Project on

Review on Childhood Asthma in Bangladesh: Diagnosis and Management

[In the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy]

Submitted To

The Department of Pharmacy,

Faculty of Allied Health Sciences,

Daffodil International University

Submitted By

Sabiha Nazmin

Student ID: **191-29-1490**

Department of Pharmacy

Faculty of Allied Health Sciences

Daffodil International University

……..

May 2023

APPROVAL

This project paper, "**Review on Childhood Asthma in Bangladesh: Diagnosis and Management",** submitted to the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.

BOARD OF EXAMINERS

…….

Dr. Muniruddin Ahmed

Professor and Head,

Department of Pharmacy,

Faculty of Allied Health Sciences,

Daffodil International University

…… Internal Examiner 1

……. Internal Examiner 2

…… External Examiner 3

DECLARATION

I hereby declare that this project report, **"Review on Childhood Asthma in Bangladesh: Diagnosis and Management".** I am declaring that this Project is my original work. I also declare that neither this project nor any part thereof has been submitted elsewhere for the award of Bachelor or any degree.

Supervised by

……

Ms. Sultana Juhara Mannan

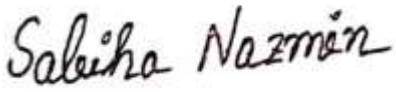
Assistant Professor

Department of Pharmacy

Faculty of Allied Health Sciences

Daffodil International University

Submitted By



……

ID: 191-29-1490

Department of Pharmacy

Faculty of Allied Health Sciences

Daffodil International University

ACKNOWLEDGEMENT

I might want to communicate my profound applause to the All-powerful Allah who has given me the capacity to finish my undertaking work and the chance to concentrate in this subject.

I'm a lot of thankful to my honorable project supervisor of Ms. Sultana Juhara Mannan Assistant Professor, Department of Pharmacy, Daffodil International University for his brilliant direction and steady oversight just as for giving essential data in regards to the task and furthermore for her help in finishing the project.

I would like to express my humble regards to Dr. Muniruddin Ahmed, Professor and Head, Department of Pharmacy, Daffodil International University.

I also wish to offer my respect to all of the teachers of Pharmacy Department, Daffodil International University and thankful to other members for their excellent cooperation with us.

Finally, I would like to express my gratitude towards my parents and other family members for their kind cooperation and encouragement which helped me in completion of this project.

Dedication…….

My Parents

The persons who always encourage me in every sphere of my life

Abstract

The incidence of asthma has increased dramatically throughout this period, with the greatest increases occurring in the urban areas of advanced nations, and it seems that the prevalence in nations that are developing may follow this pattern as well. The purpose of this review to gain a systematic considerate of the bug, as well as its cause, signs and symptoms, consequences, and medical and nursing management choices. Methods for assembling and evaluating data were gathered from a variety of linked reviews published between 1995 and 2022. Allergen evasion, as environmental testing for allergens and irritants, patient education, allergy testing, routine lung function surveillance, and the use of asthma management plans, asthma control tests, peak flow meters, and asthma diaries are a few non-pharmacological methods for asthma management. Reaching treatment objectives for asthma minimizes the disease's direct and indirect expenses and is financially wise. Diagnostic and management issues are particular to pediatric treatment. Challenges in diagnosis include consideration of other diseases such as viral respiratory illnesses or vocal cord dysfunction. Challenges in management include evaluation of the child’s ability to use inhalers and peak flow meters and the management of exercise-induced asthma.

Keywords: Asthma, Allergies, Exercise-induced asthma, Pediatric asthma

- # Contents

List of figures

Chapter 1
Introduction

1. Introduction

A chronic condition of the bronchial tree, asthma is marked by fluctuating airway blockage that can either clear up on its own or require medical attention. The narrowing of the airways in response to a range of stimuli, including diseases, unspecified activates and allergens, is known as airway hyper responsiveness. According to the Global Initiative for Asthma (GINA) recommendations, 300 million people throughout the world suffer from asthma, which is a chronic condition that can affect both children and adults [1]. Despite a boost in asthma prevalence over the past few decades, particularly in children [2], there is currently no conclusive reason for this rise. The quality of life is further decreased by persistent wheezing, coughing, chest tightness, and dyspnea, which are more common at night and in the morning [3]. Asthma symptoms can manifest as early as infancy; almost one-third of children wheeze during the first three years of life [4]. Around the age of six, nearly all of these kids will no longer be wheezing, but 40% will still be wheezing because they have asthma or will acquire it later in life. By the time they reach school age, up to 10-15% of youngsters may have asthma-related problems [5]. Early puberty often causes symptoms in youngsters to become less severe or even go away entirely, particularly in those who have mild asthma. Yet, it is commonly acknowledged and recognized that symptoms can reappear in adolescence or in children with severe asthma. The histology of a chronic inflammatory condition in the conducting airways is what distinguishes asthma in older children. Asthma development may be influenced by genetic predisposition as well as environmental variables including allergens and viral infections. The epithelial layer sheds, the airway wall becomes inflamed and swollen, and t-lymphocytes, eosinophils, and basophilic cells infiltrate the tissue. This inflammatory process may result in (or is accompanied by) additional structural alterations include expansion of the basal membrane and hyperplasia of goblet cells and smooth muscle in the airways, a condition referred to as airway remodeling [6]. The histology of a chronic inflammatory condition in the connecting airways is what distinguishes asthma in older children. Asthma development may be influenced by a family history as well as environmental variables including allergens and viral infections. The epithelial layer sheds, the airway wall becomes inflamed and swollen, and t-lymphocytes, eosinophils, and basophilic cells infiltrate the tissue. This inflammatory process may result in (or is accompanied by) additional structural alterations

include expansion of the basal membrane and hyperplasia of goblet cells and smooth muscle in the airways, a condition referred to as airway remodeling [7]. Despite significant advancements in asthma therapy over the past few decades, the condition is still incurable. Better disease control and a decrease in asthma exacerbations have been achieved as a consequence of increased awareness of potential contributory triggers and, in particular, the implementation of inhaled corticosteroids in the 1980s. With the help of modern drugs, kids can lead more or less "normal" lives that include taking part in sports and other physical and social activities. The exception continues to be a tiny number of kids with severe asthma that is difficult. This paper focuses on the diagnosis and management of pediatric asthma [8].

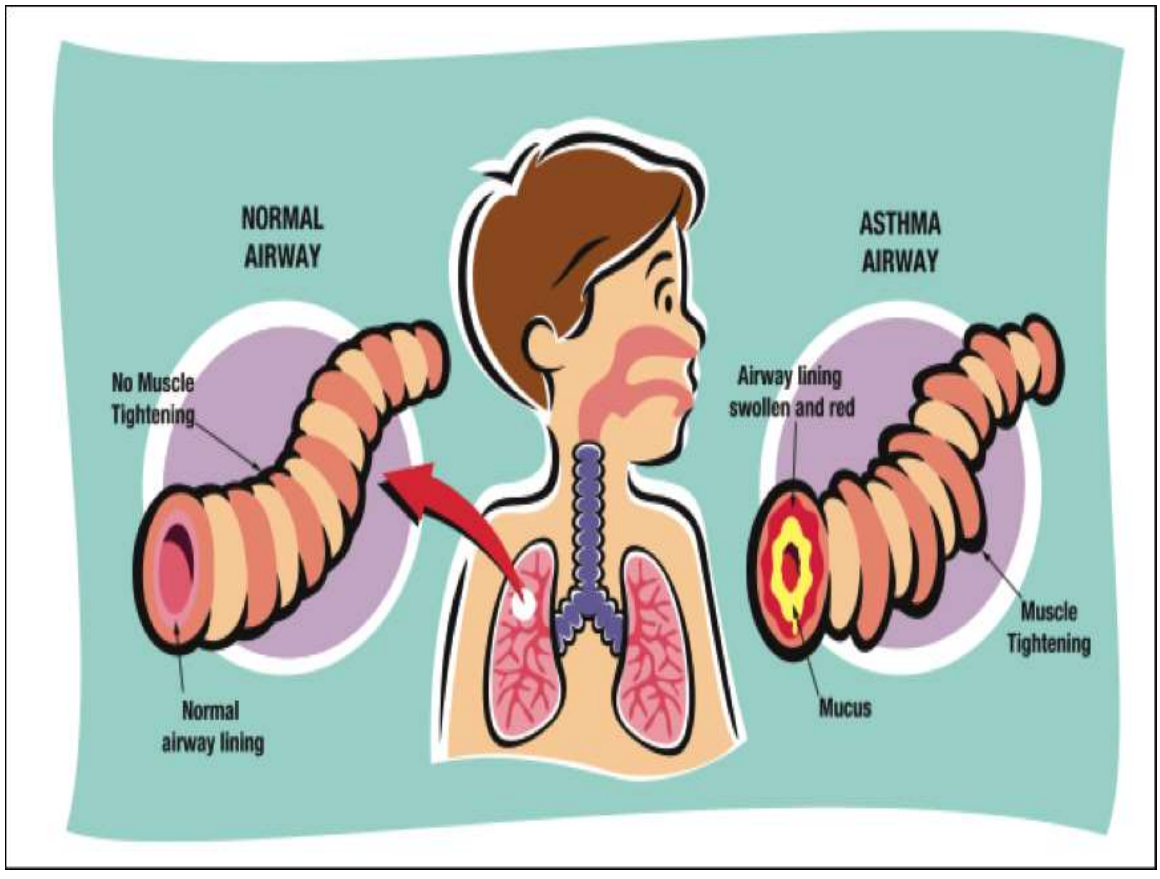


Figure 1: Asthma in children [9]

1.1 Epidemiology

Despite the fact that the epidemiology of asthma in children has been extensively written about, released data are heterogeneous due to the absence of a uniform definition and consistent data collection techniques. The most recent information on the terms used to diagnose asthma in pediatric cohort research (children within the ages of 6 and 18) were retrieved from PubMed [9]. In 122 works, sixty different definitions were found. Predictions of prevalence ranged from 15.1% to 51.1%. The International Investigation of Asthma and Allergies in Childhood (ISAAC) program was created in response to the need for systematic international comparisons of the prevalence of asthma and for a better understanding of various causal and preventive variables [10]. The initiative sought to clarify the frequency in youngsters between the ages of 6-7 and 13–14. The objective was to establish a simple, reliable approach for estimating the prevalence of allergy and asthmatic disorders globally. In 13 to 14-year-old youngsters from various nations, the first incidence of expressed wheezing during the preceding 12 months ranged from 1.6% to 36.7%. The equivalent prevalence for wheeze as reported by parents in children aged 6 to 7 ranged from 0.8% to 32.1%. The largest prevalence of asthma was seen in AngloSaxon nations, while it was less common in developing nations. The study's findings could possibly lead to other conclusions [11]. Additionally, despite countries sharing a comparable genetic or racial background, there were notable disparities in asthma frequency that could not be solely attributed to genetic variations. In addition, the incidence of asthma, allergic rhinitis, and atopic eczema varied internationally but also showed commonality. The incidence of these three disease types varied significantly, according to the authors, depending on which nation had the highest prevalence rates, whereas in the nation with the lowest prevalence rates, it was rather consistent. The varying risk factors and onset times of the various disease entities in the various nations may provide a justification [12]. Furthermore, it appears that the local environment has a significant impact on the variations in prevalence. The found disparities among genetically similar groups may be explained by environmental factors as allergies and lifestyle, according to research of emigrant and immigrant populations as well as of Germany after the reunification of East and West [13]. Although having a similar genetic basis, Wang et al.'s research showed that Chinese teenagers living in China and Canada had dramatically

different asthma prevalence rates. In the Western world, a rise in the incidence and prevalence of asthma was seen over the latter two decades of the previous century. Strackan put forth a fresh, if speculative, hypothesis for the rise in allergic asthma cases and other allergy disorders in 1989. He noticed that early childhood illnesses, which are spread through unclean contact with older siblings, appeared to protect against allergy conditions. This justification, which was first put forth as "the hygiene hypothesis," sparked a flurry of research [14]. But there is still no clear explanation for the rise in allergy illness incidence and prevalence. According to a cross-sectional study by Shirakawa et al., tuberculin skin testing may have decreased the incidence and prevalence of allergy illness in Japanese children. This data seems to support the theory while also indicating that infections that induce type I immunity might be used to steer away from allergy illness. However, in a prospective, randomized, double-blind, and placebo-controlled investigation of Dutch children at risk for allergy illness, tuberculin skin testing had no benefit [15].

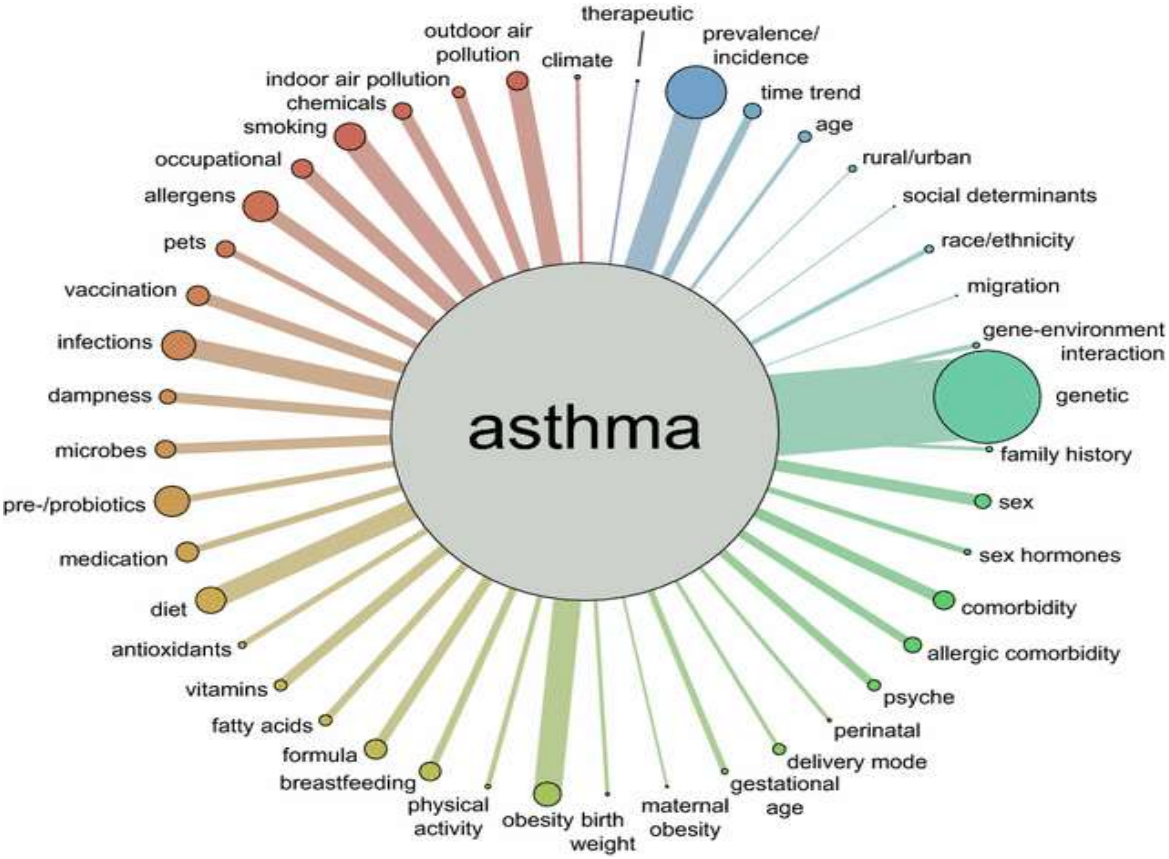


Figure 2: Epidemiology of asthma [16]

1.2 Childhood Asthma

When preschoolers exhibit persistent wheezing, coughing, chest tightness, and shortness, it is simpler to identify asthma in school-aged children (6 years and older), where the proverb "not all that wheezes is asthma" is valid. A medical condition is typically recognized in younger children because of a common past of persistent wheeze, cough, chest tightness, and shortness of breath. These signs and symptoms might not necessarily indicate asthma. In contrast, the majority of other respiratory diseases that exhibit these persistent signs are uncommon, and it is usual practice to start treating asthma without first ruling out these other respiratory diseases [17].

1.2.1 The Burden of Childhood Asthma

is widespread in the West but underdiagnosed in minority populations in both Europe and the US. Minority populations bear a disproportionate burden of asthma morbidity and experience higher rates of hospitalization, emergency department visits, and even fatalities [55]. Controlling asthma has an impact on enjoyment of life (QoL) in children with the condition. The QoL improves as asthma control improves. Uncontrolled asthma has been linked to poorer QoL, decreased lung function, and difficulty exercising. Asthma symptoms mainly manifest at night. A university hospital's outpatient clinic saw nearly half of the youngsters with asthma who also had nocturnal symptoms [18]. Lack of sleep is a result of nocturnal symptoms. The quality of sleep suffers even in kids with stable asthma. Sleep deprivation affects everyday life, including participation and academic achievement at school. Nighttime awakening could also Differential asthma diagnosis in school-aged children. breathing too quickly and voice chord damage alterations in the anatomy of the airways (Undiagnosed) heart abnormalities Dysplastic Fibrosis First-degree ciliary dyskinesia an obstruction to the airway Immune system problems can impair family life and cause parental job absences [19]. More severe asthma results in more frequent absences from school, which can have a detrimental impact on one's educational status and, possibly, career choice. Additionally, recurring nighttime awakenings may result in despair, aggressive behavior, and attention issues in adults. For children with asthma, exercise-induced airway obstruction (EIAO) is yet another challenge. EIAO may interfere with social interactions together with the frequent nighttime awakenings brought on by dyspnea. Exercise is a frequent bronchial hyper responsiveness trigger and may result in

coughing, wheezing, and heaviness in the chest. EIAO is a sign of asthma that has not been adequately treated [20]. Up to 23% of school-aged children can have EIAO, which significantly lowers their standard of life. EIAO restricts children's ability to play and participate in sports, and 79% of kids say that EIAO is the most difficult aspect of their asthma. Since EIAO is a sign of airway inflammation, it is very selective for childhood asthma [21]. In summary, asthmatic kids with poor cardiovascular health and/or high BMI will have a higher risk of developing lung disease than their peers. respiration rate when playing and exercising. is, in turn, a greater EIAO cause, further impairing athletic achievement and standard of life. The start of chronic diseases like asthma appears to be substantially correlated with childhood socioeconomic level in the United States. Paternal education was found to be inversely linked with the probability of having asthma in a long-term population-based study conducted in the USA. High school dropout was linked to maternal education [22]. Hatzmann et al. investigated the effects on quality of life (QoL) among Dutch parents of children with various chronic conditions.

1.2.2 Pathogenesis of asthma in children

A type 2 inflammatory response to early life exposures or events plays a crucial role in the etiology of asthma in children. The occurrence of wheezing sickness and the possibility of developing asthma are influenced by interactions among infections, atopy, genetic vulnerability, and environmental triggers (such as contact with cigarette smoke, air pollution, and farmyard environments). The microbiome in the stomach and airways, the immune system, and lung function all grow concurrently, and microbiome dysbiosis may play a significant role in the onset of asthma. The occurrence of asthma and a decline in lung function are also risk factors for higher baby weight gain and preterm birth. The variety of asthma in children can be explained by the intricate interactions between these components [23]. Patients' subgroups might be classified as endotypes or phenotypes based on particular pathophysiological mechanisms or clinical criteria. a combination of clinical, chronological, growing, or inflammatory traits, pediatric asthma phenotypes and endotypes may eventually aid in improving asthma diagnosis, asthma development prediction, and medical management of specific children. To more accurately characterize phenotypes, unbiased, data-driven clustering using a multidimensional or systems biology approach may be required. With the effective application of biologicals in the treatment of children

with significant therapy-resistant asthma, the current understanding of the inflammatory phenotypes of pediatric asthma has now been successfully implemented. It is to be anticipated that additional individualized treatment choices may become accessible [24]

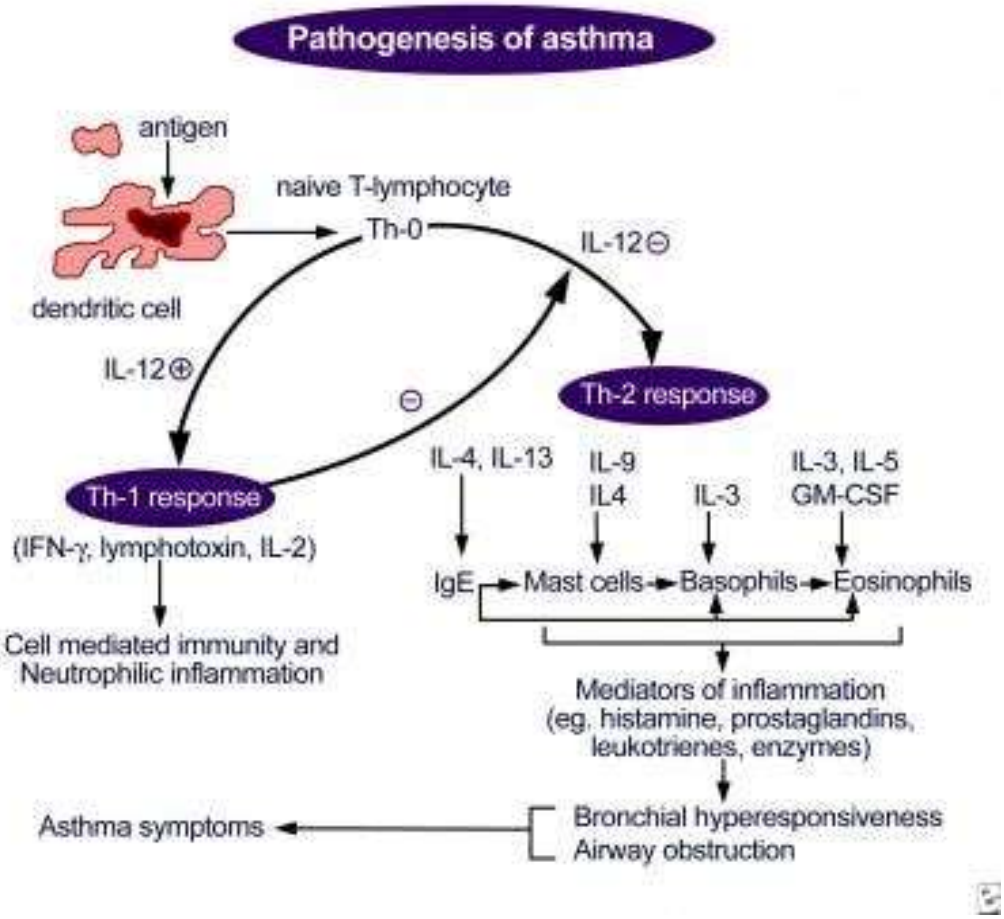


Figure 3: Pathogenesis of asthma in children [25]

Chapter 2
Purpose of the Study

2.1 Purpose of the Study

When exposed to specific triggers, the lungs and airways quickly swell up with inflammation in children with asthma. Inhaling pollen or contracting a cold or another respiratory ailment are examples of such triggers. Children with asthma may experience bothersome daily symptoms that disrupt sleep, play, sports, and school. The purpose of this review mentioned following points:

- The goals of this project are to get a comprehensive thoughtful of the medical problem being researched.
- To learn more about the variables that subsidize to the expansion of Asthma infection.
- To have a better grasp of the many diagnostic measures used to detect this ailment.
- To gain a systematic considerate of the bug, as well as its cause, signs and symptoms, consequences, and medical and nursing management choices.
- The determination of this investigation was to recognize more about children asthma infection in the Bangladesh.
- To find out the possible treatment of childhood asthma in Bangladesh.
- To know the diagnostic process of children asthma.

Chapter 3
Literature Review

3.1 Management of severe asthma in children

Children who have asthma that is difficult or severe and who are sent to a specialist Asthma sufferers are a diverse population with high morbidity. The scientific basis for care is thin and primarily based on data from studies of kids with mild to moderate asthma and on extrapolation of data from those studies. research on adults who have severe asthma. Many children with severe asthma have incorrect diagnoses or have poor adherence to medication. After excluding comorbidities ("asthma plus"), a multidisciplinary approach is used to determine whether the child has difficult asthma (which improves when the fundamental management requirements, such as adherence and inhaler technique, are met) or true, therapy-resistant asthma (which persists in causing symptoms even after the fundamental management requirements are met). Identification of environmental factors that contribute to secondary steroid resistance is very important. According to the clinical and pathophysiological characterization, a customized therapy plan should be created. High-dose inhaled steroids, the Symbiont upkeep and reliever (SMART) program (with budesonide and formoterol fumarate), and anti-IgE treatment are all approved therapeutic modalities. Methotrexate, azathioprine, cyclosporine, and subcutaneous terbutaline infusions are examples of unapproved therapies. On cytokine-specific monoclonal antibody treatments and bronchial thermoplasty, pediatric data are required. Getting the fundamentals right in managing children with asthma that appears to be severe will continue to be the cornerstone of therapy, notwithstanding interest in novel techniques [26].

3.2 Global burden of asthma among children

Asthma affects around 334 million people globally, though this number may be underestimated. It is the most prevalent chronic illness in kids. Asthma ranks among the top 20 chronic conditions for children globally in terms of disability-adjusted life years, as well as the top 10 causes for children between the ages of 5 and 14 years old. Around the world, children's asthma-related death rates range from 0.0 to 0.7 per 100,000. With up to 13-fold disparities between nations, there are notable global variations in the prevalence of asthma symptoms in children (wheeze in the previous 12 months). While many high-income countries (HICs) have higher cases of asthma symptoms, several low- and middle-income nations (LMICs) also have high rates of asthma symptom prevalence. In some high-prevalence areas in HICs, asthma symptoms increased from the 1990s to the 2000s;

in many cases, the prevalence remained constant or even dropped. The incidence of asthma increased simultaneously in many LMICs with sizable populations, which suggests that the global burden is rising and that regional inequalities in asthma prevalence are narrowing. Asthma-related expenditures are often high where they have been evaluated. It is necessary to continuously monitor the expenditures associated with childhood asthma globally using standardized techniques [27].

3.3 Asthma in Children

A IMPORTANT understanding of the pathogenesis of asthma has been developed over the past 20 years. National statistics show rising morbidity and mortality from this illness notwithstanding our increased understanding.1, 2 A reevaluation of therapy has resulted from this paradox.3 This review covers the most current recommendations for the five main classes of asthma drugs and discusses how our understanding of asthma has advanced. It also looks at the potential causes of asthma mortality. Also outlined is the significance of Nonpharmacological therapy. While the focus of this study is on pediatric asthma, when there are no studies that are similar in children, research studies including adults are cited. Deficits in our knowledge of pediatric-specific disease processes and therapeutic approaches are also observed [28].

Chapter 4
Methodology

4.1 Methodology

Methods for assembling and evaluating data were gathered from a variety of linked reviews published between 1995 and 2022 utilizing search engines like PubMed, Research Gate, Google Scholar, and Medline, among others. The procedures employed in the investigation are covered in this chapter. Some basic terms, such as "Childhood asthma pathogenesis," "Childhood asthma treatment," "Childhood asthma diagnostic technique," and "Childhood asthma preventive measures," were used to search for me. I learned more by reading every collected review paper. The information acquired has been finally summarized.

Chapter 5
Results & Discussion

5.1 Non-pharmacologic Management of Childhood Asthma

A plan of action for asthma entails taking three separate approaches to the issue: environmental control, pharmacological intervention, and immunotherapy. Furthermore, regular monitoring and independent evaluation of asthma status are both beneficial. It is obvious that the creation of new medications is just a portion of a larger treatment plan for asthma. The asthmatic child's treatment strategy must include non-pharmaceutical means for therapy in along with medication [33].

5.1.1 Environmental Control

According to investigations on allergen challenges, contact to an allergen to which an asthmatic has become sensitized is likely to cause an asthma attack. On the other hand, avoiding such allergies can cause the aggravation to go away. As a result, it is now understood that avoiding allergens is a crucial component of an asthma management strategy. The patient's sensitivities and exposure pattern must be understood in order for an allergy avoidance plan to be effective. Since seasonal allergens, primarily pollens, are windborne and can travel for kilometers, avoiding them without making unjustified lifestyle modifications is challenging [34]. On the contrary, there are tried-and-true methods for keeping indoor allergies at bay. When creating an indoor allergy avoiding program, the bedroom should be given top importance since we spending up to a third of our time sleeping next to dust mites. Dust mites need water for sustenance, and moist conditions encourage their growth. Maintaining the relative humidity of the house between 50 and 55 percent will aid in reducing the number of dust mites present. High-efficiency particle air filters and mattress and pillow encasings are two more control techniques that could be advantageous. Vacuuming shouldn't likely be done by the asthmatic youngster either because it can disturb dust mite reservoirs and discharge the mites' particles into the breathing area [35]. The best way to avoid pet allergens is to get rid of the pet completely. As a result of the emotional relationship that people, particularly children, have to their pets, completing this chore is frequently impossible. If eliminating of the animal is not an option, maintaining it out of the bedroom might be helpful. Regular pet washing may not always be beneficial. There are also many "denaturing" preparations accessible, however, as before, there is debate concerning their efficacy. Molds are typical allergens that come from the outside environment and are more prevalent in humid settings. A water leak or at

least a great deal of interior humidity is likely the cause of a high indoor to outside mold count ratio [36]. Mold can develop on a variety of surfaces, including damp paper, books, and household plants as well as decomposing living things. Concentration of indoor mold spores may be lowered by removing these substrates. The American Academy of Allergy, Asthma and Immunology's National Allergy Bureau website offers patients and their parents information on outdoor exposures despite the fact that pollens are harder to prevent than dust, as was previously indicated. The website provides data on pollen and mold counts obtained from counting facilities managed by trained counters. There were 85 counting stations in the USA as of October 2010, along with two in Canada and two in Argentina [37].

5.2 Pharmacologic Management

5.2.1 Inhaled Corticosteroids

In 1949, it was demonstrated that ACTH had a positive impact on the management of asthma. Oral corticosteroids were eventually demonstrated to be effective as well, but their widespread usage was constrained by adverse effects. Since their introduction in 1972, inhaled corticosteroids have been the first-line medication for the management of asthma, ushering in a new era in asthma treatment. Via their relationship with the glucocorticoid receptor and the activation of histone deactylase-2, corticosteroids inhibit the expression of inflammatory genes. They have a variety of anti-inflammatory actions via controlling the transcription of inflammatory genes or their promoter sequences [42].

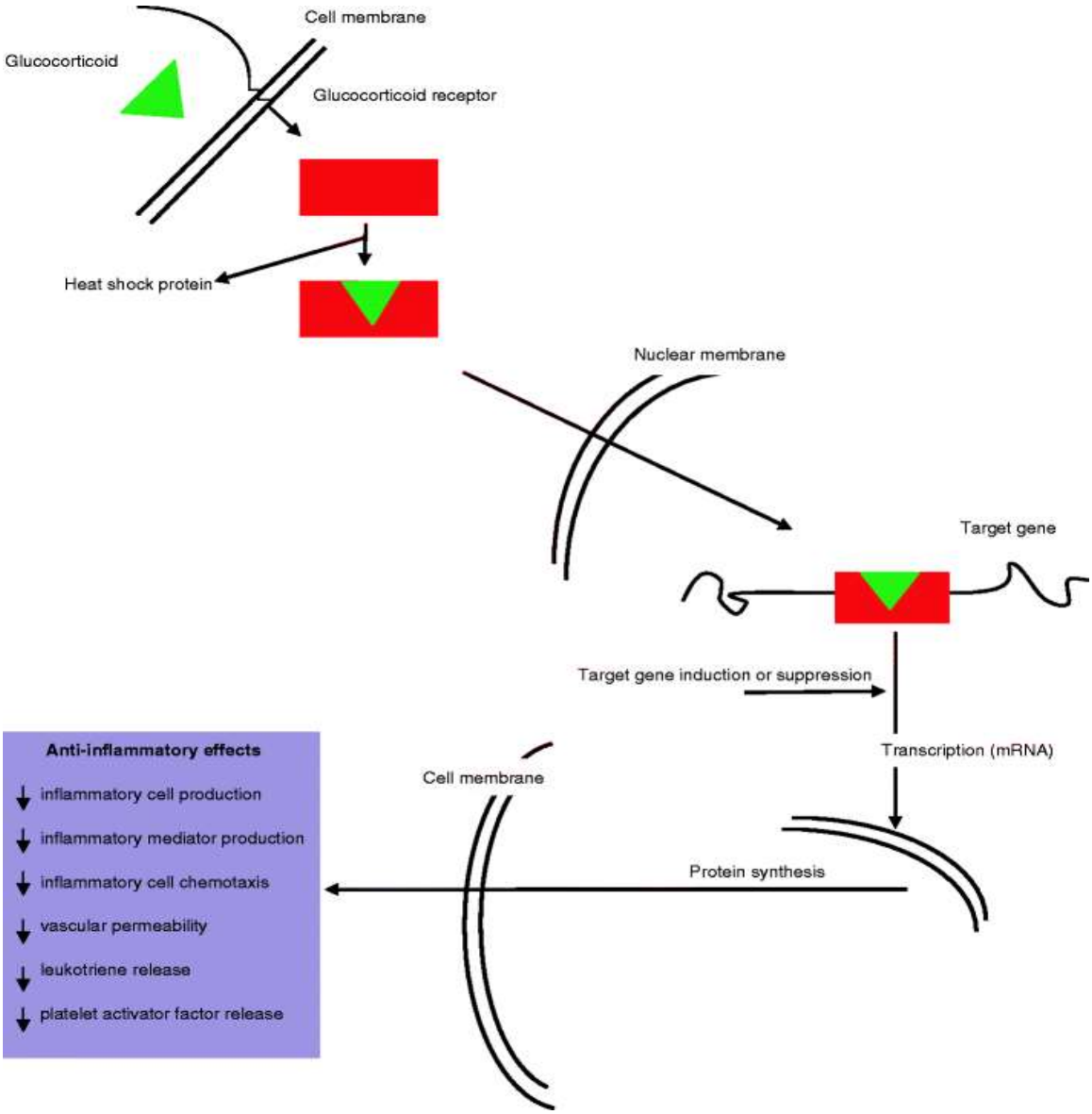


Figure 4: Mechanism of action of glucocorticoids [43]

There has been a lot of research done on the subject of the harmful consequences of inhaled steroids in children. Numerous negative effects are connected to steroids. The majority of these have been linked to parenteral or oral steroids. The impact on growth in children with asthma has been the main worry with regards to inhaled or nebulized steroids. Due to the fact that asthma has been linked to growth mental retardation, it is challenging to undertake studies to ascertain whether inhaled corticosteroids do truly have this effect. The majority of the research implies that even if there is growth retardation, it is typically reversible and there is a time of "catch-up" growth, despite the fact its consequences have been variable

[44]. Furthermore, even if corticosteroids do slow down growth, it is only to a minor degree. Therefore, the danger of growth retardation is minimal compared to the possibility of severe asthmatic flare-ups. In youngsters using inhaled steroids, adrenal insufficiency is also not a serious issue. In a trial with 14 kids using a dry powder beclomethasone dipropionate inhaler, the hypothalamic-pituitary-adrenal (HPA) axis was not suppressed. The beclomethasone dosage was 12–25 g/kg/day. Other research has not been able to show harmful effects on the HPA axis. On the other side, it has been demonstrated that using fluticasone at large doses suppresses the HPA axis [45].

5.2.2 Long-Acting β-Agonists

LABAs, or long-acting -agonists, can be used alone or in conjunction with an inhaled corticosteroid. The two long-acting -agonists that are presently on the market are formoterol fumarate and salmeterol xinafoate. A significant hydrocarbon chain runs from the bonding site to the site of action of salmeterol xinafoate. The binding site is firmly bonded to a different location on the cell membrane, and the lengthy chain serves as a tether, which potentially enables recurrent engagement among the active site and the target receptor. Down to age 4, salmeterol is recommended. It was previously offered as both an MDI and a diskus, but is currently only offered as a diskus. The diskus should be used twice daily and has a 50 g dose per puff [46]. Salmeterol has a final elimination half-life of 5.5 hours. Formoterol is sold in an aerolizer, a dry powder machine that requires puncturing a capsule in a particular chamber. One capsule has a total medication content of 12 g. Additionally, formoterol is administered twice daily. Formoterol has an average half-life of 10 hours in healthy persons. Currently, it is advised to utilize LABAs as an adjunctive therapy rather than as the primary treatment for persistent asthma. Several case reports about mortality related to asthma linked to salmeterol use have been published in the literature. The LABA class of medications subsequently received a black box warning from the FDA regarding a rise in asthma-related mortality. Due to the existence of additional complicating factors that may or may not have been taken into account in the investigations, the matter is, nevertheless, still heavily contested. A new guideline for the use of LABAs states that the patient should be weaned off the LABA once he or she has stabilized on the combination medication [47].

5.2.3 Cromolyn and Nedocromil

These two unconnected substances have a very good safety profile. Their chemical compositions are shown. Both are mast cell stabilizers and also prevent eosinophils from becoming activated and releasing inflammatory mediators. Chloride channels appear to be the mechanism by which this is regulated. Allergen challenge responses are suppressed in both their early and late phases. Bishop's weed, also known as Ammi visnaga, is the source of the chemical cromolyn. Both nebulized and MDI administration methods are available for the commercial item. The amount of cromolyn administered by MDI is 1 mg per action, while the dose of nedocromil administered via inhalation devices is 2 mg per activation from the valve and 1.75 mg per actuation from the mouthpiece. Nedocromil sodium has a terminal elimination half-life of 3.3 hours. The use of nedocromil sodium is recommended for children older than 6 years old. Very young children frequently utilize nebulizers to provide cromolyn sodium [48].

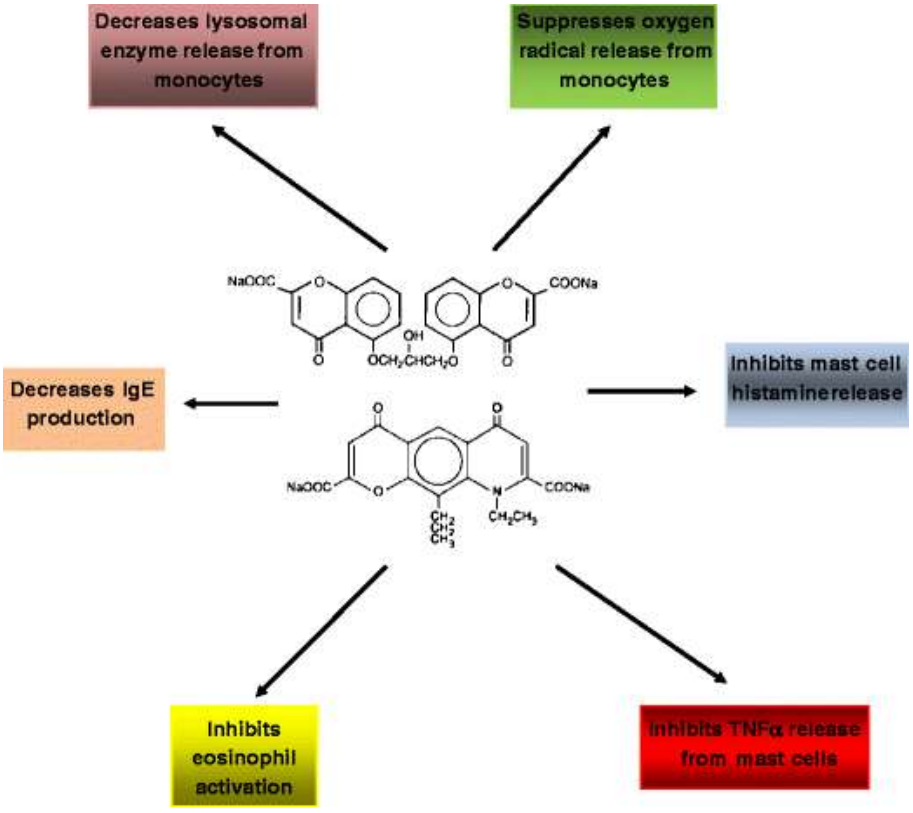


Figure 5: Structure and anti-inflammatory effects of cromolyn and nedocromil [49]

5.2.4 Leukotriene Pathway Drugs

Leukotriene-blocking medications were initially made available in the early 1990s. These medications were created using one of two methods: stopping their synthesis or preventing their function at the Cys-LT receptor level. Liver damage has been linked to medications like zileuton that prevent the production of leukotrienes. The more popular drugs have been leukotriene receptor antagonists since they have a much better safety profile and dose regimen. Fig. 6 depicts the leukotrienes' method of action [50].

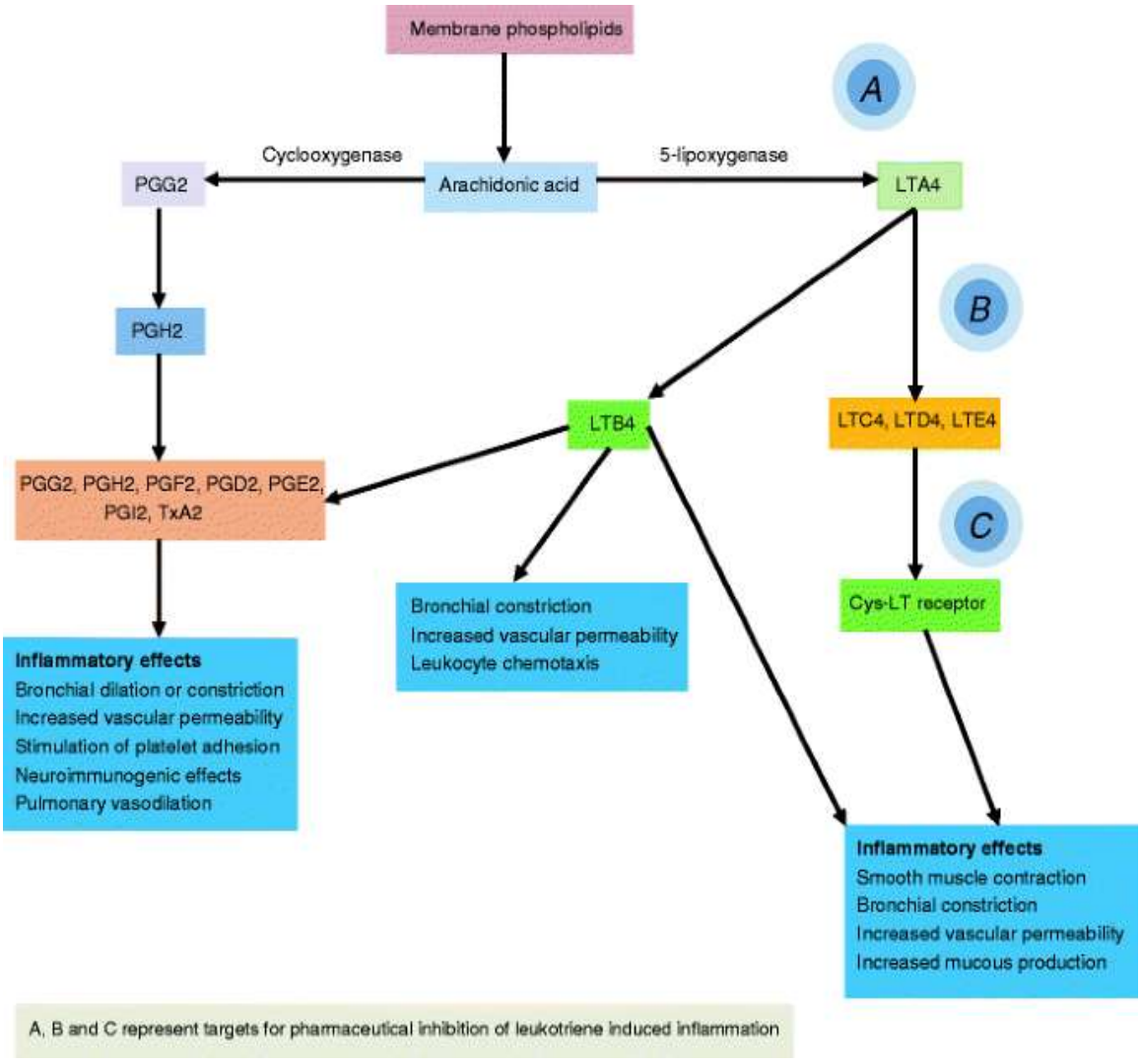


Figure 6: Mechanism of action of leukotriene pathway modifiers [51]

Leukotrienes are a 1000 times more potent inflammatory mediators in asthma than histamine. Amplification of neutrophil and eosinophil migration, restriction of bronchial

smooth muscle, and promotion of monocyte aggregate are some of the effects of LTC4, LTD4, and LTE4 on the Cys-LT receptor. The Churg-Strauss syndrome, a vasculitis characterized by peripheral eosinophilia, increased serum total IgE, patchy lung infiltrates, cutaneous purpuric lesions, and pleural effusions, is a distinct exception to the leukotriene receptor antagonists' generally minor negative consequences. Theophylline metabolism as well as that of a variety of other medications may be impacted by leukotriene system modifiers [52].

5.2.5 Antihistamines

The use of antihistamines in asthmatic children has been strongly contested. The FDA initially issued a class impact caution on the use of antihistamines in asthma, thus any subsequent antihistamines produced all had the same warning. Nevertheless, whereas the initial generation of antihistamines had side effects that could exacerbate an asthma attack, such as dripping and sedative effects on the anticholinergic system, the second generation antihistamines have significantly fewer of these negative effects and should be safe for people with asthma. They should also have some advantages, particularly for kids whose asthma is more frequently brought on by allergies. The second-generation antihistamines that are now offered in the USA are fexofenadine, loratadine, desloratadine, and levocetirizine. These medications prevent the allergic response to environmental allergens, but cetirizine also reduces late leukocyte migration into antigen-challenged skin blister fluid chambers [53]. It also suppresses leukocyte recruitment and activation as well as eosinophil migration. Neutrophils, eosinophils, and basophils—all three inflammatory cell lines—were impacted.

5.2.6 Theophylline in Childhood Asthma

In the 1980s, when practically every child with an asthma exacerbation necessitating hospital admission was started on an aminophylline drip, theophylline and aminophylline were at the height of their popularity. Similar to this, theophylline was given to the majority of asthma patients as a maintenance medication. Due to its limited treatment window and possibly serious side effects, the use of this class of drugs has considerably declined since then. Theophylline, which is produced from aminophylline, is converted into caffeine.

As a phosphodiesterase inhibitory agents, theophylline works. (Fig. 7). It works similarly to inhaled steroids in terms enhancing symptom scores and pulmonary function test metrics [54].

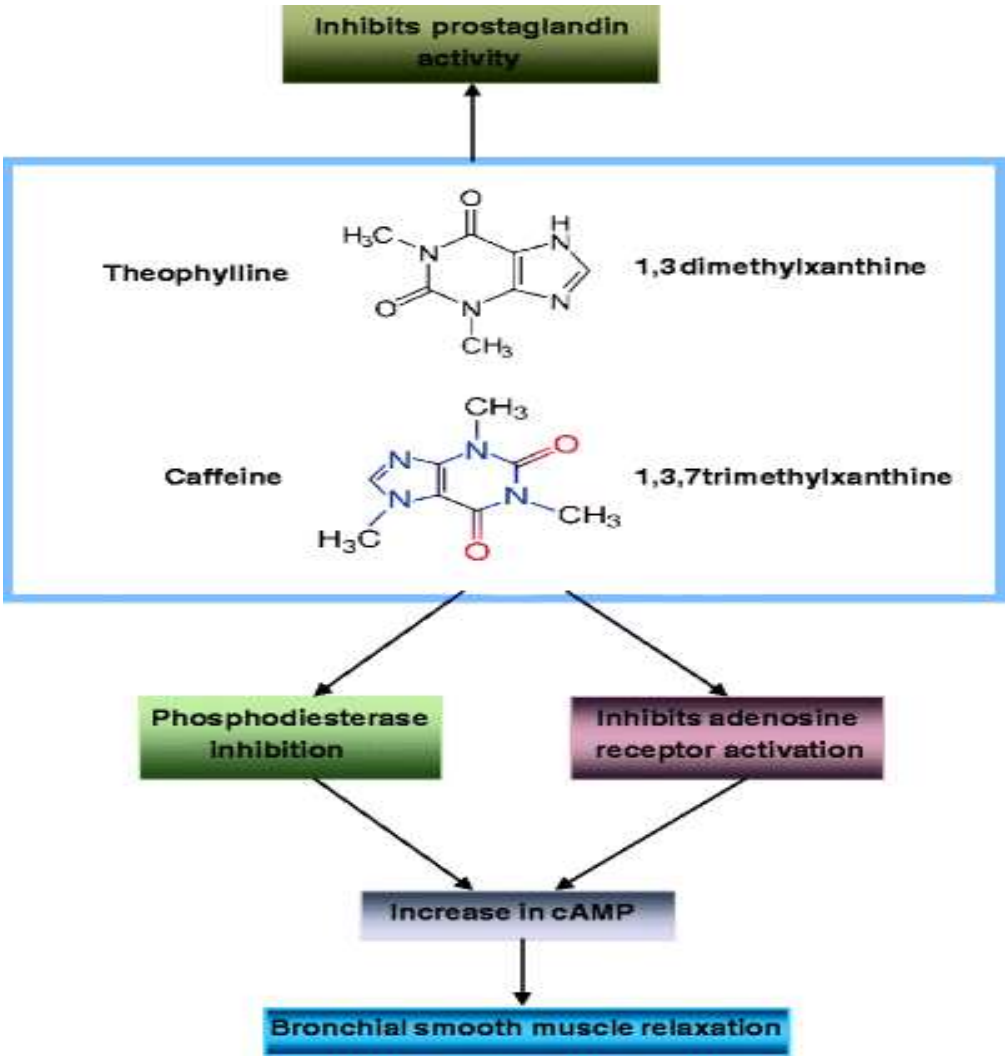


Figure 7: Structure and bronchodilator effects of theophylline [55]

Every 2 to 3 months, or more frequently if there are dosage adjustments, warning signals of side effects, or a lack of effectiveness, theophylline levels should be checked.

5.2.7 Monoclonal Anti-IgE

Omalizumab (Xolair) is a humanized IgG1a monoclonal antibody generated from recombinant DNA that binds only to human IgE. Omalizumab's binding to IgE prevents asthmatic early- and late-phase responses. Omalizumab has effects that include lowering serum IgE levels and reducing allergic bronchoconstriction. Patients with IgE levels between 30 and 700 IU/ml with moderate to severe recurrent allergic asthma who have a positive skin or blood allergy test are eligible to receive omalizumab. Patients must be 12 years of age or older. The dosage plan for omalizumab is displayed. Malignancies, allergic reactions, and local injection reactions are examples of side effects. Savings on the cost of asthma exacerbations may be enough to offset the high cost of Xolair [56].

5.2.8 Short-Acting β-Agonists

The -agonists work by activating the 2-adrenergic transmitters on the smooth muscle cells of the airways, which then causes adenyl cyclase to become active. Cyclic adenosine monophosphate (cAMP) quantity inside of cells rises as a result of this. As a consequence of protein kinase A being activated by cAMP, myosin phosphorylation is inhibited and intracellular calcium levels are decreased, which relaxes bronchial smooth muscle. All airways, from the trachea to the terminal bronchioles, have 2-adrenergic receptors. The reduction of mediator release from mast cells is another result of the rise in cAMP content. Paradoxical bronchospasm, cardiovascular issues, central nervous system excitement, fever, tremors, nausea, vomiting, and an unpleasant taste are some of the negative effects of –agonists [57]. The short-acting beta-agonists (SABA) utilized are terbutaline, albuterol, levalbuterol, pirbuterol, bronkosol, and isoproterenol. Older, less-specific medications like metaproterenol and isoproterenol are no longer used since freshly created -agonists are more particular to 2-adrenergic receptors, maximizing the effects on bronchial smooth muscle while lowering cardiac adverse effects [58].

5.2.9 Anticholinergics

Although they are recommended for the management of chronic obstructive pulmonary disease, anticholinergic inhalers may also be useful for treating asthmatics throughout an exacerbation. Ipratropium bromide works by inhibiting M2 and M3 muscarinic cholinergic receptors in an antagonistic manner. As a result, mucous gland output and vagal tone in the

airways both decline. Anticholinergic medications help prevent bronchoconstriction [86]. Both nebulized ipratropium bromide (2.5 ml of a 0.02% solution = 500 g) and HFA MDI (17 g/dose from the mouthpiece) are forms of the medication. The gastrointestinal system is not very effective in absorbing ipratropium bromide. Ipratropium bromide has a 1-hour elimination half-life when given orally or intravenously [59].

5.2.10 Mucolytic

It is debatable whether mucolytics like N-acetylcysteine and S-carboxymethycysteine should be used to treat childhood asthma. Mucolytics work by dissolving the disulfide bonds that hold the chains of mucins together, facilitating mucous drainage. However, they can also lead to bronchoconstriction. Although N-acetylcysteine has been shown to increase gas exchange following a methacholine challenge in animal experiments, there is presently no clinical evidence to support the use of mucolytic in the management of pediatric asthma [60].

5.2.11 Oral or Parenteral Steroids

thankfully in nations where access to proactive, controller drugs is simple and unrestricted, the use of systemic steroids in the treatment of asthma has declined. Chronic oral or parenteral use of systemic steroids is linked to a wide range of negative side effects, many of which have the potential to be more severe than the disease they are intended to treat. Osteonecrosis is a significant adverse effect that is occasionally overlooked. When treating an asthmatic child who has been on steroids for a long period, one should still have a high index of suspicion because corticosteroid-induced osteonecrosis is more common in people with autoimmune disorders and people who have had organ transplants than it is in asthma patients [61]. In general, from a risk-benefit perspective, treating an asthma exacerbation with a brief process of steroids is reasonable. If the administration of corticosteroids in this instance lasts fewer than seven days, there is no need to taper the dose. For patients receiving steroids for a period longer than a week, a tapering schedule should be created. The potential for major adverse effects should be taken into account if the patient needs numerous courses of steroids. For the treatment of asthmatic flare-ups, a variety of corticosteroids are accessible [61].

Chapter 6
Conclusion

6.1 Conclusion

At least amongst allergy and asthma specialists, the management of childhood asthma has improved. All age groups now receive asthma therapy with inhaled corticosteroids as a first line option. Growing the dose of steroids, adding a leukotriene receptor antagonist, or incorporating a long-acting -agonist are all suitable choices that should be tailored and tailored for each individual child with asthma. The chose add-on therapy remains up for controversy. Though we have not yet arrived at this stage, future study may be able to determine what course of action might be chosen depending on the patient's pharmacogenetic. Over the past two or three many years, environmental control has established itself as a cornerstone in the management of asthma, and novel immunotherapy techniques have significantly reduced morbidity. Children with asthma are now less likely to be admitted to hospitals, medications with serious side effects like theophylline have been substituted, and their standard of life has increased. As long as they follow their asthma care plan, the majority of children with asthma are able to lead remarkably normal lives, participate at a high level in sports, and miss relatively few days of school or work. The asthma education element is always being developed. Access to specialized care is a significant concern that could get worse in the face of cost-cutting measures brought on by various health care restructuring concepts. Pediatric asthma has a promising future. Investigation is still being done to better understand the pathophysiology of asthma and to create novel medications to treat it. We can create a personalized care plan for each child with asthma by using our understanding of the genetic foundation for asthma and how kids respond to asthma treatments. Perhaps this will result in even better outcomes for kids with asthma.

Chapter 7
Reference

Reference

1. Pearce N, Douwes J (2006) The global epidemiology of asthma in children. Int J Tuberc Lung Dis 10:125–132

2. Bateman ED, Hurd SS, Barnes PJ et al (2008) Global strategy for asthma management and prevention: GINA executive summary. Eur Respir J 31:143–178

3. New NHLBI (1997) Guidelines for the diagnosis and management of asthma. National Heart, Lung and Blood Institute. Lippincott Health Promot Lett 2(1):8–9

4. Expert Panel Report 3 (EPR-3) (2007) Guidelines for the diagnosis and management of asthma-summary report 2007. J Allergy Clin Immunol 120:S94–S138

5. Priftis KN, Mantzouranis EC, Anthracopoulos MB (2009) Asthma symptoms and airway narrowing in children growing up in an urban versus rural environment. J Asthma 46:244–251

6. Chang CC, Phinney SD, Halpern GM, Gershwin ME (1993) Asthma mortality: another opinion is it a matter of life and bread? J Asthma 30:93–103

7. Dixon AE, Holguin F, Sood A et al (2010) An official American Thoracic Society Workshop report: obesity and asthma. Proc Am Thorac Soc 7:325–335

8. Vollmer WM, Buist AS, Osborne ML (1992) Twenty year trends in hospital discharges for asthma among members of a health maintenance organization. J Clin Epidemiol

45:999–1006

9. Berce V, Potocnik U (2010) Functional polymorphism in CTLA4 gene influences the response to therapy with inhaled corticosteroids in Slovenian children with atopic asthma. Biomarkers 15:158–166

10. Vonk JM, Postma DS, Maarsingh H, Bruinenberg M, Koppelman GH, Meurs H (2010) Arginase 1 and arginase 2 variations associate with asthma, asthma severity and beta2 agonist and steroid response. Pharmacogenet Genomics 20:179–186

11. Polimanti R, Piacentini S, Moscatelli B, Pellicciotti L, Manfellotto D, Fuciarelli M (2010) GSTA1, GSTO1 and GSTO2 gene polymorphisms in Italian asthma patients. Clin Exp Pharmacol Physiol 37:870–872

12. Piacentini S, Polimanti R, Moscatelli B et al (2010) Glutathione S-transferase gene polymorphisms and air pollution as interactive risk factors for asthma in a multicentre Italian field study: a preliminary study. Ann Hum Biol 37:427–439

13. Vergara CI, Acevedo N, Jimenez S et al (2010) A six-SNP haplotype of ADAM33 is associated with asthma in a population of Cartagena, Colombia. Int Arch Allergy Immunol 152:32–40

14. Hesselmar B, Bergin AM, Park H et al (2010) Interleukin-4 receptor polymorphisms in asthma and allergy: relation to different disease phenotypes. Acta Paediatr 99:399–403

15. Sleiman PM, Flory J, Imielinski M et al (2010) Variants of DENND1B associated with asthma in children. N Engl J Med 362:36–44

16. Via M, De Giacomo A, Corvol H et al (2010) The role of LTA4H and ALOX5AP genes in the risk for asthma in Latinos. Clin Exp Allergy 40:582–589

17. Reijmerink NE, Bottema RW, Kerkhof M et al (2010) TLR related pathway analysis: novel gene-gene interactions in the development of asthma and atopy. Allergy 65:199–207

18. Gao J, Li W, Willis-Owen SA et al (2010) Polymorphisms of PHF11 and DPP10 are associated with asthma and related traits in a Chinese population. Respiration 79:17–24

19. Wang TN, Tseng HI, Kao CC et al (2010) The effects of NOS1 gene on asthma and total IgE levels in Taiwanese children, and the interactions with environmental factors. Pediatr Allergy Immunol 21:1064–1071

20. Jonsson UB, Hakansson LD, Jogi R, Janson C, Venge P (2010) Associations of ECP (eosinophil cationic protein)-gene polymorphisms to allergy, asthma, smoke habits and lung function in two Estonian and Swedish sub cohorts of the ECRHS II study. BMC Pulm Med 10:36

21. Harada M, Hirota T, Jodo AI, et al (2011) TSLP promoter polymorphisms are associated with susceptibility to bronchial asthma. Am J Respir Cell Mol Biol. doi:10.1165/rcmb.2009- 0418OC

22. Zhang YG, Huang J, Zhang J et al (2010) RANTES gene polymorphisms and asthma risk: a meta-analysis. Arch Med Res 41:50–58

23. Polk S, Sunyer J, Munoz-Ortiz L et al (2004) A prospective study of Fel d1 and Der p1 exposure in infancy and childhood wheezing. Am J Respir Crit Care Med 170:273–278

24. Wennergren G, Ekerljung L, Alm B, Eriksson J, Lotvall J, Lundback B (2010) Asthma in late adolescence—farm childhood is protective and the prevalence increase has levelled off. Pediatr Allergy Immunol 21:806–813

25. Sheehan WJ, Rangsithienchai PA, Wood RA et al (2010) Pest and allergen exposure and abatement in inner-city asthma: a work group report of the American Academy of Allergy, Asthma & Immunology Indoor Allergy/Air Pollution Committee. J Allergy Clin Immunol 125:575–581

26. Chang C (2010) The immune effects of naturally occurring and synthetic nanoparticles. J Autoimmun 34:J234–J246

27. Randolph C (2010) The challenge of asthma in adolescent athletes: exercise induced bronchoconstriction (EIB) with and without known asthma. Adolesc Med State Art Rev 21:44–56, viii

28. Peroni DG, Pietrobelli A, Boner AL (2010) Asthma and obesity in childhood: on the road ahead. Int J Obes (Lond) 34:599–605

29. Lund TK (2009) Asthma in elite athletes: how do we manage asthma-like symptoms and asthma in elite athletes? Clin Respir J 3:123

30. Stickland MK, Spooner CH, Dryden DM, Rowe BH (2010) The need for standardization in exercise challenge testing for exercise-induced asthma/bronchoconstriction. J Allergy Clin Immunol 126:878–880.e6

31. Rosenthal LA, Avila PC, Heymann PW et al (2010) Viral respiratory tract infections and asthma: the course ahead. J Allergy Clin Immunol 125:1212–1217

32. Jackson DJ, Johnston SL (2010) The role of viruses in acute exacerbations of asthma. J Allergy Clin Immunol 125:1178– 1187, quiz 88–9

33. Sly PD, Kusel M, Holt PG (2010) Do early-life viral infections cause asthma? J Allergy Clin Immunol 125:1202–1205

34. Bizzintino J, Lee WM, Laing IA et al (2011) Association between human rhinovirus C and severity of acute asthma in children. Eur Respir J. doi:10.1183/09031936.00092410

35. Jackson DJ (2010) The role of rhinovirus infections in the development of early childhood asthma. Curr Opin Allergy Clin Immunol 10:133–138

36. Johnston SL, Pattemore PK, Sanderson G et al (1996) The relationship between upper respiratory infections and hospital admissions for asthma: a time-trend analysis. Am J Respir Crit Care Med 154:654–660

37. McBride JT (1999) Pulmonary function changes in children after respiratory syncytial virus infection in infancy. J Pediatr 135:28–32

38. Dimova-Yaneva D, Russell D, Main M, Brooker RJ, Helms PJ (2004) Eosinophil activation and cysteinyl leukotriene production in infants with respiratory syncytial virus bronchiolitis. Clin Exp Allergy 34:555–558

39. Sigurs N, Gustafsson PM, Bjarnason R et al (2005) Severe respiratory syncytial virus bronchiolitis in infancy and asthma and allergy at age 13. Am J Respir Crit Care Med 171:137–141

40. Sigurs N, Aljassim F, Kjellman B et al (2010) Asthma and allergy patterns over 18 years after severe RSV bronchiolitis in the first year of life. Thorax 65:1045–1052

41. Naclerio RM, Meier HL, Kagey-Sobotka A et al (1983) Mediator release after nasal airway challenge with allergen. Am Rev Respir Dis 128:597–602

42. Gelfand EW, Cui ZH, Takeda K, Kanehiro A, Joetham A (2002) Fexofenadine modulates T-cell function, preventing allergen induced airway inflammation and hyperresponsiveness. J Allergy Clin Immunol 110:85–95

43. Gelfand EW, Cui ZH, Takeda K, Kanehiro A, Joetham A (2003) Effects of fexofenadine on T-cell function in a murine model of allergen-induced airway inflammation and hyperresponsiveness. J Allergy Clin Immunol 112:S89–S95

44. Ducharme FM, Zemek RL, Chalut D et al (2011) Written action plan in pediatric emergency room improves asthma prescribing, adherence and control. Am J Respir Crit Care Med 183:195–203

45. Sapien RE, Fullerton-Gleason L, Allen N (2004) Teaching school teachers to recognize respiratory distress in asthmatic children. J Asthma 41:739–743

46. Byrnes CA, Dinarevic S, Shinebourne EA, Barnes PJ, Bush A (1997) Exhaled nitric oxide measurements in normal and asthmatic children. Pediatr Pulmonol 24:312–318

47. Mattes J, Storm van's Gravesande K, Reining U et al (1999) NO in exhaled air is correlated with markers of eosinophilic airway 134 Clinic Rev Allerg Immunol (2012) 43:98–137 inflammation in corticosteroid-dependent childhood asthma. Eur Respir J 13:1391–1395

48. Warke TJ, Fitch PS, Brown V et al (2002) Exhaled nitric oxide correlates with airway eosinophils in childhood asthma. Thorax 57:383–387

49. Baraldi E, Azzolin NM, Zanconato S, Dario C, Zacchello F (1997) Corticosteroids decrease exhaled nitric oxide in children with acute asthma. J Pediatr 131:381–385

50. del Giudice MM, Brunese FP, Piacentini GL et al (2004) Fractional exhaled nitric oxide (FENO), lung function and airway hyperresponsiveness in naive atopic asthmatic children. J Asthma 41:759–765

51. Bastain TM, Islam T, Berhane KT et al (2011) Exhaled nitric oxide, susceptibility and new-onset asthma in the children's health study. Eur Respir J. doi:10.1183/09031936.00021210

52. Korn S, Telke I, Kornmann O, Buhl R (2011) Measurement of exhaled nitric oxide: comparison of different analysers. Respirology 15:1203–1208

53. Caudri D, Wijga AH, Hoekstra MO et al (2010) Prediction of asthma in symptomatic preschool children using exhaled nitric oxide, Rint and specific IgE. Thorax 65:801–807

54. Pedrosa M, Cancelliere N, Barranco P, Lopez-Carrasco V, Quirce S (2010) Usefulness of exhaled nitric oxide for diagnosing asthma. J Asthma 47:817–821

55. Sandrini A, Taylor DR, Thomas PS, Yates DH (2010) Fractional exhaled nitric oxide in asthma: an update. Respirology 15:57–70

56. Shields MD, Brown V, Stevenson EC et al (1999) Serum eosinophilic cationic protein and blood eosinophil counts for the prediction of the presence of airways inflammation in children with wheezing. Clin Exp Allergy 29:1382–1389

57. Peona V, De Amici M, Quaglini S et al (2010) Serum eosinophilic cationic protein: is there a role in respiratory disorders? J Asthma 47:131–134

58. Ahlstedt S (1995) Clinical application of eosinophilic cationic protein in asthma. Allergy Proc 16:59–62

59. Perng DW, Huang HY, Lee YC, Perng RP (2004) Leukotriene modifier vs inhaled corticosteroid in mild-to-moderate asthma: clinical and anti-inflammatory effects. Chest 125:1693–1699

60. Basyigit I, Yildiz F, Kacar Ozkara S, Boyaci H, Ilgazli A, Ozkarakas O (2004) Effects of different anti-asthmatic agents on induced sputum and eosinophil cationic protein in mild asthmatics. Respirology 9:514–520

61. Kocak AK, Bor O, Yildiz B, Erdogan L, Us T (2006) T-lymphocyte activation and the levels of eosinophilic cationic protein and interleukin-5 in asthmatic children with acute exacerbation and effect of glucocorticoid treatment. Allergy Asthma Proc 27:371–377