ASTHMA – A REVIEW

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Summary

Asthma is a predisposition to chronic inflammation of the lungs in which the airways (bronchi) are reversibly narrowed. During asthma attacks (exacerbations of asthma), the smooth muscle cells in the bronchi constrict, the airways become inflamed and swollen, and breathing becomes difficult. This is often referred to as a tight chest and is a sign to immediately take medication. Asthma affects 7% of the population of the United States, 6.5% of British people and a total of 300 million worldwide. Public attention in the developed world has recently focused on the predisposition because of its rapidly increasing prevalence, affecting up to one quarter of urban children. Although asthma is more common in affluent countries, it is by no means a problem restricted to the affluent; the WHO estimate that there are between 15 and 20 million people with asthma in India. In the U.S., urban residents, Hispanics, and African Americans are affected more than the population as a whole. Striking increases in asthma prevalence have been observed in populations migrating from a rural environment to an urban one, or from a third-world country to Westernized one. Therefore this review is undertaken to provide a glimpse on the causes, pathophysiology, diagnosis and types of treatment options available for asthamatic patients.

Keywords: - Asthma, bronchi, inflammation

Introduction

The word asthma has originated from an ancient Greek word meaning panting. Essentially asthma is a chronic inflammation of the air ways (Bronchi) that result in obstruction of air flow [1].

Asthma is a predisposition to chronic inflammation of the lungs in which the airways (bronchi) are reversibly narrowed. Asthma affects 7% of the population of the United States [2, 3], 6.5% of British people and a total of 300 million worldwide [4].

Although asthma is a chronic obstructive condition, it is not usually considered as a part of chronic obstructive pulmonary disease as this term refers specifically to combinations of bronchiectasis, chronic bronchitis, and emphysema. Unlike these diseases, the airway obstruction in asthma is usually reversible; however, if left untreated, asthma can result in chronic inflammation of the lungs and irreversible obstruction. In contrast to emphysema and bronchiectasis, asthma affects the bronchi, not the alveoli [5]. The National Heart, Lung and Blood Institute defines asthma as a common chronic disorder of the airways characterized by variable and recurring symptoms, airflow obstruction, bronchial hyperresponsiveness (bronchospasm), and an underlying inflammation [6].

Public attention in the developed world has recently focused on the predisposition because of its rapidly increasing prevalence, affecting up to one quarter of urban children [7].

The International Study of Asthma and Allergies in Childhood (ISAAC), a monumental study which involved 155 centers in 56 countries was one of the first to reliably compare the prevalence of asthma worldwide [8]. Surveying nearly half a million children 13–14 years of age, this study found great disparities (as high as a 20 to 60-fold difference) in asthma prevalence across the world, with a trend toward more developed and westernized countries having higher asthma prevalence.

Rote westernization however does not explain the entire difference in asthma prevalence between countries, and the disparities may also be affected by differences in genetic, social and environmental risk factors [9]. There are also worldwide disparities in asthma mortality, which is most common in low to middle income countries [10]. Asthma symptoms were most prevalent (as much as 20%) in the United Kingdom, Australia, New Zealand, and Republic of Ireland; they were lowest (as low as 2–3%) in Eastern Europe, Indonesia, Greece, Uzbekistan, India, and Ethiopia [11].

Although asthma is more common in affluent countries, it is by no means a problem restricted to the affluent; the WHO estimate that there are between 15 and 20 million people with asthma in India. In the U.S., urban residents, Hispanics, and African Americans are affected more than the population as a whole. Striking increases in asthma prevalence have been observed in populations migrating from a rural environment to an urban one [12], or from a third-world country to Westernized one [13].

Causes

Asthma is caused by environmental and genetic factors [14], which can influence how severe asthma is and how well it responds to medication [15]. Some environmental and genetic factors have been confirmed by further research, while others have not been. Underlying both environmental and genetic factors is the role of the upper airway in recognizing the perceived dangers and protecting the more vulnerable lungs by shutting down the airway.

Environmental

Many environmental risk factors have been associated with asthma development and morbidity in children, but a few stand out as well-replicated or that have a meta-analysis of several studies to support their direct association.

Environmental tobacco smoke, especially maternal cigarette smoking, is associated with high risk of asthma prevalence and asthma morbidity, wheeze, and respiratory infections [16]. Low air quality, from traffic pollution or high ozone levels, has been repeatedly associated with increased asthma morbidity and has a suggested association with asthma development that needs further research [17, 18].

Caesarean sections have been associated with asthma when compared with vaginal birth; a meta-analysis found a 20% increase in asthma prevalence in children delivered by Caesarean section compared to those who were not. It was proposed that this is due to modified bacterial exposure during Caesarean section compared with vaginal birth, which modifies the immune system [19].

Psychological stress has long been suspected of being an asthma trigger, but only in recent decades has convincing scientific evidence substantiated this hypothesis. Rather than stress directly causing the asthma symptoms, it is thought that stress modulates the immune system to increase the magnitude of the airway inflammatory response to allergens and irritants [20, 21].

Genetic

Over 100 genes have been associated with asthma in at least one genetic association study [22]. However, such studies must be repeated to ensure the findings are not due to chance. Through the end of 2005, 25 genes had been associated with asthma in six or more separate populations [23]:

• GSTM1 • IL10 • CTLA-4 • SPINK5 • LTC4S	• LTA • GRPA • NOD1 • CC16 • GSTP1	• STAT6 • NOS1 • CCL5 • TBXA2R • TGFB1	• IL4 • IL13 • CD14 • ADRB2 (β-2 adrenergic receptor) • HLA-DRB1	• HLA-DQB1 • TNF • FCER1B • IL4R • ADAM33

Many of these genes are related to the immune system or to modulating inflammation. However, even among this list of highly replicated genes associated with asthma, the results have not been consistent among all of the populations that have been tested [24]. This indicates that these genes are not associated with asthma under every condition, and that researchers need to do further investigation to figure out the complex interactions that cause asthma. One theory is that asthma is a collection of several diseases, and that genes might have a role in only subsets of asthma. For example, one group of genetic differences (single nucleotide polymorphisms in 17q21) was associated with asthma that develops in childhood [25].

Gene–environment interactions

Research suggests that some genetic variants may only cause asthma when they are combined with specific environmental exposures, and otherwise may not be risk factors for asthma [26].

The genetic trait, CD14 single nucleotide polymorphism (SNP) C-159T and exposure to endotoxin (a bacterial product) are a well-replicated example of a gene-environment interaction that is associated with asthma. Endotoxin exposure varies from person to person and can come from several environmental sources, including

environmental tobacco smoke, dogs, and farms. Researchers have found that risk for asthma changes based on a person's genotype at CD14 C-159T and level of endotoxin exposure [27].

CD14-endotoxin interaction based on CD14 SNP C-159T		
Endotoxin levels	**CC genotype**	**TT genotype**
High exposure	Low risk	High risk
Low exposure	High risk	Low risk

Typical symptoms and signs of asthma [28]

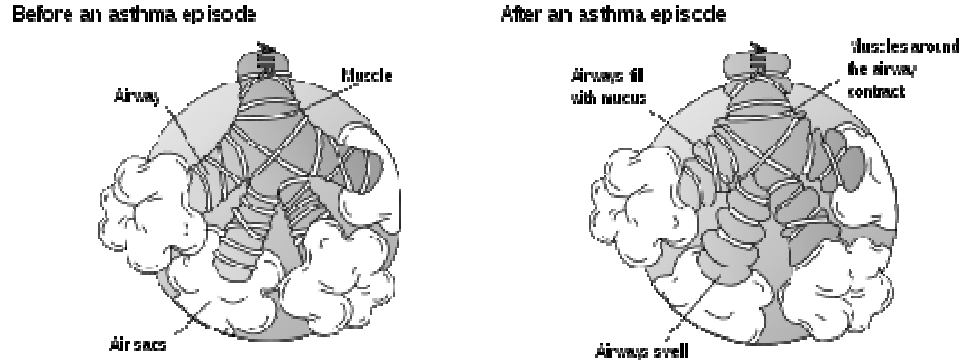
The symptoms of asthma vary from person to person and in any individual from time to time. It is important to remember that many of these symptoms can be subtle and similar to those seen in other conditions. All of the symptoms mentioned below can be present in other respiratory, and sometimes, in heart conditions. This potential confusion makes identifying the settings in which the symptoms occur and diagnostic testing very important in recognizing this disorder.
The following are the four major recognized asthma symptoms:

Shortness of breath, especially with exertion or at night
Wheezing is a whistling or hissing sound when breathing out
Coughing may be chronic, is usually worse at night and early morning, and may occur after exercise or when exposed to cold, dry air
Chest tightness may occur with or without the above symptoms

Pathophysiology

Asthma is an airway disease that can be classified physiologically as a variable and partially reversible obstruction to air flow, and pathologically with overdeveloped mucus glands, airway thickening due to scarring and inflammation, and bronchoconstriction, the narrowing of the airways in the lungs due to the tightening of surrounding smooth muscle. Bronchial inflammation also causes narrowing due to edema and swelling caused by an immune response to allergens.

Bronchoconstriction



Inflamed airways and bronchoconstriction in asthma. Airways narrowed as a result of the inflammatory response cause wheezing.

During an asthma episode, inflamed airways react to environmental triggers such as smoke, dust, or pollen. The airways narrow and produce excess mucus, making it difficult to breathe. In essence, asthma is the result of an immune response in the bronchial airways [29].

The airways of asthma patients are "hypersensitive" to certain triggers, also known as *stimuli*. (It is usually classified as type I hypersensitivity. [30, 31]) In response to exposure to these triggers, the bronchi (large airways) contract into spasm (an "asthma attack"). Inflammation soon follows, leading to a further narrowing of the airways and excessive mucus production, which leads to coughing and other breathing difficulties. Bronchospasm may resolve spontaneously in 1–2 hours, or in about 50% of subjects, may become part of a 'late' response, where this initial insult is followed 3–12 hours later with further bronchoconstriction and inflammation [32].

The normal caliber of the bronchus is maintained by a balanced functioning of these systems, which both operate reflexively. The parasympathetic reflex loop consists of afferent nerve endings which originate under the inner lining of the bronchus. Whenever these afferent nerve endings are stimulated (for example, by dust, cold air or fumes) impulses travel to the brain-stem vagal center, then down the vagal efferent pathway to again reach the bronchial small airways. Acetylcholine is released from the efferent nerve endings. This acetylcholine results in the excessive formation of inositol 1,4,5-trisphosphate (IP3) in bronchial smooth muscle cells which leads to muscle shortening and this initiates bronchoconstriction.

Bronchial inflammation

The mechanisms behind allergic asthma—i.e., asthma resulting from an immune response to inhaled allergens—are the best understood of the causal factors. In both people with asthma and people who are free of the disease, inhaled allergens that find their way to the inner airways are ingested by a type of cell known as antigen-presenting cells, or APCs. APCs then "present" pieces of the allergen to other immune system cells. In most people, these other immune cells (T_H0 cells) "check" and usually ignore the allergen molecules. In asthma patients, however, these cells transform into a different type of cell (T_H2), for reasons that are not well understood.

The resultant T_H2 cells activate an important arm of the immune system, known as the humoral immune system. The humoral immune system produces antibodies against the inhaled allergen. Later, when a patient inhales the same allergen, these antibodies "recognize" it and activate a humoral response. Inflammation results: chemicals are produced that cause the wall of the airway to thicken, cells which produce scarring to proliferate and contribute to further 'airway remodeling', causes mucus producing cells to grow larger and produce more and thicker mucus, and the cell-mediated arm of the immune system is activated. Inflamed airways are more hyper-reactive, and will be more prone to bronchospasm.

The "hygiene hypothesis" postulates that an imbalance in the regulation of these T_H cell types in early life leads to a long-term domination of the cells involved in allergic responses over those involved in fighting infection. The suggestion is that for a child being exposed to microbes early in life, taking fewer antibiotics, living in a large family, and growing up in the country stimulate the T_H1 response and reduce the odds of developing asthma [33].

Stimuli

- Allergens from nature, typically inhaled, which include waste from common household pests, the house dust mite and cockroach, as well as grass pollen, mold spores, and pet epithelial cells [34];
- Indoor air pollution from volatile organic compounds, including perfumes and perfumed products. Examples include soap, dishwashing liquid, laundry detergent, fabric softener, paper tissues, paper towels, toilet paper, shampoo, hairspray, hair gel, cosmetics, facial cream, sun cream, deodorant, cologne, shaving cream, aftershave lotion, air freshener and candles, and products such as oil-based paint [35, 36].
- Medications, including aspirin [37], β-adrenergic antagonists (beta blockers) [38], and penicillin [39].

- Food allergies such as milk, peanuts, and eggs. However, asthma is rarely the only symptom, and not all people with food or other allergies have asthma [40]
- Sulfite sensitivity Asthma can occur in reaction to ingestion or inhalation of sulfites, which are added to foods and wine as preservatives [41].
- Salicylate sensitivity Salicylates can trigger asthma in sensitive individuals. Salicylates occur naturally in many healthy foods. Aspirin is also a salicylate [42].
- Use of fossil fuel related allergenic air pollution, such as ozone, smog, summer smog, nitrogen dioxide, and sulfur dioxide, which is thought to be one of the major reasons for the high prevalence of asthma in urban areas [43].

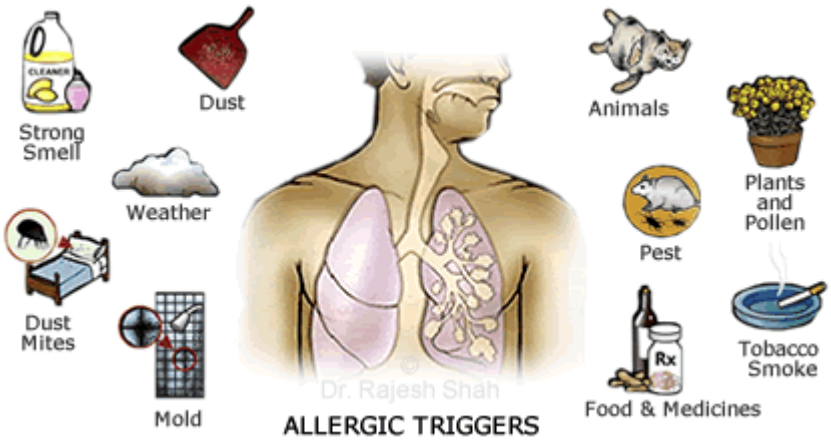
Various industrial compounds (e.g. toluene diisocyanate [44]) and other chemicals, notably sulfites; chlorinated swimming pools generate chloramines—monochloramine (NH_2Cl), dichloramine ($NHCl_2$) and trichloramine (NCl_3)—in the air around them, which are known to induce asthma [45].

- Early childhood infections, especially viral upper respiratory tract infections. Children who suffer from frequent respiratory infections prior to the age of six are at higher risk of developing asthma [46], particularly if they have a parent with the condition. However, persons of any age can have asthma triggered by colds and other respiratory infections even though their normal stimuli might be from another category (e.g. pollen) and absent at the time of infection. In many cases, significant asthma may not even occur until the respiratory infection is in its waning stage, and the person is seemingly improving [47]. In children, the most common triggers are viral illnesses such as those that cause the common cold [48].
- Exercise or intense use of respiratory system—the effects of which differ somewhat from those of the

other triggers, since they are brief. They are thought to be primarily in response to the exposure of the airway epithelium to cold, dry air.

- Hormonal changes in adolescent girls and adult women associated with their menstrual cycle can lead to a worsening of asthma. Some women also experience a worsening of their asthma during pregnancy whereas others find no significant changes, and in other women their asthma improves during their pregnancy [49].
- Psychological stress. There is growing evidence that psychological stress is a trigger. It can modulate the immune system, causing an increased inflammatory response to allergens and pollutants [50].
- Cold weather can make it harder for patients to breathe [51]. Whether high altitude helps or worsens asthma is debatable and may vary from person to person [52].

Common triggers for asthma [1]

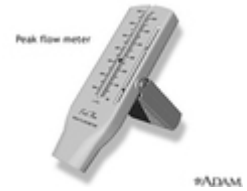


Diagnosis [53]

During the process of being diagnosed with asthma or during the course of your treatment, you are likely to undergo

different types of tests. Some of the tests you may undergo fairly frequently, while you may never undergo others. Some you can do at home, while others may require you to go to your asthma provider's office or you may even need to be referred to a more specialized physician.

1. Peak Flow



Peak Flow is probably the simplest test that you can use to see how well your asthma is doing and will be an integral part of your asthma care plan. Peak flows can easily be done at home with an inexpensive device called a peak flow meter. Peak flow measure how quickly air can be blown out of your lungs.

2. Spirometry

Spirometry is slightly more complicated than peak flow in that it is usually done in your doctors office and measures both *how much* and *how quickly* air moves out of your lungs. It is important in both the diagnosis and management of asthma over time.

3. Complete Pulmonary Function Testing

Your asthma care provider may want to determine your lung volumes and diffusing capacity. This is often done if your asthma diagnosis is unclear. The test requires you to sit inside a special box that helps determine how much air you breathe in and out.

- **Lung Volumes:** Your asthma care provider may order body plethysmography test to determine your lung volumes. Asthma may cause certain changes in lung volumes that will assist your asthma care provider in diagnosing or treating your asthma.
- **Diffusion Capacity:** Diffusion capacity measures how well oxygen flows from the lungs into your blood. Poor diffusion indicates damage to the lung where the oxygen and blood meet in the lungs. Diffusion capacity is usually normal in asthmatics.

4. Chest X-Ray

A chest x-ray is a test commonly preformed for patients who wheeze. An asthma care provider will usually order one to make sure there is not some other condition that may be causing your symptoms like a lung infection.

5. Bronchoprovocation Challenge Testing

When your asthma provider orders a bronchoprovocation test, you will inhale a specific substance through a nebulizer, often methacholine or histamine. This is done to see if your lungs become irritated, hyperresponsive, and lead to the development of asthma symptoms. The test has a high negative predictive value. This means that if the test is negative it is unlikely you have asthma.

6. Pulse Oximetry

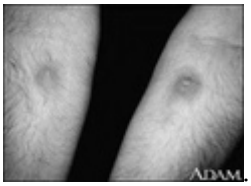
Pulse oximetry is a non-invasive way to measure oxygenation of blood or how well oxygen is being exchanged between the lungs and the blood. A sensor is placed on the fingertip or other thin part of the body with blood vessels close to the skin. The sensor measures changes in wavelengths of light and is able to estimate oxygenation in the blood.

7. Arterial Blood Gas (ABG)

An arterial blood gas (ABG) is an arterial blood sample used to determine how well blood is oxygenated -- a marker for oxygen exchange between the lungs and the blood. Commonly, a blood sample will be obtained from one of the

arteries near your wrist. This test may likely be preformed during an acute asthma exacerbation and is more reliable than pulse oximetry.

8. Allergy Testing



The relationship between allergies and asthma has been known for a long time. Allergens you normally breathe in can increase the inflammatory reaction and hyperresponsiveness in your lungs. However, your doctor cannot reliably determine if a particular allergen is responsible for your symptoms on clinical grounds alone. Because of this, your asthma care provider may recommend allergy testing. Not all asthmatics are tested. But if you have persistent asthma, your asthma care provider will probably recommend testing.

Prevention and control

Prevention of the development of asthma is different from prevention of asthma episodes. Aggressive treatment of mild allergy with immunotherapy has been shown to reduce the likelihood of asthma development. In controlling symptoms, the crucial first step in treatment is for patient and doctor to collaborate in establishing a specific plan of action to prevent episodes of asthma by avoiding triggers and allergens, regularly testing for lung function, and using preventive medications [54].

Current treatment protocols recommend controller medications such as an inhaled corticosteroid, which helps to suppress inflammation and reduces the swelling of the lining of the airways, in anyone who has frequent (greater than twice a week) need of relievers or who has severe symptoms.

If symptoms persist, additional controller drugs are added until almost all asthma symptoms are prevented. With the proper use of control drugs, patients with asthma can avoid the complications that result from overuse of rescue medications.

Patients with asthma sometimes stop taking their controller medication when they feel fine and have no problems breathing. This often results in further attacks after a time, and no long-term improvement.

The only preventive agent known is allergen immunotherapy. Controller medications include the following:

- Inhaled glucocorticoids are the most widely used prevention medications and normally come as inhaler devices (ciclesonide, beclomethasone, budesonide, flunisolide, fluticasone, mometasone, and triamcinolone). Long-term use of corticosteroids can have many side effects including a redistribution of fat, increased appetite, blood glucose problems and weight gain. High doses of steroids may cause osteoporosis. These side effects are generally not seen with the inhaled steroids when used in conventional doses for control of asthma due to the smaller dose which is targeted to the lungs, unlike the higher doses of oral or injected preparations. Patients on the highest doses of inhaled steroids should take prophylactic treatment (usually Calcium and exercise, but sometimes Fosamax or similar) to prevent osteoporosis. Deposition of steroids in the mouth may result in oral thrush. Deposition near the vocal cords can cause hoarse voice. These may be minimised by rinsing the mouth with water after inhaler use, as well as by using a spacer. Spacers also generally increase the amount of drug that reaches the lungs. A new agent, ciclesonide, is inactive until activated in the lung. For this reason changing to ciclesonide can relieve dysphonia in some patients. In November 2007 *The New York Times* reported a

review of more than 500 studies finding that independently backed studies on inhaled corticosteroids are up to four times more likely to find adverse effects than studies paid for by drug companies [55,56].

- Leukotriene modifiers (montelukast, zafirlukast, pranlukast, and zileuton) provide both anti-spasm and anti-inflammatory effects. In general they are weaker than inhaled corticosteroids, but the do not have any steroid side-effects and the benefit is additive with inhaled steroid.
- Mast cell stabilizers (cromoglicate (cromolyn), and nedocromil). These medications are believed to prevent the initiation of the allergy reaction, by stabilizing the mast cell. They are not effective once the reaction has already begun, and typically must be used 4 times a day for maximal effect. But they do truly prevent asthma symptoms and are nearly free of side-effects.
- Antimuscarinics/anticholinergics (ipratropium, oxitropium, and tiotropium). These agents both relieve spasm and reduce formation of mucous. They are more effective in patients with empysema or 'smokers lung.' They are rarely effective in asthma and are not true asthma controller medications.
- Methylxanthines (theophylline and aminophylline). These agents are bronchodilators with minimal anti-inflammatory effect. At one time they were the only effective asthma medications available. They are sometimes considered if sufficient control cannot be achieved with inhaled glucocorticoid, leukotriene modifier, and long-acting β-agonist combinations.
- Antihistamines are often used to treat the nasal allergies which can accompany asthma. Older agents are too drying and can result in thick mucous so should be avoided. Newer antihistamines which do not have this effect can safely be used by patients with asthma.
- Allergy Desensitization, also known as allergy immunotherapy, may be recommended in some cases where allergy is the suspected cause or trigger of

asthma. Allergy shots are dangerous in severe asthma and in uncontrolled asthma. However if allergy immunotherapy is started early in the disease there is a good chance that a remission of asthma can be induced (aka "asthma cure"). Typically the need for medication is reduced by about half with injection allergy immunotherapy, when done correctly. If a patient is only allergic to one or two items, oral allergy immunotherapy can be used. This is safe, much easier in young children, and is about half as effective. Unfortunately if a patient is allergic to more than 2 or 3 items then oral therapy cannot be given in a dose which is proven safe and effective.

- Omalizumab, an IgE blocker, can help patients with severe allergic asthma that is not well controlled with other drugs. It is expensive, but not compared with hospitalization(s). It requires regular injections.
- Methotrexate is occasionally used in some difficult-to-treat patients.
- If chronic acid indigestion (GERD) contributes to a patient's asthma, it should also be treated, because it may prolong the respiratory problem.
- Chronic sinus disease may be a contributing factor in difficult to control asthma, and should be evaluated.

Trigger avoidance

As is common with respiratory disease, smoking is believed to adversely affect patients in several ways, including an increased severity of symptoms (likely due to increased inflammation [57]), a more rapid decline of lung function, and decreased response to preventive medications [58]. Automobile emissions are considered an even more significant cause and aggravating factor. Patients with asthma who smoke or who live near traffic typically require additional medications to help control their disease. Furthermore, exposure of both non-smokers and smokers second-hand smoke is detrimental, resulting in more severe asthma, more emergency room visits, and more asthma-related hospital admissions, but the effect of woodstove and gas stove fumes is uncertain [59]. Smoking cessation and

avoidance of second-hand smoke is strongly encouraged in people who have asthma [60]. Air filters and room air cleaners may help prevent some asthma symptoms [61]. Ozone is also considered as a major factor in increasing asthma [62]. The report by the National Heart, Lung and Blood Institute supports the idea of an asthma management plan that includes the avoidance of as many allergens as possible to which the individual is sensitive. This report, and others [63, 64] also agree that no one single approach is sufficient to reduce allergens; a multifactorial approach is required. The Asthma and Allergy Friendly Certification Program that is operated in the USA by the Asthma and Allergy Foundation of America and in Canada by the Asthma Society of Canada is based on this multifactorial approach to trigger control.

For those in whom exercise can trigger an asthma attack (exercise-induced asthma), higher levels of ventilation and cold, dry air tend to exacerbate attacks. For this reason, activities in which a patient breathes large amounts of cold air, such as skiing and running, tend to be worse for people with asthma, whereas swimming in an indoor, heated pool with warm, humid air is less likely to provoke a response [9].

Treatment

The prevention of severe life threatening attacks and the normalization of activity within the patient's life style are the primary goals in the therapy of asthma. A more ideal goal is the normalization of the patient's lung function.

Approaches towards treatment of Bronchial Asthma [65]

1. **Prevention of AG: AB reaction**

Avoidance of antigen.

2. **Non- specific reduction of bronchial hyperreactivity**

Corticosteroids

3. **Prevention of release of mediators**

Mast cell stabilizers

4. Antagonism of released mediators
Antihistamincs, PAF antagonists
5. Blockade of constrictor neurotransmitter
Anticholinergics
6. Mimicking dilator neurotransmitter
Sympathomimetics
7. Directly acting bronchodilators
Methylxanthines

Classification of Anti- asthmatic drugs

(I) Bronchodilators
(a) Sympathomimetics
Adrenaline, ephedrine, isoprenaline, orciprenaline, salbutamol, terbutaline, salmeterol
(b) Methylxanthines
Theophylline, hydroxyethyl theophylline, aminophylline.
(c) Anticholinergics
Atropine methonitrate, ipratropium bromide, tiotropium bromide.
(II) Mast Cell Stabilizers
Sodium cromoglycate, ketotifen, nedocromil
(III) Corticosteroids
(a) Systemic
Hydrocortisone, prednisolone.
(b) Inhalational
Beclomethasone dipropionate, budesonide, triamcinolone.
(IV) Leukotriene pathway inhibitors
(a) LTD_4 receptor antagonist
Zafirlukast, montelukast.
(b) H_1 and LT receptor antagonist
Azelastine.
(c) LT synthesis inhibitors
(i) 5- lipoxygenase inhibitor
Zileuton
(ii) Pranlucast.
(V) Ca^{++} channel blockers
Nifedipine, verapamil

(VI) **K^+ channel openers**
Cromakalim
(VII) **Th_2 cell inhibitors**
Keiximab

Types of Asthma Medication [66]

Asthma medication can be divided into two categories:

- Quick relief or rescue asthma medication
- Controller asthma medication

Quick-relief asthma medication treats acute asthma symptoms such as:

- Wheezing
- Chest tightness
- Shortness of breath
- Cough

Controller asthma medication, on the other hand, attempts to prevent these same symptoms.

For the most part, all asthma medication is inhaled, although some do come in a liquid form and one is given as an infusion.

1. <u>Inhaled Steroids</u>

Inhaled steroids are your most important asthma medication because they are the most potent and effective asthma medication available for the long term control of your

asthma. The anti-inflammatory properties of inhaled steroids are responsible for the significant improvement that is often seem with the use of this asthma medication.

Inhaled steroids prescribe to you may include:

- Aerobid
- Alvesco
- Asmanex
- Azmacort
- Flovent
- Pulmicort
- Qvar

2. Short Acting Beta Agonists (SABA) such as Albuterol

SABAs are a type of drug class commonly used rescue for quick-relief asthma medication. This type of asthma medication is the drug of choice for the acute relief of asthma symptoms and is also used to prevent exercise induced asthma. Because this asthma medication can prevent your asthma symptoms from getting worse, it is important to always keep this asthma medication with you.

Some of the SABAs include:

- Albuterol
- Proventil
- Ventolin
- Xopenex
- Maxair

3. Long Acting Beta Agonists (LABA)

This type of asthma medication is preferred when your inhaled steroids are not adequately controlling your symptoms, otherwise known as adjunctive therapy. LABAs are not used as a single asthma medication for the treatment and prevention of asthma symptoms and are not used to treat acute asthma symptoms or asthma exacerbations.
LABAs include:

- Brovana
- Foradil
- Perforomist
- Serevent

4. Leukotriene Modifiers

This type of asthma medication is considered an alternative treatment for patients with mild persistent asthma and can be used as adjunctive therapy with inhaled steroids. Exercise-induced asthma can also be controlled with this asthma medication.

Three leukotriene modifiers are currently available:

- Accolate
- Singulair
- Zyflo

5. Oral Steroids

Oral steroids are used for the treatment of moderate and severe asthma exacerbations to help improve symptoms and prevent the late phase response of the allergic cascade. Oral steroids are only used as a controller medication after failing multiple other medications.

6. Anticholinergics

Anticholinergics act as a bronchodilator and are often used in combination with SABAs in the acute treatment of asthma symptoms in the emergency department or hospital. An example of an anticholinergic is Atrovent.

7. Cromolyn Sodium and Nedocromil

Cromolyn and nedocromil are considered alternative treatments for patients with mild persistent asthma. Both help prevent inflammation in the lungs. These drugs are never used for the treatment of acute asthma symptoms.

- Cromolyn Sodium (Intal)
- Nedocromil (Tilade)

8. Combination Asthma Medication

A number of pharmaceutical companies have combined asthma medication products with more than one type of asthma medication in a single inhaler. Most commonly this includes an inhaled steroid plus a LABA.

The LABA widens your lung airways and the inhaled steroid decreases and prevents airway inflammation. Patients find this type of asthma medication more convenient and often feel like they have better control of their asthma.

Examples include

- Advair
- Symbicort

9. Immunomodulators

Immunomodulators are a group of drugs that either provide long-term control of asthma or are considered steroid sparing. These medications alter your immune system's response to asthma triggers. In general, these treatments decrease your IgE response to asthma triggers.

The currently available immunomodulator is Xolair.

10. Methylxanthine

This works as a mild bronchodilators and is considered an alternative adjunctive treatment to be used with inhaled steroid.

Homeopathic treatment [1]:
Homeopathy offers excellent treatment for asthma, which can do following jobs:
a. Reduce frequency of asthmatic attacks
b. Reduce severity of asthmatic attacks

c. Reduce duration of attacks
d. Reduce need for bronchodilators, cortisone and antibiotic (in case of infections)

Limitation of homeopathic medicines:
Homeopathy may not easily control acute attacks, which are better taken care of by conventional medicines.

Duration of treatment for Asthma:
The total length of treatment varies form case to case, depending of the following factors:

- Duration of Asthma
- Severity and frequency of attacks
- Environmental factors such as exposure to dust, allergens, industrial pollution, etc. Extent of spread (Small or large; one or multiple spots)
- Previous and current medication (Extensive inhaled and oral cortisone)
- Associated diseases eczema, pollen allergy, Ischemic heart disease, bronchiactasis, pulmonary fibrosis, etc.

One may expect a definite change in about three to five months. The total length of treatment varies from patient to patient.

Asthma home remedies and natural cures [67]

Asthma treatment using Honey

Honey is one of the most common home remedies for asthma. It is said that if a jug of honey is held under the nose of an asthma patient and he inhales the air that comes into contact with it, he starts breathing easier and deeper.

Asthma treatment using Figs

Among fruits, figs have proved very valuable in asthma. They give comfort to the patient by draining off the phlegm.

Three or four dry figs should be cleaned thoroughly with warm water and soaked overnight.

Asthma treatment using Lemon

Lemon is another fruit found beneficial in the treatment of asthma. The juice of one lemon, diluted in a glass of water and taken with meals, will bring good results.

Asthma treatment using Indian Gooseberry

Indian gooseberry has also proved valuable in asthma. Five grams of gooseberry mixed with one tablespoon of honey forms an effective medicinal tonic for the treatment of this disease. It should be taken every morning

Asthma treatment using Bitter Gourd Roots

The roots of the bitter gourd plant have been used in folk medicine for asthma since ancient times. A teaspoon of the root paste, mixed with an equal amount of honey or juice of the holy basil leaves, given once every night for a month, acts as an excellent medicine for this disease.

Asthma treatment using Drumstick Leaves

A soup prepared from drumstick leaves, and taken once daily, has been found beneficial in the treatment of asthma. This soup is prepared by adding a handful of leaves to 180ml of water and boiling it for five minutes. After being allowed to cool, a little salt, pepper, and lime juice may be added to this soup.

Asthma treatment using Ginger

A teaspoon of fresh ginger juice, mixed with a cup of fenugreek decoction and honey to taste, acts as an excellent expectorant in cases of asthma. The decoction of fenugreek can be made by mixing one tablespoon of fenugreek seeds in a cupful of water. This remedy should be taken once in the morning and once in the evening.

Asthma treatment using Garlic

Garlic is another effective home remedy for asthma. Ten garlic cloves, boiled in 30 ml of milk, make an excellent medicine for the early stages of asthma. This mixture should he taken once daily by the patient. Steaming ginger tea with two minced garlic cloves in it, can also help to keep the problem under control, and should be taken in the morning and evening.

Asthma treatment using Bishop's Weed

The herb bishop's weed has been found valuable in asthma. Half a teaspoon of bishop's weed should be mixed in a glass of buttermilk and taken twice daily. It is an effective remedy for relieving difficult expectoration caused by dried-up phlegm. A hot poultice of the seeds should be used for dry fomentation to the chest twice daily. The. patient can also inhale steam twice a day from boiling water mixed with carom seeds. It will dilate the bronchial passages.

Asthma treatment using Safflower

Safflower seeds are beneficial in the treatment of bronchial asthma. Half a teaspoon of powder of the dry seeds, mixed with a tablespoon of honey, can be taken once or twice a day in treating this disease. This acts as an expectorant and reduces the spasms by liquefying the tenacious sputum. An infusion of five grams of flowers mixed with one tablespoon of honey, taken once daily, is also useful in this disease.

Diet for Asthma

Carbohydrates, fats and proteins

The patient should avoid common dietetic errors. Ideally, his diet should contain a limited quantity of carbohydrates, fats and proteins which are 'acid-forming' foods, and a liberal quantity of alkali-forming foods consisting of fresh fruits, green vegetables, sprouted seeds, and grains. The patient should avoid foods which tend to produce phlegm, such as

rice, sugar, lentils, and yoghurt. He should also avoid fried and other difficult to-digest foods, strong tea, coffee, alcoholic beverages, condiments pickles, sauces and all refined and processed foods.

Other Suggestions for Asthma

Fasting and exercises

The patient should also follow the other laws of nature. Air, sun, and water are great healing agents. Regular fasting once a week, an occasional enema, breathing exercises, fresh air, a dry climate, light exercises, and correct posture go a long way in treating the disease.

Conclusion

Asthma is a complicated disease with a multitude of clinical presentations. The exact defect in asthma has not been defined, and it may be that asthma is a common presentation of a heterogeneous group of diseases. Asthma is defined and characterized by excessive reactivity of the bronchial tree to a wide variety of noxious stimuli. The reaction is characterized by bronchospasm, excessive mucus production, and inflammation. The central role of inflammation in inducing and maintaining bronchial hyper-responsiveness is now becoming widely appreciated and studied. The goal of asthma therapy is to normalize, as much as possible, the patient's life and prevent chronic irreversible lung changes. Drugs are the mainstay of asthma therapy. The goal of drug therapy is to use the minimum amount of medications possible to completely control the disease. In chronic asthma, therapy should be aimed at both bronchospasm and inflammation in order to produce the best results. Patients should be followed and monitored diligently for toxicities. Although death from asthma is an uncommon event, the most common cause of death is underassessment of the severity of obstruction either by the patient or by the clinician; the next common cause is under treatment. A cornerstone of any therapy is education and the realization that most asthma deaths are avoidable.

References

1. http://www.asthma.net.in/app/asthma.asp
2. http://www.merck.com/mmhe/sec04/ch044/ch044a.html
3. http://www.merck.com/mmpe/sec05/ch048/ch048a.html
4. Fanta CH. Asthma. N Engl J Med 2009; 360:1002-1014
5. Weiss ST, Tager IB, Munoz A, Speizer FE: "The relationship of respiratory infections in early childhood to the occurrence of increased levels of bronchial responsiveness and atopy." Am Rev Respir Dis 1985; 131:573-578.
6. http://www.nhlbi.nih.gov/guidelines/asthma/03_sec2_def.pdf
7. Lilly CM. "Diversity of asthma: evolving concepts of pathophysiology and lessons from genetics". J. Allergy Clin. Immunol. 2005; 115 (4): S526–31.
8. Ball TM, Castro-Rodriguez JA, Griffith KA, et al.: "Siblings, day-care attendance, and the risk of asthma and wheezing during childhood. N Engl J Med 2000; 343:538-543.
9. McFadden ER, Jr. "Asthma" In: Kasper DL, Fauci AS, Longo DL, et al. eds. Harrison's Principles of Internal Medicine 16th ed. New York: McGraw-Hill. 2004: 1508–1516.
10. Longmore, Murray et al. Oxford Handbook of Clinical Medicine 7th ed. Oxford University Press 2007: 1206
11. Martinez FD. Genes, environments, development and asthma: a reappraisal. Eur. Respir. J. 2007; 29 (1): 179–184.
12. http://www.arb.ca.gov/research/chs/chs.htm.
13. Salam M. Adverse effects of residential proximity to traffic sources on asthma. Current Opinion Pulmonary Medicine 2008; 14 (1):58
14. Thavagnanam S, Fleming J, Bromley A, Shields MD, Cardwell CR. A meta-analysis of the association between Caesarean section and childhood asthma. Clin. and Exper. Allergy 2007: 629.
15. Chen E, Miller GE. Stress and inflammation in exacerbations of asthma. Brain Behav Immun. 2007; 21 (8): 993–999.
16. Richeldi L, Ferrara G, Fabbri LM, Lasserson TJ, Gibson PG. Macrolides for chronic asthma. Cochrane Database Syst Rev 2005; (4): CD002997.
17. Marra F, Lynd L, Coombes M. Does antibiotic exposure during infancy lead to development of asthma?: a systematic review and meta analysis. Chest 2006; 129 (3): 610–618.
18. http://www.belfasttelegraph.co.uk/health/article3056797.ece.

19. Ober C, Hoffjan S, Hoffjan S. Asthma genetics 2006: the long and winding road to gene discovery. Genes Immun 2006; 7 (2): 95–100.
20. Bouzigon E, Corda E, Aschard H. Effect of 17q21 Variants and Smoking Exposure in Early-Onset Asthma. N Engl J Med 2008; 359 (19): 1985.
21. Martinez FD. CD14, endotoxin, and asthma risk: actions and interactions. Proc Am Thorac Soc 2007; 4 (3): 221–225.
22. Bai TR, Mak C, Barnes PJ. A comparison of beta-adrenergic receptors and in vitro relaxant responses to isoproterenol in asthmatic airway smooth muscle. Am J Respir Cell Mol Biol 1992; 6:647-651.
23. Ronmark E, Lundback B, Jonsson EA, et al. Incidence of asthma in adults: Report from the obstructive lung disease in northern Sweden study. Allergy 1997; 52:1071-1081.
24. Burrows B, Martinez FD, Holonen M et al.: Association of asthma with serum IgE levels and skin-test reactivity to allergens. N Engl J Med 1989; 320:271-277.
25. Simpson BM, Custovic A, Simpson A et al. NAC Manchester Asthma and Allergy Study (NACMAAS): Risk factors for asthma and allergic disorders in adults. Clin Exp Allergy 2001; 31:391-399.
26. Peat JK, Tovey E, Toelle BG, et al. House dust mite allergens: A major risk factor for childhood asthma in Australia. Am J Respir Crit Care Med 1996; 153:141-146.
27. Custovic A, Smith AC, Woodcock A. Indoor allergens are a primary cause of asthma: Asthma and the environment. Eur Respir Rev 1998; 53:155-158.
28. http://www.medicinenet.com/asthma/page6.htm
29. F. E. R. Simons. Epidemiology of Asthma and Allergic Diseases — Risk factors for Asthma In: N. F. Adkinson, B. S. Bochner, W. W. Busse, S. T. Holgate, R. F. Lemanske eds. Middleton's Allergy Principles & Practice. Elsevier 2008, 85(2):412
30. F. E. R. Simons. Adverse Reactions to Foods: Respiratory Food Hypersensitivity Reactions In: N. F. Adkinson, B. S. Bochner, W. W. Busse, S. T. Holgate, R. F. Lemanske eds. Middleton's Allergy Principles & Practice. Elsevier 2008, 63(5):559
31. http://www.allergy.org.au/content/view/128/1/
32. Towns S. J, Mellis C. M. Role of acetyl salicylic acid and sodium metabisulfite in chronic childhood asthma. Pediatrics 1984; 73(5): 631-637.

33. Mapp CE, Boschetto P, Maestrelli P, Fabbri LM. Occupational Asthma. American Journal of Respiratory and Critical Care Medicine 2005; 172 (1): 280–305.
34. Nemery B, Hoet PH, Nowak D. Indoor swimming pools, water chlorination and respiratory health". Eur. Respir. J. 2002; 19 (5): 790–3.
35. Grant EN, Wagner R, Weiss KB: "Observations on emerging patterns of asthma in our society." J Allergy Clin Immunol 1999; 104:S1-S9.
36. Zhao J, Takamura M, Yamaoka A, Odajima Y, Iikura Y. Altered eosinophil levels as a result of viral infection in asthma exacerbation in childhood. Pediatr Allergy Immunol 2002; 13 (1): 47–50.
37. Johansen HK. House dust mite control measures for asthma. Cochrane Database Syst Rev 2008; 7(2):52
38. McCarney RW, Brinkhaus B, Lasserson TJ, Linde K. Acupuncture for chronic asthma. Cochrane Database Syst Rev 2004; 9(1):75
39. Szentivanyi A. The Beta Adrenergic Theory of the Atopic Abnormality in Asthma. J. Allergy 1968; 42: 203.
40. Lockey, Richard, In lasting tribute: Andor Szentivanyi, MD. J. Allergy and Clinical Immunology 2006; 19 (5): 790–793.
41. Szentivanyi A., Ali K., Calderon EG., Brooks SM., Coffey RG., Lockey RF. The *in vitro* effect of Imunnoglobulin E {IgE} on cyclic AMP concentrations in A549 human pulmonary epithelial cells with or without beta adrenergic stimulation. J. Allergy Clin Immunol. 1993; 91(4): 379.
42. Kowalak JP, Hughes AS eds., Professional Guide To Diseases 7th ed. Springhouse 2001, 6(2):366
43. http://www.med.umich.edu/opm/newspage/2005/asthmasleep.htm.
44. http://www.sleepapnea.org/resources/pubs/asthma-osa.html.
45. Leggett JJ, Johnston BT, Mills M, Gamble J, Heaney LG. Prevalence of gastroesophageal reflux in difficult asthma: relationship to asthma outcome. Chest 2005; 127 (4): 1227–1231.
46. Pinnock H, Shah R. Asthma. BMJ 2007; 334 (7598): 847–850.
47. Hirsch L, Pohl CA. "How Old Is Old Enough to Report on Asthma Symptoms? Consultant for Pediatricians 2007; 6 (2):236
48. Sapp J, Niven AS. Making the most of pulmonary function testing in the diagnosis of asthma. Journal of Respiratory Diseases 2008; 115:272-277.
49. http://www.asthma.org.uk/document.rm?id=29.

50. Corbo J, Bijur P, Lahn M, Gallagher EJ. Concordance between capnography and arterial blood gas measurements of carbon dioxide in acute asthma. Annals of emergency medicine 2005; 46 (4): 323–327.
51. http://www.consultantlive.com/asthma/article/1145425/1405157.
52. Hargreave FE, Parameswaran K. "Asthma, COPD and bronchitis are just components of airway disease". European Respiratory Journal 2006; 28 (2): 264–267.
53. http://asthma.about.com/od/adultasthma/tp/asthma_tests.htm
54. http://www.nhlbi.nih.gov/guidelines/asthma/06_sec3_comp3.pdf
55. Burchard EG, Avila PC, Nazario S. Lower bronchodilator responsiveness in Puerto Rican than in Mexican subjects with asthma. Am J Respir Crit Care Med 2004; 169 (3): 386–392
56. Ram FSF, Rowe BH, Kaur B. Vitamin C supplementation for asthma. Cochrane Database of Systematic Reviews 2004; Issue 3. Art. No.: CD000993.
57. Sarir H, Mortaz E, Karimi K. et al. Cigarette smoke regulates the expression of TLR4 and IL-8 production by human macrophages. J Inflamm. 2009; 1 (6):12.
58. Thomson NC, Spears M. The influence of smoking on the treatment response in patients with asthma. Curr Opin Allergy Clin Immunol 2005; 5 (1): 57–63.
59. Eisner MD, Yelin EH, Katz PP, Earnest G, Blanc PD. Exposure to indoor combustion and adult asthma outcomes: environmental tobacco smoke, gas stoves, and woodsmoke. *Thorax* 2002; 57 (11): 973–8.
60. National Asthma Education and Prevention Program. Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma. National Institutes of Health, Bethesda, MD, 2007: 175.
61. http://www.webmd.com/asthma/guide/do-you-need-an-air-filter.
62. Reitze Arnold W. Air Pollution Control Law. Environmental Law Institute 2001: 5.
63. George T O'Connor. Allergen avoidance in asthma: what do we do now? J Allergy Clin Immunol 2005; Vol. 116 (1): 26-30.
64. Platts-Mills TA. Allergen avoidance in the treatment of asthma: problems with the meta-analyses. J Allergy Clin Immunol. 2008; 122(4):694-696.
65. Tripathi KD. Essentials of Medical Pharmacology5th ed. Jaypee Brothers Medical Publishers (P) Ltd., New Delhi 2004: 199,209
66. http://asthma.about.com/od/treatmentoptions/a/asthmamedication_hub.ht
67. http://www.home-remedies-for-you.com/remedy/Asthma.html