary health care settings have a respiratory illness. While the majority of patients presenting at primary health care settings will have a minor acute respiratory illness, a proportion of them will have chronic lung disease such as asthma or chronic obstructive airways disease, while others will have serious and potentially life threatening conditions such as pneumonia and tuberculosis. At the primary health care setting the majority of patients presenting with respiratory symptoms will be managed using a syndromic approach with minimal use of laboratory or other tests. It is essential that all patients presenting at the primary health care setting are managed properly to reduce morbidity and to prevent deaths from respiratory disease. In particular it is important to rapidly identify patients who may have more serious or chronic lung disease in order to offer appropriate care and reduce suffering. A systematic approach to the care of patients presenting with respiratory illness would be expected to improve case finding for the four respiratory diseases that pose the greatest public health threat: pneumonia, TB, asthma and COPD.

The Practical Approach to Lung Health (PAL) strategy is a syndromic management

of patients with respiratory symptoms presenting to primary health care facilities. The approach focuses on persons over the age of 5 years (younger children are managed according to the algorithms of the integrated management of childhood illness (IMCI) and is designed to optimize care for patients with TB, acute respiratory infections, principally pneumonia and chronic respiratory diseases especially asthma and COPD. The primary objective of the PAL approach is to provide the best possible quality of care for patients presenting with respiratory symptoms at the primary health care setting and to enhance the efficiency of health care delivery for respiratory disease.

The PAL approach or strategy has two main components: standardization of health care procedures through the development and implementation of clinical care guidelines and enhanced coordination at the various levels of the health care system and within components of the health care system at the district level. The PAL strategy is therefore a patient centered approach for the diagnosis and treatment of respiratory illnesses at the primary health care setting which attempts to promote a symptom based, standardized and integrated approach to the management of respiratory disease with enhanced linkages and coordination within the district health delivery service.

The Step Wise Approach for PAL Development and Implementation.

A step wise approach to the introduction of PAL has been defined. They key steps include:

- 1. Approval by national health authorities to pursue PAL. The national health authorities must be made aware of the necessity for PAL and the problems that the PAL strategy will attempt to address. The ministry of health may then request a relevant technical agency to carry out a preliminary assessment to explore the possibilities for PAL development in the country. Kenya has already made the decision to pursue PAL and has sought funding for PAL implementation through funding channels such as TBREACH and the Global Fund to Fight AIDS, TB and Malaria (GFATM).
- 2. A preliminary assessment which should include the demographic and epidemiological situation, evaluation or assessment of the burden of respiratory disease, health resource utilization by respiratory patients, current management practices for patients presenting with respiratory disease and health resources available for the care of respiratory patients. In addition there should be an assessment of the health care system to understand system opportunities and assets that may favor PAL development and also to appreciate system bottlenecks that may challenge the development and implementation of PAL. The health system assessment should include a review of the major health sector reforms taking place, health care financing and organization of health care services such as health service coverage, human resource cadres available and their distribution and the balance between

public and private health care provision. This step should assist in designing the best PAL approaches adapted to the country's own epidemiological profile of disease and health resources. This critical step is yet to be carried out in Kenya but there are indications that studies to define the burden of respiratory disease in Kenya are about to be undertaken though collaborative efforts of the DLTLD, KEMRI and KAPTLD.

- 3. Establishment of a National Working Group with representation from all key stakeholders to design a country specific approach to PAL implementation and to monitor implementation. The stakeholders that may be included in the national technical working group include the national TB control programme, the primary health care department of the Ministry of Health, the department responsible for the Health Management Information System and academic and research institutions.
- 4. Development of the PAL guideline, which will outline the do's and don'ts when providing care to patients with respiratory symptoms at the various levels of the health care system but especially at the primary health care setting. The PAL guidelines should define the syndromic management approach based on respiratory symptoms. Some countries have included a disease specific approach in the same guideline. As far as feasible an evidence based approach should be followed when developing the guideline. The guideline(s) need to be adapted to the available resources to make it implementable.
- 5. Development of training materials including training guides and manuals to be used to transfer knowledge and skills to health care workers who will be managing patients with respiratory symptoms according to the PAL guidelines.
- 6. It is wise to use a phased approach to PAL implementation in a country by initiating PAL in a limited number of sites. This initial phase of PAL implementation should be used to learn lessons that can then be used to modify approaches appropriately during the scale up of the strategy. This step will include the assessment of respiratory case management by health care workers before and after PAL implementation in the pilot sites.
- 7. The further development of the PAL strategy and its scale up should be informed by the lessons learnt during the initial phase of implementation. A plan for country wide implementation with the health resources needed and the cost of these resources should then be developed.
- 8. A multi -year, progressive and costed plan should be developed through a consultative process with all relevant stakeholders. Once agreed upon by stakeholders the comprehensive plan should be presented to the relevant health authorities for adoption.
- 9. Mobilization of the resources to implement the PAL expansion plan. Funds for PAL implementation may be sourced from domestic sources or from external



sources. The availability of domestic financial resources for PAL is a measure of the political commitment to this strategy.

10. To institutionalize the PAL strategy in a country so that it becomes the way of doing things, institutions that train health care workers should adopt their training curricula to fit the PAL implementation needs.

PAL Implementation - documented country experiences.

Several countries have implemented the PAL strategy and the experiences documented. These countries include Algeria, Bolivia, Chile, El Salvador, Guinea, Jordan, Kyrgyzstan, Morocco, Nepal, Syria, South Africa and Tunisia. The country experiences have demonstrated clear benefits in the care of respiratory patients. These benefits include decreased referral to upper levels of the health care system suggesting better or more comprehensive care was provided at the lower level; an increase in the proportion of patients evaluated appropriately for TB suggesting an improvement in the quality of the process of TB diagnosis; improved TB case finding among patients presenting with respiratory symptoms; a reduction in number and type of medicines prescribed to patients with respiratory symptoms and in particular a reduction in the prescription of unnecessary antibiotics and adjuvant drugs such as cough syrups; and an increase in the prescription of PAL has also been documented to result in a reduction of the average cost of drug prescription per respiratory patient.

The implementation of PAL activities has been associated with positive changes in the health care system such as the modification of the outpatient register to include chronic respiratory disease. This important change enables the health care system to have a better grasp of the burden of respiratory disease, the treatment provided to respiratory patients, the outcomes of treatment of respiratory patients and to monitor trends in these parameters. In some countries the implementation of PAL activities has led to an update of the national essential drug list and the procurement of essential equipment for the management of respiratory patients such as spirometers, peak flow meters and x-ray machines at lower levels of the health care system. The overall impact of these effects of PAL implementation is a strengthened health care system.

Suggested further reading

- 1. World Health Organization. Practical Approach to Lung Health (PAL). A primary health care strategy for the integrated management of respiratory conditions in people five years of age and over. WHO/HTM/STB/2005.351. WHO/NMH/CHP/CPM/CRA/05.3. Geneva, Switzerland: World Health Organization, 2005.
- World Health Organization. Practical approach to lung health. Manual on initiating PAL implementation. WHO/HTM/TB/2008.410; WHO/NMH/ CHP/CPM/0.8.02. Geneva, Switzerland: World Health Organization, 2008.

Chapter 7 Monitoring and Evaluation of Asthma Care Programmes

Chapter objectives

This chapter highlights the importance of monitoring and evaluation of the proposed national asthma care programme in order to obtain critical information on the health care resource utilization by asthma patients, the treatment provided to asthma patients and the treatment outcomes of patients managed within the asthma care programme. This information is critical for advocacy purposes, resource mobilization and refinement of the programme to promote access to quality asthma care services.

The primary audience for this chapter includes health programme developers and managers, health programme financiers, asthma activists, patients and their families.

The monitoring and evaluation of the national asthma care programme will be based on the usual monitoring and evaluation framework. This framework will include the tracking of inputs such finances; outputs such as persons trained, equipment and drugs procured and distributed and outcomes such as patients identified and treated and their treatment outcomes. The tracking of inputs, outputs and outcomes will be a continuous process (monitoring). Periodically the programme will be evaluated to determine a number of programme related measures that cannot be routinely monitored such the efficiency with which programme resources are utilized, the efficiency of asthma service delivery, adherence to asthma management guidelines, the reach of the programme especially in relation to gender and socio economic status (equity) and very importantly to determine the impact of the programme. Impact assessment will include an assessment of the impact of the programme on quality of life of asthma patients, asthma hospitalization and emergency room utilization which are measures of the impact of the programme on asthma morbidity. It should also be possible to measure the impact of the programme on in hospital asthma mortality but the overall impact of the programme on asthma mortality may be difficult to discern if a significant proportion of asthma patients remain undiagnosed or die at home. It will also be difficult to evaluate the impact of the asthma care programme on asthma incidence and prevalence since the determinants of the incidence and prevalence of asthma are currently poorly understood and the interventions of the asthma care programmes are not primarily intended to influence the epidemiology of the disease.

The Asthma Indicators

The asthma care programme will be interested in tracking key patient level indicators that will provide an indication of the success or failure of the programme. These indicators include

Asthma Case Notification:

- a) New asthma case notification which will be defined as the number of new asthma cases identified and recorded over a specific time period. Figures will be provided as cases per 100,000 population
- b) All asthma case notification which will be defined as new plus previously notified asthma cases recorded over a specific time period. The figures will be provided as cases per 100,000 population
- c) The cases notified will be categorized by gender, age, HIV status and initial severity status (mild, moderate and severe) at the time of identification.

Asthma treatment outcomes

The asthma care programme will also monitor the outcomes of treatment for all registered patients. A system similar to what is used in the HIV care programme will be used. Thus at the end of every reporting period the following outcomes will be recorded:

- a) Number and proportion of patients in the register who are controlled, partly controlled or uncontrolled based on the most recent clinical assessment.
- b) Number and proportion of patients registered in the previous/preceding quarter who are lost to follow up (defaulted) , transferred out or dead
- c) The treatment outcomes of patients on register will be linked to treatment provided, recorded level of adherence, age, and gender and HIV status.

Reporting units

The basic reporting units will be counties (or districts if districts will remain in the county system)

The monitoring tools

The reporting tools will include

- Asthma treatment cards (individual case records) at service delivery points
- Asthma treatment register at the service delivery points
- Asthma county/district registers at the county/district level

Frequency of reporting

A quarterly reporting system will be used.

Annexes 1: The Asthma Control Test

1A: Adult Asthma Control Test

The Following test can help people with asthma (12 years or older) assess their asthma control.

Please circle the appropriate score for each question. There are five questions in total

You can calculate your total Asthma Control Test score by adding up the numbers for each of your responses. Be sure to review your results with your health care provider (doctor, clinical officer or nurse)

Step 1. Circle the score for each question and write the number in the box. Please answer as honestly as possible. This will help you and your doctor to discuss what your asthma is really like.

Step 2. Add up your score to get your total

Step 3. Use the scale provided to know what your score means.

During the past 4 weeks, how often did your asthma prevent you from getting as much done at work, school or home?				Score	
1=All the time	2= Most of the time	3= Some of the time	4=A little of the time	5=None of the time	
During the pas	st 4 weeks, hov	v often have you	had shortness o	of breath?	
1=More than once a day	2=Once a day	3= 3 to 6 times a week	4=Once or twice a week	5=Not at all	
During the past 4 weeks, how often did your asthma symptoms (wheezing, cous shortness of breath, chest tightness or pain) wake you up at night or earlier than in the morning?					
1=4 or more times a week	2=2 to 3 nights a week	3=Once a week	4=Once or twice	5= Not at all	
During the past 4 weeks, how often have you used your reliever inhaler or nebulizer medication?					ılizer
1=3 or more time a day	2=1or 2 times a day	3=2 or 3 times a week	4=Once a week or less	5= Not all	
How would you rate your asthma control during the past 4 weeks					

1=Not	2=Poorly	3=Somewhat	4=Well	5=Completely	
controlled	controlled	controlled	controlled	controlled	
Total Score					

Interpretation of the Asthma Control Test

Score 25: Great: There is Total Control. See your health care provider if this changes

Score 20-24: on Target – Asthma is Well Controlled but not Totally Controlled. Your health care provider may be able to be able to help you get to Total Control

Score less than 20: Off Target- Asthma is Not Controlled. Your health care provider can recommend an asthma action plan to help improve your asthma control.

1B: Childhood Asthma Control Test

For children 4 to 11 years old

Please fill this together with your child now and discuss the results afterwards with your health care provider.

How to fill the Childhood Asthma Control Test.

Step 1: Let your child answer the first four questions (1 to 4). If your child needs help reading or understanding the question, you may help, but let your child choose the answer. Complete the remaining three questions (5 to 7) on your own, without letting the child's answers to influence your answers. There is no right or wrong answers.

Step 2: Write the number of answer in the score box provided.

Step 3: Add up the scores in each box to calculate the total score

Step 4: Take the test score to your health care provider (doctor, clinical officer or nurse) to talk about your child's total score.

Ask your child to answer these questions					
1. How does your asthma make you feel today? Score					
0=I feel very ill 1=I feel ill today 2=I feel well today 3=I feel very well today					
2. How much does your asthma bother you when you run , exercise or play sports?					

0=It bothers me a lot, I can't do what I want to do	1=It bothers me and I don't like it	2=It bothers me a bit but its okay	3=It doesn't bother me
3. Do you	cough because o	of your asthma?	
0=Yes, always	1=Yes, most of the time	3=Yes, some of the time	4=No, never
4. Do you	wake up during	the night because	of your asthma?
0=Yes, always	1=Yes, most of the time	2=Yes, some of the time	3=No , never

Please complete the following questions on your own.						
5. During the past 4 weeks, how many days did your child have any daytime symptoms?						Score
5=Not at all	4=1-3 days	3=4-10 days	2=11-18 days	1=19-24 days	0= everyday	
6. During the past 4 weeks, how many days did your child wheeze during the day because of asthma?						
5=Not at all	4=1-3 days	3=4-10 days	2=11-18 days	1=19-24 days	0= everyday	
7. During the past 4 weeks, how many days did your child wake up during the night because of asthma?						
5=Not at all	4=1-3 days	3=4- 10days	2=11- 18days	1=19- 24days	0=everyday	
Total Score (Question 1-7)						

Interpretation of Childhood Asthma Control Test

Score 20 or more: Child's asthma may be under control. Discuss your child's asthma with your health care provider. Your health care provider may consider other factors when assessing your child's asthma control.

Score 19 or less: Child's asthma may not be as well controlled as it should be. Discuss with your health care provider and ask if your child's asthma treatment plan should be changed.



Annex 2: Illustrations on the use of asthma devices

Annex 2A: How to use the pressurized meter dose (pMDI) inhaler without a spacer.

- 1. Remove mouth piece cover
- 2. Shake inhaler
- 3. Breath out
- 4. Place inhaler in mouth sealing mouthpiece with mouth(do insert tongue into inhaler
- 5. Simultaneously press the inhaler canister to release dose and using a suction like action deeply, strongly but slowly breathe in the released dose
- 6. Hold breath for about 10 seconds or as long as is comfortable.

Annex 2B: How to use the pMDI with a spacer

1. Remove cap of inhaler





- 2. Shake inhaler
- 3. Insert inhaler into flat end of device







- 4. Place mouth piece in mouth and press inhaler canister to release a dose of medication. Ask the patient to breathe (using a suction like action) in slowly, deeply and strongly
- 5. Hold breaths for at least ten seconds or as long as comfortable.

For children or elderly patients who need to be assisted.

Step 1-3 remain the same

Step 4. Place mouth piece in child's/patient's mouth or face mask onto child and press inhaler canister to release a dose of medication. Ask the patient to breathe in and out (deeply if possible) for 7 - 10 breaths.

Note

- Older children > 7 years should try to hold their breath after inhaling for upto 6 -10 seconds.
- If a face mask is used it must be fitted firmly around the child's mouth and nose.
- Shake inhaler between every puff and NEVER spray two or more puffs at the same time. So give one puff, breath 7-10 times then shake the inhaler and give the second puff.
- If you spray straight into the mouth without using a spacer then you only deliver < 1% of the dose ALWAYS USE THE SPACER.
- Static electricity accumulates on spacers with time, attracting drug particles and thus delivers less drug to the lungs.

A simple way of reducing static is wash spacer in soapy water and drip dry

DO NOT RINSE WITH CLEAR WATER NOR WIPE THE INNER SURFACE WITH A CLOTH.



Wash once every 2 weeks.

INHALERS DO NOT FINISH WHEN THE LAST SPRAY COMES OUT:

• Get to know how many doses are in the inhaler device. Note how many doses you are taking every day. Indicate in your diary the date when your inhaler is expected to become empty. Do not use it after this date even if "something" seems to come out. What comes out after the inhaler is finished contains no medicine and may result in loss of asthma control.

Annex 2C: How to use commonly available dry powder devices

2C1: Using the Accuhaler

- 1. Place finger in the space provided and push anti- clockwise
- 2. Action 1 will reveal a lever, which you should also push anti-clockwise until the end to load a dose
- 3. Place device in mouth sealing lips around the mouth piece
- 4. Inhale deeply, strongly and slowly
- 5. Hold breath for at least 10 seconds or as long as is comfortable



- 6. Place finger back in the space and push clockwise to "close" the device. Do not touch the lever when "closing " the device.
- 7. Examine the counter to know how many doses are remaining



8. Do not use the device when the number 0 appears.



2C2: Using the Turbuhaler

1. Remove the protective cover of the device



- 2. Hold device upright
- 3. Twist the base anti-clockwise until it reaches the end , then turn it back until it makes a clicking sound. When this happens a dose has been loaded ready to be inhaled
- 4. Turn the device to a horizontal position, place mouth into the space provided, ensuring that the lips do not go beyond this area, inhale deeply, slowly and strongly
- 5. Hold breath for at least 10 seconds or for as long as is comfortable



- 6. Do not move the base after inhaling the medicine unless you wish to load and inhale another dose.
- 7. Examine the counter to obtain an estimate of the doses remaining in the device
- 8. Return the device to its protective housing/cover.

Remember

To note the number of doses in your device the first time you use it. Depending on the average number of doses you inhale daily, record in your diary the expected date when the doses in your device will finish. The sound that the device makes when you shake it should not be used to indicate that there are doses remaining in the device. If a red mark appears on the counter only a few doses remain in the device and this is a warning that you should seek to replace your device.



Annex 3: An Example of an Asthma Action Plan

For Relief of asthma symptoms (cough, wheeze, chest tightness, shortness of breath)

Inhale ______inhaler_____puff_____as needed

If you need more than – puffs in a day your asthma may getting out of control and take the following action

For prevention of asthma symptoms inhale ----- inhaler ----- puffs ----- times a day, **every day**.

Take the following additional medicines to control the other associated symptoms

- 1. ----- tablet a day for control of nasal symptoms
- 2. nasal spray sprays into each nostril --- times a day to control nasal symptoms
- 3. Others

In an emergency situation

Call ---- on this ---- number

Go to ----

Annex 4: The Asthma Register

Annex 5: FLOW CHART FOR ASTHMA DIAGNOSIS



66