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A Review on Epidemiology, Pathophysiology and Management of Asthma

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ABSTRACT

Asthma is a chronic inflammatory disorder of respiratory airway. The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night and in morning. 300 million people are affected with asthma worldwide which is increasing 50% every decade. The disease can affect any age but prevalence of this disease is more common in children. Asthma is a multifactorial disease which includes environment, allergen, infection, genetic, exercise, obesity, and component. The pathophysiology of asthma includes inflammation. The purpose of therapy is to reduce the airway inflammation and increase the life style. Non pharmacological treatment avoidance of allergen, pollutant, smoking, use of antioxidant, mineral and plant are beneficial in asthma treatment. The physical exercise like yoga, massage is also helpful. Pharmacological treatment with short-acting beta-agonists, anti-inflammatory drugs, and anticholinergics. Generally, pharmacological treatments are divided into 2 groups: quick-relief medications and controller medications. This review is focus on Asthma disease's definition, causes, pathophysiology and management of Asthma disease in brief.

Keywords: Airway inflammation, airway hyperresponsiveness, Exercise induce asthma, mast cell etc.

INTRODUCTION

Bronchial asthma is a chronic inflammatory disorder of the airways associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing particularly at night or in the early morning (Col SP *et al.*, 2007). Airway inflammation produces airflow limitation through acute bronchoconstriction, chronic mucus plug formation and airway wall swelling or remodeling. These symptoms may be relieved either spontaneously or after treatment. Asthma can occur at any age. However, in half the cases the onset is before 10 years of age (Johnston and Holgate, 2003). Asthma is a multifactorial disease process associated with genetic, allergic, environmental, infection, emotional and nutritional component. Because of their symptomatology the majority of individual experience a significant no of missed work or school day. This can create a severe disruption in quality of life (Store *et al.*, 1998).

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EPIDIMIOLOGY

Approximately 300 million people worldwide currently have Asthma, with estimates suggesting that Asthma prevalence increases globally by 50% every decade. With the projected increase in the proportion of the world's urban population from 45% to 59% in 2025, there is likely to be a marked increase in the number of Asthmatics worldwide over the next two decades. It is estimated that there may be an additional 100 million persons with Asthma by 2025 (Masoli et al., 2004). A wide variation in prevalence rates has been documented: studies of both children and adults have revealed low prevalence rates (2%–4%) in Asian countries (especially China and India) and high prevalence rates (15%–20%) in the United Kingdom, Canada, Australia, New Zealand and other developed countries. The highest Asthma prevalence rates are found in the United Kingdom (>15%) and New Zealand (15.1%). In Western Europe, the Asthma prevalence rate has doubled over the last decade (European Lung White Book 2003) and in Japan; the number of Asthma patients treated by medical facilities has tripled over the past 30 years (Subbarao et al., 2009)

RISK FACTOR

Environmental factor

Indoor air pollution

The indoor pollution such as smoke and fumes, use of solid cooking fuels (use of biomass fuels) and poor housing may be important risk factors for developing asthma (Perzanowski et al., 1998). Where house dust mite level is low, sensitizations to mould or cat dander is associated with increased risk of asthma (Halonen et al., 1997). Children in home with a increased surface area of plastic flooring and wall coverings, and increased surface airborne concentration of common organic chemicals, such as formaldehyde and volatile/semivolatile organic compounds (VOC/SVOCs), for example phthalates, have more wheeze and physician-diagnosed allergic and asthma.

Outdoor air pollution

There are two main types of outdoor pollution: **industrial smog** (sulfur dioxide particulate complex) and **photochemical smog** (ozone and nitrogen oxides). The role of outdoor air pollution in causing asthma remains controversial. Outdoor air pollution is of particular interest in asthma for three main reasons: firstly, it can cause a worsening of symptoms and cause asthma to spiral out of control (O'Connor et al., 2008), secondly, if this worsening of symptoms progresses sufficiently and in a sustained or ever-increasing manner, it can result in an acute asthma exacerbation or attack meaning possible hospitalisation (Andersen et al., 2012) or, in the most severe cases, death (Braback et al., 2009); and thirdly, it is thought to potentially have a role in increasing the likelihood of asthma developing in the first place. Children raised in a polluted environment have diminished lung function, but the relationship of this loss of function to the development of asthma is not known. Outbreaks of asthma exacerbations have been shown to occur in relationship to increased levels of air pollution, and this may be

related to a general increase in the level of pollutants or to specific allergens to which individuals are sensitized. However, the role of pollutants in the several studies has implicated various pollutants as aggravating asthma (Koenig, 1999). For example: the prevalence of asthma in children in New Zealand attending schools located in heavy traffic zones (with high air pollution) was higher compared to those attending schools in less polluted areas (Burney, 2002). Similarly, in India the prevalence of asthma in traffic police personnel in Bangalore was 26.1% compared to 14.1% among non-traffic police personnel, indicating an 85% increase in their risk of developing asthma. But exposure to traffic, particularly to diesel exhaust, may exacerbate pre-existing allergic conditions but does not necessarily induce the development of new cases of asthma and atopy. Diesel particles have also been shown to absorb allergens from grass pollen onto their surface and may therefore act as potential carriers to increase deposition of pollen allergens in the lung (Knox et al., 1997; Diaz-Sanchez et al., 1997; Nel et al., 1998). In this way, both the allergen dose and the antigenicity of pollen allergen may be enhanced by automobile related pollution.

Viral Infection

The burden of health care costs associated with hospitalizations and emergency department visits for virus-induced wheezing during the first 3 years of life is significant, and development of specific therapies is a huge unmet medical need. Virus-induced wheezing in infancy is associated with an increased risk for recurrent wheezing as children grow older (Jakson et al., 2008; Sigus et al., 2005). Moreover, there is substantial evidence that early-life virus-induced wheezing illnesses are associated with subsequent childhood asthma. Respiratory syncytial virus (RSV) is the most frequent infection causing bronchiolitis and pneumonia in children 1 year of age and younger and commonly presents as a wheezing illness during the late fall, winter, and early spring in temperate climates (Heymann et al., 2004). The timing of infant birth in relationship to the peak of bronchiolitis hospitalizations for that winter season predicted the likelihood of clinically significant bronchiolitis. In addition, children who were about 121 days old at the winter virus peak also had the greatest risk of asthma. Similarly, seasonal epidemiologic analysis has been used to demonstrate that infantile wheezing illnesses during HRV seasons are important predictors of the development of persistent wheezing and asthma later in childhood (Wu et al., 2008; Lemanske et al., 2005). These studies suggest the possibility that respiratory tract viral infections in early childhood contribute to asthma causality. The incorporation of improved viral diagnostics into long-term studies suggests that the type of virus causing the wheezing illness could be a significant indicator of asthma risk.

Occupational Asthma

Occupational asthma can be defined as "variable airways narrowing causally related to exposure in the working environment to airborne dust, gases and fumes" (Tylor et al., 1980; Waren et al., 1985). About 250 agents can cause occupational asthma (Chan-Yeung et al., 1994). Two types of OA have been recognized: (1) OA

with latency period is most common and develop after a period of exposure for few weeks, to several years (Chan-yeung *et al.*, 1995). It is caused by exposure to high molecular weight agents (MW > 5000 daltons) eg. cereals and enzymes etc. or exposure to low molecular weight agents (MW < 5000 daltons) eg. acid anhydrides and platinum salts ... etc. Agents at the workplace cause occupational asthma through immunologic and nonimmunologic mechanisms. Most of the high molecular weight compounds induce asthma by producing specific IgE and sometimes specific IgG antibodies. Some of the low molecular weight compounds such as acid anhydrides and platinum salts act as haptens and induce specific IgE antibodies by combining with a body protein (Novoy *et al.*, 1989; Chan-yeung *et al.*, 1988). OA without latency period which includes reactive airways dysfunction syndrome (RADS) and here it follows exposure to high concentration of irritant gases, fumes or chemicals on one or several occasions.

Bacterial Infection

Much less is known about the role of bacteria in the pathogenesis of asthma. Serological evidence of an immune response to *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* can be found in 20% of wheezing children. *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* were identified in 5–25% of children with asthma exacerbations. A significantly greater reduction in asthma symptoms and a larger improvement from baseline lung function was found in adult patients treated with a macrolide for acute asthma exacerbations (Lehtinen *et al.*, 2006).

Drugs Induce Asthma

Aspirin, non-steroidal anti-inflammatory drugs (NSAIDs) and β -blockers have been associated with asthma exacerbations. Aspirin-induced asthma is a clinical syndrome which involves intolerance to aspirin and other NSAIDs which inhibit cyclo-oxygenase. This results in alterations in arachidonic acid metabolism and an overproduction of leukotrienes resulting in asthmatic attacks when these drugs are ingested. Beta-blockers in general and non-selective β -blockers (e.g. propranolol) in particular have the potential for worsening bronchospasm and inhibiting therapeutic responses to inhaled β -agonists.

Genetic Factor

Asthma runs strongly in family and is about half due to genetic susceptibility and about half due to environmental factors. Five asthma genes or gene complexes have now been identified by positional cloning including ADAM3, PHF11, DPP10, GRPA and SPINKS (10-1A). The function of all of these genes are observed, but the expression of DPP10, GRPA and SPINKS in terminally differentiating epithelium suggests that they deal with threat or damage from the external environment. Many of these genes identified by candidate gene studies may also exert their effect within the cell that make up mucosa. These include IL13 which modified the mucus production. Fc ϵ RI-BC modified. The allergic

trigger on mast cell and microbial pattern recognition receptors of the innate immune system (Cookson *et al.*, 2004).

Obesity And Asthma

Most cross-sectional and prospective studies in children and adults support a link between obesity and asthma. In addition, most prospective studies in children show that obesity precedes the development of asthma. Obesity is characterized by low-grade systemic inflammation with increased levels of inflammatory cytokines, adipokines, and acute phase proteins, including leptin, interleukin 6, tumor necrosis factor- α , and C reactive protein (Shore *et al.*, 2001). It is thought that obesity may upregulate airway inflammation, resulting in asthma. Exhaled nitric oxide (eNO) is a surrogate marker of inflammation that has been recently studied to evaluate inflammation in the airway of obese people with asthma. Obesity is associated with changes in airway mechanics that may lead to respiratory symptoms without the airway inflammation typical of asthma. Obesity causes a higher oxygen cost of breathing leading to dyspnea because of decreased compliance from excess weight compressing the chest wall, fatty infiltration of the chest wall, and an increase in blood volume (Beuther *et al.*, 2006). In addition, obesity causes a decrease in functional residual capacity, and decreases in both forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC), with a normal FEV1/FVC ratio, resulting in rapid shallow breathing (Beuther *et al.*, 2006).

Sex Factor

Male sex is a risk factor for asthma in children. Prior to the age of 14, the prevalence of asthma is nearly twice as great in boys as in girls. As children get older the difference between the sexes narrows and by adulthood the prevalence of asthma is greater in women than in men. The reasons for this sex-related difference are not clear. However, lung size is smaller in males than in females at birth but larger in adulthood.

Exercise Induced Asthma

Exercise induced asthma (EIA) is mainly characterized by symptoms of coughing, wheezing, shortness of breath, and chest tightness during or after exercise, and associated with airway obstruction after exercise, as noted by a drop in FEV1 or other spirometric parameters. The symptoms are not always straightforward; patients may present with cramps, stomach pain, headache, etc. EIA can be seen in subjects at any level of exercise, from children in gym class to elite Olympic athletes. Some patients with EIA only have symptoms with exercise and have no signs or symptoms of asthma at rest, and they have a normal physical examination and spirometry. It is only with exercise that these patients have respiratory symptoms and a drop in pulmonary function after exercise. They have EIA with no evidence of underlying chronic asthma. Other patients may have chronic asthma, as evidenced by reduced lung function at rest and they will usually have exercise-related increase in symptoms and reduction in lung function. These individuals may also have symptoms of

asthma when exposed to pollens, animal danders, or with an upper respiratory infection. In other words, there is chronic asthma present that can be triggered by other stimuli than exercise. In all likelihood, these individuals need daily medication for chronic asthma plus preexercise medication for the exercise-induced exacerbation. Up to 50% of cold weather athletes will have respiratory symptoms after exercise and a drop in FEV1 that is compatible with exercise-induced asthma. Many of these athletes have neither prior history of asthma nor a family history of asthma (Mannix *et al.*, 1996; Mahler, 1993).

Other Factor

There is a strong association between gastroesophageal reflux, psychological dysfunctioning, obstructive sleep apnoea and recurrent exacerbations of asthma. Pathological gastro-oesophageal reflux is considered a potential trigger of asthma. Mechanisms of this acid-induced bronchoconstriction include a vagally mediated reflex and microaspiration. A subgroup of patients gains improved control of asthma with treatment of gastro-oesophageal reflux. Although psychological dysfunctioning has been strongly associated with recurrent asthma exacerbations, more studies are needed to clarify whether psychological disturbances are the cause or consequence of the loss of control in asthma. Snoring and obstructive apnoea may trigger nocturnal asthma attacks. In some unstable asthmatic patients, improvement in asthma control has occurred after nasal continuous positive airway pressure.

PATHOPHYSIOLOGY

Airway narrowing is the final common pathway leading to symptoms and physiological changes in asthma. It had been recognised for many years that patients who die from acute asthma attacks have grossly inflamed airways. The airway lumen is occluded by a tenacious mucus plug composed of plasma proteins exuded from airway vessels and mucus glycoproteins secreted from surface epithelial cells. There is evidence that the degree of inflammation is related to airway hyperresponsiveness (AHR), as measured by histamine or methacholine challenge. Different inflammatory cells are involved in asthma, although the precise role of each cell type is not yet certain. It is evident that no single inflammatory cell is able to account for the complex pathophysiology of allergic disease, but some cells predominate. Role of different chemical mediators are now recognized to be involved in asthma and mediate the complex inflammatory response in the airway.

Inflammatory Cell In Asthma

Mast cells

Activation of mast cells are important in initiating the acute bronchoconstrictor responses to allergen and probably to other indirect stimuli, such as exercise and hyperventilation (via osmolality or thermal changes) and fog. Patients with asthma are characterised by a marked increase in mast cell numbers in airway smooth muscle (Brightling *et al.*, 2002). Treatment of asthmatic patients with prednisone results in a decrease in the

number of tryptase positive mast cells (Bentley *et al.*, 1996). Furthermore, mast cells appear to play a role in airway remodelling, as this mast cell product stimulates human lung fibroblast proliferation (Akers, 2000). Mast cells also secrete certain cytokines, such as interleukin (IL)-4 that may be involved in maintaining the allergic inflammatory response and tumour necrosis factor (TNF)- α . These cells are activated by allergens through high-affinity IgE receptors, as well as by osmotic stimuli (accounting for exercise-induced bronchoconstrictor). Increased mast cell numbers in airway smooth muscle may be linked to airway hyperresponsiveness.

Eosinophils

Increased numbers of eosinophils exist in the airways of most, but not all, persons who have asthma (Chu and Martin 2001; Sampson 2000; Williams 2004). Eosinophils present in increased numbers in the airways, release basic proteins that may damage airway epithelial cells. They may also have a role in the release of growth factors and airway remodeling (Kay *et al.*, 2004). **T**

Lymphocytes

Increased numbers in the airways, it causes release of specific cytokines, including IL-4, IL-5, IL-9, and IL-13, that orchestrate eosinophilic inflammation and IgE production by B lymphocytes. An increase in Th2 cell activity may be due in part to a reduction in regulatory T cells that normally inhibit Th2 cells. There may also be an increase in T helper 1 (Th1) and Th2 cytokines (Akbari *et al.*, 2006). Dendritic cells sample allergens from the airway surface and migrate to regional lymph nodes, where they interact with regulatory T cells and ultimately stimulate production of Th2 cells from naïve T cells (Kuijpers *et al.*, 2004).

Macrophages

Macrophages are the most numerous cells in the airways and also can be activated by allergens through low-affinity IgE receptors to release inflammatory mediators and cytokines that amplify the inflammatory response (Peters-Golden, 2004). Macrophages are increased in number in the airways and may be activated by allergens through low-affinity IgE receptors to release inflammatory mediators and cytokines that amplify the inflammatory response (Peter *et al.*, 2004).

Neutrophil

Neutrophil numbers are increased in the airways and sputum of patients with severe asthma and in smoking asthmatics, but the pathophysiological role of these cells is uncertain and their increase may even be due to glucocorticosteroid therapy (Wenzel *et al.*, 2003).

Resident cells of the airway

Airway smooth muscle is not only a target of the asthma response (by undergoing contraction to produce airflow obstruction) but also contributes to it (via the production of its own family of pro-inflammatory mediators). As a consequence of airway

inflammation and the generation of growth factors, the airway smooth muscle cell can undergo proliferation, activation, contraction, and hypertrophy—events that can influence airway dysfunction of asthma.

Epithelial cells

Airway epithelium is another airway lining cell critically involved in asthma (Polito *et al.*, 1998). The generation of inflammatory mediators, recruitment and activation of inflammatory cells, and infection by respiratory viruses can cause epithelial cells to produce more inflammatory mediators or to injure the epithelium itself. The repair process, following injury to the epithelium, may be abnormal in asthma, thus furthering the obstructive lesions that occur in asthma.

Chemical Mediator

Chemokines are important in the recruitment of inflammatory cells into the airways and are mainly expressed in airway epithelial cells (Miller *et al.*, 2004). Eotaxin is relatively selective for eosinophil, whereas thymus and activation-regulated chemokines (TARC) and macrophage-derived chemokines (MDC) recruit Th2 cells. Cysteinyl leukotrienes are potent bronchoconstrictors and proinflammatory mediators mainly derived from mast cells and eosinophils. They are the only mediator whose inhibition has been associated with an improvement in lung function and asthma symptoms. Cytokines orchestrate the inflammatory response in asthma and determine its severity (Barnes, 2002). Key cytokines include IL-1 and TNF- α , which amplify the inflammatory response, and GM-CSF, which prolongs eosinophil survival in the airways. Th2-derived cytokines include IL-5, which is required for eosinophil differentiation and survival; IL-4, which is important for Th2 cell differentiation; and IL-13, needed for IgE formation. Nitric oxide (NO), a potent vasodilator, is produced predominantly from the action of inducible nitric oxide synthase in airway epithelial cells (Ricciardolo, 2004). Exhaled NO is increasingly being used to monitor the effectiveness of asthma treatment, because of its reported association with the presence of inflammation in asthma (Smith *et al.*, 2005). Prostaglandin D₂ is a bronchoconstrictor derived predominantly from mast cells and is involved in Th2 cell recruitment to the airway.

Structural Change In Airway

Subepithelial fibrosis results from the deposition of collagen fibers and proteoglycans under the basement membrane and is seen in all asthmatic patients, including children, even before the onset of symptoms but may be influenced by treatment. Fibrosis occurs in other layers for the airway wall, with deposition of collagen and proteoglycans. Airway smooth muscle increases, due both to hypertrophy and hyperplasia, and contributes to the increased thickness of the airway wall (Hirst *et al.*, 2004) this process may relate to disease severity and is caused by inflammatory mediators, such as growth factors. Blood vessels in

airway walls proliferate the influence of growth factors such as vascular endothelial growth factor (VEGF) and may contribute to increased airway wall thickness. Mucus hypersecretion results from increased numbers of goblet cells in the airway epithelium and increased size of submucosal.

Air Way Hyperresponsiveness

Airway hyperresponsiveness, the characteristic functional abnormality of asthma, results in airway narrowing in a patient with asthma in response to a stimulus that would be innocuous in a normal person. In turn, this airway narrowing leads to variable airflow limitation and intermittent symptoms. Airways hyperresponsiveness is linked to both inflammation and repair of the airways and is partially reversible with therapy. Its mechanisms are incompletely understood.

MANAGEMENT OF ASTHMA

Non Pharmacological Treatment

Intensive house dust mite avoidance may reduce exposure to a range of other factors including endotoxin. Epidemiological studies suggest that close contact with a cat or a dog in early life may reduce the subsequent prevalence of allergy and asthma (Remes *et al.*, 2001; Muraro *et al.*, 2004).

Fish oils have a high level of omega-3 polyunsaturated fatty acids (n-3 PUFAs). Western diets have a low intake of n-3 PUFAs with a corresponding increase in intake of n-6 PUFAs. This change has been associated with increasing rates of allergic disease and asthma. Evidence suggests that early life ETS exposure is associated with later persistent asthma (Arshad *et al.*, 2005; Jaakkola *et al.*, 2004) with a strong interaction with genetic polymorphisms which affect antioxidant activity (Kabesh *et al.*, 2004).

Oxidative stress may have many detrimental effects on airway function include airway smooth muscle contraction, induction of airway hyperresponsiveness, mucus hypersecretion, epithelial shedding and vascular exudation. Observational studies have reported that low vitamin C, vitamin E and selenium intakes are associated with a higher prevalence of asthma. Intervention studies suggest that neither supplementation with vitamin C, vitamin E or selenium is associated with clinical benefits in people with asthma (Allam *et al.*, 2004; Pearson *et al.*, 2004; Ram *et al.*, 2004).

Several studies have reported an association between increasing body mass index and symptoms of asthma (one randomised parallel group study has shown improved asthma control following weight reduction in obese patients with asthma (Stenius *et al.*, 2000)). Weight reduction is recommended in obese patients with asthma to promote general health and to improve asthma control.

In vitro studies suggest that supplementing the diet with omega n-3 fatty acids, which are most commonly found in fish oils, might reduce the inflammation associated with asthma (Prescott *et al.*, 2004; Stephensen *et al.*, 2004).

Complementary and alternative medicine

Herbal and traditional Chinese medicine

In Chinese medicine, asthma is known as *Xiao Chuan* and is the result of Phlegm. Phlegm is a by-product of a weak Lung, Spleen or Kidney, the three main organs that control water metabolism in the body. If any of these are unbalanced, water becomes stagnate and turns into Phlegm. No matter where Phlegm is formed in the body, it is stored in the Lung. This impedes the Lung, causing shallow breathing, wheezing, chest oppression, sweating, coughing that is sometimes productive, susceptible to colds and flu, slight fever, etc. Chinese herbals are used in the treatment and management of asthma. For example, the Chinese herb *Scutellaria*—first listed some 2,200 years ago in *The Divine Husbandman's Classic of the Materia Medica*, the oldest known textbook of medicine—has been touted as a method for helping ease “hot lungs,” coughing, fever and tension. Modern testing has found that this herb impacts histamine without sedation, possibly affecting the number of asthma attacks triggered by allergies (Nakajima et al., 2001). Ma Huang (*Ephedra Sinica*) is the Chinese herbal equivalent of salbutamol. It can only be administered orally, within a mixed herbal formula, either in an herbal tea or in tablet form and usually accompanies other herbs such as GuiZhi (*Ramulus Cinnamomi Cassiae*), Xing Ren (*Semen Pruni Armeniacae*), Shi Gao (*Gypsum*), Huang Qin (*Radix Scutellariae Baicalensis*), etc. She Gan Ma Huang Tang (*Belamcanda and Ephedra Decoction*), which contains She Gan (*Rhizoma Belamcandae Chinensis*) 9 grams. Ma Huang (*Herba Ephedrae*) 12g. Zi Wan (*Radix Asteris Tatarici*) 9 grams. Kuan Dong Hua (*Flos Tussilaginis Farfarae*) 9 grams. Fa Ban Xia (*Processed Rhizoma Pinelliae Ternatae*) 9 grams, Xi Xin (*Herba cum Radice Asari*) 9 grams, Wu Wei Zi (*Fructus Schisandrae Chinensis*) 3 grams, Sheng Jiang (*Rhizoma Zingiberis Officinalis*) 12g and Da Zao (*Fructus Zizyphi Jujubae*) 3 pieces. This formula stops coughing, warms the Lung, transforms Cold and congested fluids lingering in the chest and redirects rebellious Qi downwards (Attilio D'Alberty, 2005). A more recent double blind placebo controlled trial of a Chinese herb decoction (Ding Chuan Tang) showed improvement in airway hyper-responsiveness in children with stable asthma (Chan et al., 2006). It is difficult to disentangle the effects of multiple ingredients; Ding Chuan Tang for example contains nine components. In a second study, 100 children with asthma found that a five-herb mixture gave some benefits in relation to lung function and symptoms compared with placebo (Hsu et al., 2005). If you are open to adding a specially-formulated nutritional supplement in order to maximize your own lung health, the following also may be some noteworthy nutrients to consider:

- Capsaicin (Cayenne extract) and *Glycyrrhiza Glabra* (licorice) seem to have a soothing effect on the throat, which can sometimes become irritated in people with asthma.
- The authoritative *Complete German Commission E Monographs* states that Fenugreek gently soothes the lining of the throat.

- Marshmallow and Mullein provide mucilages to add bulk to phlegm, making it easier to expectorate.
- Turnip Powder is a terrific natural source of the amino-acid histidine, which is particularly helpful in supporting nose, eyes and throat health.

Anti-asthma Herbal Medicine Intervention (ASHMI), Modified Mai Men Dong Tang (mMMDT), Ding Chuan Tang, STA-1, *Sophora flavescens* Ait, are Chinese herbal medicine used in the treatment of asthma.

Air Ionisers

Ionisers have been widely promoted as being of benefit for patients with asthma. A Cochrane review of five studies using negative ion generators and one with a positive ion generator found no evidence of benefit in reducing symptoms in patients with asthma (Blackhall et al., 2003). One study demonstrated an increase in night-time cough to a level which approached statistical significance (Warner et al., 1993).

Homeopathy

People suffering from asthma often have allergic tendencies; a genetic predisposition is common. Constitutional homeopathic care (with the guidance of an experienced professional) can help to improve a person's general health on deeper levels and possibly reduce the tendency toward asthma. Correctly-chosen remedies can help reduce distress during asthma attacks; however, emergency medical care must be sought in any serious attack. Some of homeopathy remedies (*Truestar Health, 2012*) are given below:

Arsenicum album

A person needing this remedy can feel exhausted, yet be very restless and anxious. Breathing problems tend to be worse while lying down, better when sitting up, and may begin, or be the most intense, between midnight and two a.m. Dry wheezing may progress to a cough that brings up frothy whitish fluid. The person can be thirsty, taking frequent tiny sips. General chilliness is usually seen, with burning pains in the chest and heat in the head. Warmth often brings improvement.

Carbo vegetabilis

This remedy may be indicated when a person feels weak or faint with a hollow sensation in the chest. Coughing jags can lead to gagging. The person may be very cold (especially hands and feet), yet feel a need for moving air, wanting to sit beside a fan or open window. Gas and digestive upset are also likely, and sitting up and burping offers some relief. Feeling worse in the evening, and worse from talking, eating, or lying down are other indications for this remedy.

Chamomilla

Asthma with a dry, hard, irritating cough that starts after being exposed to moving air, or after becoming overexcited and angry, may be helped with this remedy. The cough is often worse

around nine p.m., and may continue into the night. The person seems hypersensitive and may be extremely irritable and agitated. (Children may even shriek and hit, though they often calm down if someone carries them.)

Ipecacuanha

Coughing spasms that lead to retching or vomiting strongly indicate this remedy. Wheezing can come on suddenly with a feeling of suffocation and heaviness in the chest. Mucus collects in breathing tubes, but the person has difficulty coughing much out. The person may sweat a lot and feel clammy or nauseous, be worse from motion, and sometimes worse from warmth.

Natrumsulphuricum

This remedy is sometimes indicated when asthma attacks are brought on by exposure to mold and dampness. The person may hold the chest while coughing, because it feels so weak. Wheezing and breathing difficulties are aggravated by exertion, and episodes tend to be worse in the very early morning.

Nux vomica

Indications for this remedy include a tense, constricted feeling in the chest during asthma attacks, with pressure in the stomach. Problems are often worse in the morning. Overindulgence in stimulants, alcohol, sweets, or strong spicy food can bring on or aggravate an episode. Both physical effort and mental exertion can make things worse, and warmth and sleep often bring relief. A person needing this remedy is typically very irritable and impatient, with a general feeling of chilliness.

Pulsatilla

Wheezing that starts when a person gets too warm (especially in a stuffy room), or after eating rich food, can indicate this remedy. Coughing brings up yellow-colored mucus, with gagging and choking. Tightness in the chest tends to be worse in the evening and at night, and is relieved by cool fresh air. A person who needs this remedy is likely to be changeable and emotional, wanting a lot of attention and comforting. (*Pulsatilla* is often useful in children's illnesses.).

Spongiatosta

A hard or "barking" cough during an asthma attack is a strong indication for this remedy. Breathing can be labored, with a sawing sound, and not much mucus is produced. The person may feel best when sitting up and tilting the head back, or when leaning forward. Warm drinks may be helpful. The problems often start while the person is asleep (typically before midnight). *Spongia* is often used in croup, as well.

Homeopathy Dosage Directions

Select the remedy that most closely matches the symptoms. In conditions where self-treatment is appropriate, unless otherwise directed by a physician, a lower potency (6X, 6C,

12X, 12C, 30X, or 30C) should be used. In addition, instructions for use are usually printed on the label.

Many homeopathic physicians suggest that remedies be used as follows: Take one dose and wait for a response. If improvement is seen, continue to wait and let the remedy work. If improvement lags significantly or has clearly stopped, another dose may be taken. The frequency of dosage varies with the condition and the individual. Sometimes a dose may be required several times an hour; other times a dose may be indicated several times a day; and in some situations, one dose per day (or less) can be sufficient (*Truostar Health, 2012*).

A Cochrane review identified only three methodologically sound randomised controlled trials, two of which reported some positive effects. A criticism of the studies was that they did not employ individualised homeopathy, which is the essence of this approach to treatment (Linde *et al.*, 2001). A more recent trial of individualised homeopathy in childhood asthma, which was placebo controlled and appropriately powered, failed to show any evidence of benefit over conventional treatment in primary care (White *et al.*, 2003).

Hypnosis and relaxation therapies

A systematic review of relaxation therapies, including hypnotherapy, identified five controlled trials, two of which showed some benefits. Overall the methodology of the studies was poor and the review concluded that there was a lack of evidence of efficacy but that muscle relaxation could conceivably benefit lung function in patients with asthma (Huntley *et al.*, 2002).

Pharmacological Treatment

There is no permanent cure for asthma however the disorder can be adequately controlled with drugs. The optimal asthma control assessment of severity is important before treatment is initiated and patient should be placed in the highest category of severity. Asthma medications are divided into 2 groups: quick-relief medications and controller medications.

Quik-relief medicine

Medications in this category are meant to be used to treat an asthma episode or attack – to relieve symptoms and open airways quickly. They also may be used to pre-treat to prevent attacks, such as before exercise. These falls into three categories: short-acting beta-agonists, anti-inflammatory drugs, and anticholinergics.

Short acting b-blocker

These medications are bronchodilators and are used to relax the muscles and open airways. Short-acting beta agonists work quickly to increase airflow and are the treatment of choice for acute asthma symptoms and attacks. Example: Salbutamol, Terbutaline

Anti-inflammatory

These medications are used to prevent or reduce inflammation and swelling in the airways. Oral Corticosteroids may

be used as an alternative or in addition to other therapies. Generally, they are not the first treatment of choice. Example: Prednisone, Methylprednisolone

Anticholinergic

These medications may be used as an alternative or in addition to other therapies. Generally, they are not the first treatment of choice. Example: Ipratropium, Tiotropium

Long Term Control Medication

The medications in this category are preventive and meant to be used on an ongoing basis, as prescribed. They are not to be used now and then, or to relieve acute asthma symptoms. These medications are taken daily to achieve and maintain control of persistent asthma. The most effective long-term-control medications for asthma are those that reduce inflammation.

Anti-Inflammatory Drugs

These medications are used to prevent or reduce inflammation and swelling in the airways.

Inhaled Corticosteroids (ICS): Beclomethasone, Budesonide, Fluticasone

LTRA (Leukotriene Receptor Antagonists): Montelukast

Mast Cell Stabilisers: Sodium Cromoglycate, Nedocromil.

Long-Acting Beta-Agonists (LABA)

These medications are bronchodilators and are used to relax the muscles and open airways. Long-acting beta-agonists are used as maintenance drugs because they provide longer term control and have a slower onset of action. They should not be used as quick-relief medications. Inhaled Bronchodilators are given below:

Inhaler β_2 -agonist bronchodilators

- Salmeterol, Formoterol
- Administered by inhaled route twice a day

Oral β_2 -agonist bronchodilators

Salbutamol, Salbutamol, Terbutaline, Terbutaline, Bambuterol (Oral LABA)

Leukotriene Modifiers

These medications modify the inflammatory response in asthma.

- 5-Lipoxygenase Inhibitor: Zileuton
- LTD₄-Receptor Antagonists: Zafirlukast, Montelukast

Delivery methods

Medications are typically provided as metered-dose inhalers (MDIs) in combination with an asthma spacer or as a dry powder inhaler. The spacer is a plastic cylinder that mixes the medication with air, making it easier to receive a full dose of the drug. A nebulizer may also be used. Nebulizers and spacers are equally effective in those with mild to moderate symptoms however insufficient evidence is available to determine whether or

not a difference exists in those severe symptomatology (NHLBI Guideline, 2007)

Adverse effects

Long-term use of inhaled glucocorticoids at conventional doses carries a minor risk for adverse effects. Risks include the development of cataracts and a mild regression in stature (Dahl R, 2006)

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